Local calcium signals in pacemaker cells heart rate and body mass are self-similar from mice to humans

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Short title: Self-similarity of local calcium signals in pacemaker cells and heart rate across species

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Abstract

Long-range, power law correlations across species between heart rate (HR) and body mass (BM) have been documented. Heart rate, which varies widely across species, is determined by the frequency and rhythm at which action potentials (APs) are generated by pacemaker cells within the hearts sinoatrial node (SAN). The rate and rhythm of AP firing of SAN pacemaker cells depend upon the kinetics of activation and inactivation of molecular functions operating within a coupled-clock system of chemical (i.e. Ca^{2+}) oscillators and current oscillators that determine the cell membrane potential (Vm). Measuring Ca^{2+} signals and membrane potential in single pacemaker cells isolated from mouse, guinea-pig, rabbit and human hearts, we uncover novel self-similarity (trans-species power law correlations) between phase shifts kinetics of Ca^{2+} and Vm domains that occur during AP cycles in single pacemaker cell and (1) AP firing rates in these SAN cells *in vitro*; (2) heart rate (EKG RR intervals) *in vivo*; and (3) body mass (BM). These long-range correlations between subcellular events during AP cycles in SAN cells *in vitro*, and the rate at which heart beats *in vivo* are manifestation of self-ordered criticality of heart rate regulation across species from mouse to human within a coupled-oscillator system, i.e., phase shifting of activation-inactivation kinetics occurring within and among molecules operating within a coupled-oscillator system. Thus, self-ordered criticality of the pacemaker cells during an AP cycle underlies long-range correlations between HR and BM across these species.

Introduction

Heart rate (HR), which varies widely across species, is determined by the rate at which action potentials (APs) are generated by cells that reside within the sinoatrial node (SAN), the heart' pacemaker. The rate and rhythm of AP firing of SAN cells, in turn, are controlled by coordinated activation-inactivation kinetics of phase shifts among molecular functions operating within a coupled-system of chemical (i.e. Ca^{2+}) and current oscillators that regulates surface membrane potential (Vm)[1,2].

Phase transition kinetics in Vm and Ca^{2+} domains that can be measured in SAN cells during AP cycles reflect ensembles of phase shifts in activation-inactivation kinetics of molecules that underlie AP cycles and determine AP cycle lengths phase transitions during AP cycle. For example, studies in rabbit SAN cells indicate that sub-cellular, spontaneous, local oscillatory Ca^{2+} releases (LCRs) activate inward sodium-calcium exchange (NCX) current,[3,4] to regulate the rate of spontaneous surface membrane diastolic depolarization (DD) culminating in the generation of an AP, a cell-wide event[5,6]. Differences in spontaneous AP firing rates among isolated rabbit SAN cells are highly correlated with differences in periodicity of LCR signals at baseline and during autonomic receptors stimulation[5,7]. Numerical sensitivity analyses reveal that only models that generate intercellular calcium oscillations in addition to ion channels are able to reproduce the full range of human heart rates[8].

Intracellular Ca^{2+} oscillations are a universal property of excitable cells throughout nature[9,10]. Different models have been suggested to describe its universal properties. One of these is that long-range correlations that manifest power law behavior throughout nature (indicating self-similarity) are manifestations of self-ordered criticality[11]. It has been previously noted that cell-wide Ca^{2+} signals emerge in mouse heart ventricular myocytes when self-organization of spontaneous local **sub-cellular** calcium events achieves criticality[12]. Similarly, spontaneous action potentials (APs) in rabbit SAN cell emerge when self-organization of spontaneous local sub-cellular Ca^{2+} releases (LCRs) achieves criticality[3,5,6,13].

Because the heart is the only organ in which anatomical and physiological properties have been preserved during mammalian species evolution[14], it is not surprising that heart rates derived from EKG RR intervals manifest long-range, power law correlations with body mass (BM) across a wide range of diverse species [15-18]. The rational of present study was to test the idea that (1) like self-similarity of *in vivo* HR and BM across species, kinetics of phase transitions occurring within Vm and Ca^{2+} domains during AP cycles and AP cycle lengths are self-similar among SAN cells isolated from hearts of different species (mouse to humans), (2) whether these long-range power law correlations across species between sub-cellular Ca^{2+} and Vm domain phase transitions *in vitro* might also extend to the *in vivo* HR and BM across these species.

Results

Conservation of proteins that regulate heart pacemaker cell functions

Tantamount to testing our hypothesis regarding self-similarity of pacemaker functions across species from mouse to humans, we investigated the degree of homology of proteins that underlie these functions, and aligned protein sequences of those involved in coupled-oscillator functions of mouse, guinea-pig, rabbit and human SAN cells. Table 1 shows that sequences of these proteins are highly conserved from mouse to humans.

Table 1. Homology of proteins that regulate SAN pacemaker cell functions in mouse, guinea-pig, rabbit and human.

Function domains	**Alias**	**Gene**	***% Pairwise$^{\#}$ Identity***
Vm domain			
I_{NCX}	Ncx1	SLC8A1	93.8%
I_f HCN2	Hcn2	HCN2	77.5%^
I_f HCN4	Hcn4	HCN4	88.9%
$I_{Nav1.5}$	Nav1.5	SCN5A	88.2%
$I_{Nav1.1}$	Nav1.1	SCN1A	97.0%
$I_{Ca\text{-}L}$ α1C	Cav 1.2	CACNA1C	92.4%
$I_{Ca\text{-}L}$ α1D	Cav1.3	CACNA1D	96.6%
$I_{Ca\text{-}T}$ α1G	Cav3.1	CACNA1G	91.6%
I_{Ks} α	Kv 7.1	KCNQ1	87.4%
I_{Ks} β	MinK	KCNE1	74.8%
I_{kr}	HERG	KCNH2	94.7%
I_{BK1}	KCa1.1	KCNMA1	91.3%
I_{SK1}	KCa2.1	KCNN1	83.1%^
I_{SK2}	KCa2.2	KCNN2	95.1%
I_{SK3}	KCa2.3	KCNN3	94.1%
I_{CRAC}	Orai1	ORAI1	89.0%
I_{CRAC}	Orai2	ORAI2	94.6%
I_{CRAC}	Orai3	ORAI3	89.5%
Ca^{2+} domain			
CaATPase	Serca2a	ATP2A2	98.4%
RyR	RyR2	RyR2	97.0%
Phospholamban	Pln	PLN	98.1%
Calsequestrin	Casq2	CASQ2	89.1%
Inositol-trisphosphate 3-kinase A	IP3-kinase A	ITPKA	68.3%

FK506 binding protein 12	FKBP12	FKBP1A	98.1%
Stromal Interaction Molecule 1	Stim1	STIM1	91.8%
Stromal Interaction Molecule 2	Stim2	STIM2	91.8%
cAMP regulators			
Adenylate cyclase 1	ADCY1	ADCY1	93.7%
Adenylate cyclase 8	ADCY8	ADCY8	97.6%
Phosphodiesterase 4A	PDE4A	PDE4A	81.3%**^**

[#] *Alignment and sequence acquisition numbers are illustrated in Supplementary Table S6 and Alignments.pdf; ^ not mapped to rabbit genome.*

Electro-chemical AP ignition phase

Subcellular events in SAN pacemaker cells during spontaneous diastolic depolarization (DD) in isolated rabbit SAN cells have been conceptualized as the AP ignition phase[13]. Ignition onset is linked to the occurrence of oscillatory local Ca^{2+} releases (LCRs), that undergo self-organized phase transitions (during the diastolic depolarization) into roughly periodic, cell-wide ensemble Ca^{2+} signals, that culminate in the generation of an AP, a cell-wide event[5,6,13,19]. The AP induces a cell wide Ca^{2+} transient that faithfully informs on AP cycle length[20].

Using 2D imaging (Fig. 1A) and confocal microscopy (Fig. 1B-1E), we observed that spontaneous diastolic LCRs, the hallmark diastolic Ca^{2+} signal of the Ca^{2+} clock, are conserved in SAN cells across species from mouse to humans. Therefore, major regulators of the coupled-oscillator system (LCRs) are conserved from mouse to humans (Fig. 1).

Next, we determined whether the timing of phase transitions that occur in membrane potential (Vm) and Ca^{2+} signals during AP cycles in SAN pacemaker cells isolated from mouse, guinea-pig, rabbit and humans hearts, and the AP cycle lengths of these cells manifest (trans-species) correlations that obey power laws. Vm and Ca^{2+} domains parameters were measured and reported in subsets of SAN pacemaker cells. The diastolic LCR ensemble Ca^{2+} signal during the ignition phase accelerates diastolic membrane depolarization (Vm domain) due to Ca^{2+} activation of an inward NCX current. The time at which this Vm acceleration achieves (~0.15V/s), has been identified as ignition onset in the Vm domain[13]. Recordings of Vm in single, SAN cells isolated from hearts of species under study demonstrated that the onset of ignition across species to AP cycle length is self-similar (obeys power law relationships) (Fig. 2A). In SAN cells in which Ca^{2+} was measured, like the onsets of ignition in the Vm domain (Fig. 2A), ignition onsets in the Ca^{2+} domain (see methods) and AP-induced Ca^{2+} transient (CaT) cycle lengths were self-similar across species (Fig. 2B).

The completion of the ignition phase in Vm domain occurs when Vm depolarization markedly accelerates (take-off potential (TOP)), creating the rapid upstroke of an AP[13]. As shown in Fig. 3A, the times to the completion of the ignition phase and AP cycle lengths were self-similar across species (R^2=0.89). In the Ca^{2+} domain, the completion of ignition phase is reflected in a 3rd acceleration of the diastolic whole cell Ca^{2+} transient, i.e., the time just prior to the time of the rapid upstroke of the AP-induced global Ca^{2+} transient (see methods). As in the Vm domain, times of the ignition phase completion in the Ca^{2+} domain were self-similar to the AP-induced Ca^{2+} transient (CaT) cycle lengths across species (Fig. 3B). Thus, Figures 2 and 3 demonstrate that the onset and completion of the ignition and phase AP cycle lengths are self-similar across species.

Because the times to the beginning and completion of ignition in both Vm and Ca^{2+} domains and AP cycle lengths were self-similar across species, we reasoned that restitution kinetics of electro-chemical processes that determine AP cycle lengths must **also** be self-similar across species. The APD 90 (time to 90% AP repolarization) and CaT90 (time to 90% of decay time of AP-induced Ca^{2+} transient) were taken as restitution times in Vm and Ca^{2+} domains, respectively. We found that both APD90 and CaT90 restitution times are self-similar to AP cycle lengths across species (Fig. 4). Thus, although absolute AP cycle lengths differ markedly from mouse to humans, relationships of the kinetics of activation and inactivation in both in Vm and Ca^{2+} domains to AP cycle lengths are self-similar across these species.

Ignition onsets and repolarization times measured in Vm and Ca^{2+} domains during an AP cycle in SAN pacemaker cells isolated from mouse, guinea-pig, rabbit and human hearts are also strongly correlated (Supplementary Fig. S1). Further, strong correlations were observed among kinetic parameters **within** Vm (Supplementary Table S2A) and Ca^{2+} domains (Supplementary Table S2B). Because kinetic parameters defining ignition phase onset and completion, and restitution phases **within** either Vm or Ca^{2+} domain were self-similar across species (Figs. 2-4 and Supplementary Fig. S1 and Table S2), we reasoned that Vm domain parameters might be self-similar to Ca^{2+} domain parameters, even though Ca^{2+} and Vm were measured in different subsets of SAN cells. Indeed, Supplementary Table S3 revealed that this is indeed the case.

Phase transitions in Vm and Ca^{2+} domain parameters during AP cycles in isolated SAN cells *in vitro* and heart rates in vivo are self-similar across species

We next determined whether the self-similarity of ignition and restitution kinetics, and AP firing rate in isolated SAN cells across species *in vitro* (Figs. 1-4) extends to the HR *in vivo* (EKG RR, cycle length).

Power law correlations demonstrated self-similarity across species between heart rates (EKG RR intervals) *in vivo* and AP cycle lengths in SAN cells *in vitro* (Fig. 5A and Supplementary Table S4). Atrial-ventricular conduction times (EKG PR intervals) and ventricular depolarization-repolarization times (EKG QT intervals), and AP cycle ignition or restitution intervals in the Vm and Ca^{2+} domains in isolated SAN cells *in vitro* also were self-similar across species (Fig. 5B-5D). In addition, Supplementary Table S4, which lists Pearson correlation coefficients between Vm and Ca^{2+} domains parameters during AP cycles and EKG parameters *in vivo*, indicated that many kinetic parameters in single isolated cells and EKG intervals are self-similar across species. Supplementary Table S5 reports the extended results of the linear fit between other parameters of this study and EKG intervals.

Vm and Ca^{2+} domains kinetic parameters during AP cycles in isolated, single SAN cells *in vitro* are self-similar to body mass (BM) across species

Because kinetic parameters in Vm and Ca^{2+} domains measured during AP cycles in single, isolated pacemaker cells *in vitro* and HR *in vivo* manifested self-similarity across species in our study (Fig. 5), and because numerous prior studies have demonstrated that HR and BM are self-similar across species [15-18,21-23], we hypothesized that kinetic parameters measured in single SAN cells across species *in vitro* and BM must also be self-similar across species. Fig 6 revealed that this hypothesis is correct. Specifically, we found that the ignition phase onset (Fig. 6A), end of ignition (Fig. 6B), AP cycle lengths (Fig. 6C) and restitution times (Fig. 6D) of the AP cycle in Vm and Ca^{2+} domains in SAN cells and BM were self-similar across species with nearly the same (0.25) scaling exponent observed previously.

Discussion

Intracellular Ca^{2+} oscillations are a universal property of excitable cells [9,10] that manifest long-range correlations throughout nature (indicating self-similarity)[15-18,21-23] are manifestations of self-ordered criticality[11]. Our results uncover novel long-range (power law) correlations between phase transitions kinetics measured in cellular Ca^{2+} and Vm domains during AP cycles *in vitro* in single SAN pacemaker cells isolated from hearts of these species and: (1) AP cycle lengths of these isolated cells *in vitro*; (2) heart rates (EKG RR intervals) and (3) other EKG intervals (PR, QT intervals) *in vivo*; and (4) BM.

The phase transition kinetics measured during AP cycles in Vm and Ca^{2+} domains in single, isolated SAN cells in the present study inform on kinetics of activation and inactivation of molecular functions that underlie our functional measurements. The sarcoplasmic reticulum (SR) is a Ca^{2+} oscillator: acts as a Ca^{2+} capacitor, pumping Ca^{2+} via a CaATPase (SERCa2), storing Ca^{2+} and releasing Ca^{2+} via ryanodine receptors (RyR). The SR Ca^{2+} charge (Ca^{2+} load) is a major determinant of spontaneous, diastolic local RyR activation that initiates the ignition phase of AP by generating local Ca^{2+} releases (LCRs); Ca^{2+}

binding to NCX in the Vm domain generates an inward current (I_{NCX}), that accelerates the rate of spontaneous diastolic membrane depolarization. In addition to SERCa2, RyR and NCX, activation-inactivation of other molecules[5], operating together with HCN, Cav 3.1, Cav 1.3 and several K^+ channels in the context of the coupled-oscillator system, generates feed-forward signaling during the ignition phase[3,4,13], leading to progressive depolarization of the diastolic membrane potential. The system achieves criticality when the rate of Vm depolarization acutely accelerates (the rapid AP uptake) due activation of Vm domain Cav 1.2 channels. Achievement of criticality in the Vm domain induces criticality in the Ca^{2+} domain by triggering a global activation of RyRs, via a Ca^{2+}-induced Ca^{2+} release, resulting in a rapid global increase in Ca^{2+}, i.e., the AP-induced Ca^{2+} transient. Restitution in the Vm domain occurs as voltage-dependent activation of K^+ channels effects repolarization of the membrane potential; and in the Ca^{2+} domain, as cytosolic Ca^{2+} decays, due to pumping of a fraction of the Ca^{2+} released into cytosol from SR back to SR (Ca^{2+} recirculation fraction) and extrusion of a fraction of the Ca^{2+} from the cell via NCX[10].

Sequence similarity of proteins in Vm and Ca^{2+} domains that regulate pacemaker cell functions (e.g. LCRs, I_{NCX}, I_K and etc. (Table 1) are highly conserved from mouse to human. Moreover, proteins operative within coupled-oscillator system are highly conserved across phyla, from mammals to fishes, and many of those with similar structure (defined by presence of all functional domains in protein sequence) were also identified in insects, flies and worms (Supplementary Table S1). An exception is SCN5A, which is only expressed in mammals and birds (Supplementary Table S1). Further, within mammals', sequence proteins that regulate SAN pacemaker cells are highly conserved from mouse to human (Table 1).

In order to generate the wide range of AP cycle lengths that occur across these species studied, and yet manifest self-similarities of AP cycle lengths and sub-cellular phase transitions across species the same clock molecules shown in Table 1 must be differently "tuned" (e.g. differential protein expression levels, differential alternative splicing, and differential post translational modifications e.g. for example differential protein phosphorylation etc.) across species. Elucidating this fine-tuning across different species from the literature is difficult, due to different experimental conditions and experimental designs employed in different species being compared in different studies. The most quantitative comparison of ion channels across species in SAN was reported by Li et al.[24], who used a comprehensive normalization method to compare ion channels among four different species. We integrated information on species differences in the ion channel current density and channel protein gene expression levels in SAN of different species in the Supplementary Table S7.

In summary, we conclude that self-similarity across species (from mouse to humans) of phase transition kinetics in Vm and Ca^{2+} domains in SAN cells *in vitro*, and the rate at which heart beats *in vivo* may be conceptualized as a manifestation of self-ordered criticality of pacemaker cell molecular functions that regulate heart rate. Self-similarity of pacemaker cell molecular functions and AP cycle lengths in vitro and HR in vivo is linked to self-similarity of HR to BM across species[15-18,21-23]. Together these long-range power law correlations stem from the reality that intra-cellular calcium oscillations are a universal property of excitable cells throughout nature[9,10] .

Methods

Ethics statement. The study was performed in accordance with the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health. The experimental protocols have been approved by the Animal Care and Use Committee of the National Institutes of Health (Protocol # 457-LCS-2021). Adult human hearts not required for transplantation were procured from Washington Regional Transplant Community as previously described[19]. None of the donors, age 26-65 years, had a history of major cardiovascular diseases. LVEF: left ventricular ejection fraction. OD, drug overdose, CVA, cerebrovascular accident, CP, cardioplegic. Experimental protocols were approved by the George Washington University Institutional Review Board. Informed donor consents were obtained for all tissue used in this study.

SAN cells isolation. Single, spontaneously beating SAN cells were isolated from the hearts of adult mice (M), guinea-pigs (GP), rabbits (R) and humans (H) by enzymatic digestions as previously described [19,25,26]. All methods were performed in accordance with the National Institutes of Health guidelines on human research.

Transmembrane AP recordings and analyses in SAN cells. Membrane potential was measured in another subset of SAN cells that were not loaded with the Ca^{2+} sensitive indicator. Spontaneous AP were recorded by perforated patch-clamp technique with 0.05 mmol/L of β-escin added to the electrode solution that contained in mmol/L: 120 K-gluconate, 5 NaCl, 5 Mg-ATP, 5 HEPES, 20 KCl, 3 Na_2ATP (pH adjusted to 7.2 with KOH)[27]. SAN cells were continuously superfused with normal Tyrode solution at 35±0.5°C, containing in mmol/L: 140 NaCl, 5.4 KCl, 5 HEPES, 2 MgCl2, 1.8 CaCl2, 5 glucose (pH 7.4). APs were recorded by a standard zero-current-clamp technique (Axopatch 200B, Molecular Devices). APs were corrected for the appropriate liquid junction potential by Clampex 10 Software (Axon Instruments). The AP cycle length and AP characteristics were analyzed via a customized computer program[3,13,28]. The AP cycle length was measured as the interval between AP peaks. The program calculated dV/dt (V/s) and the ignition onset (ms) as a time at which Vm dv/dt during diastolic depolarization accelerates to 0.15V/s[13] (see also Fig. 1A). Other measured of AP parameters included: MDP (maximum diastolic potential), TOP (threshold of AP activation when dV/dt reaches 0.5 V/s),[13] end of ignition (time from MDP to take off potential (TOP, ms)) and APD90 (time from AP overshoot to 90% repolarization time, ms).

Spontaneous diastolic LCRs and AP-induced Ca^{2+} transient (CaT) recordings and analyses in SAN cells. *S*AN cells were loaded with 3-10 μM Ca^{2+} indicator (Cal-520AM or Fluo-4AM) for 10 min, and then were washed with normal Tyrode solution. AP-induced Ca^{2+} transients and spontaneous diastolic local Ca^{2+} releases (LCRs) were recorded in normal Tyrode's solution (as above) at 35±0.5°C in spontaneously beating SAN cells via confocal microscope. Our Ca^{2+} transient data include both Fluo-4AM and Cal-520AM measurements. Early in our research, we had employed the commonly used Fluo-4AM, but in recent years, a new and more robust Ca^{2+} probe -Cal- 520AM (AAT Bioquest) with a higher signal/background ratio became available. We find Cal-520 is more suitable for detecting Ca^{2+} signals in SAN cells. We did not find a significant difference in mean CaT parameters between measurements collected with Fluo-4 and Cal-520 AM indicators in SAN cells.

The line-scan mode was executed at a rate 1.92 and 3 ms per scan-line and images were processed with IDL (8.5) software. The scan-line was set along the border of the cell to the specific cell locations beneath the sarcolemma where LCR are present in SAN cells. AP-induced Ca^{2+} transient cycle length (AP cycle length), the faithful proxy of the Vm AP cycle length[20], was defined as the time interval between the peaks of two adjacent AP-triggered Ca^{2+} transients (CaT). Because the use of different indicators could potentially affect the amplitude of CaT, the amplitude of CaTs or spontaneous LCRs was expressed as normalized fluorescence, a peak value (F) normalized to its basal fluorescence (F_0) rather than just a peak value of (F) in our analysis.

Ignition phase onset was demonstrated in SAN cells in which membrane potential and Ca^{2+} were simultaneously measured, and that the ignition phase onset Vm was defined as the time when membrane potential accelerates to ~0.15V/s[13]. Ignition phase onset in the Ca^{2+} domain was a direct read out of the Ca^{2+} signal that prevailed at the Vm ignition onset. In other terms, at ignition onset in the Ca^{2+} domain, the individual LCR Ca^{2+} signals became sufficiently synchronized to generate an ensemble Ca^{2+} signal of sufficient amplitude to accelerate the rate of DD via activation of NCX that generated inward NCX current. In the present study, we used the same acceleration of DD as Lyashkov et al.[13] to define ignition onset in the Vm domain. But since we do not have simultaneous Vm and Ca^{2+} recordings in our study, it is not possible to directly detect the onset of ignition in the Ca^{2+} domain as the calcium signal at the time of ignition onset in the Vm domain. We tested various time derivatives of the Ca^{2+} signal during diastole hoping to detect an onset of ignition in the calcium domain. This approach was not satisfactory due to excessive noise in the differentiated Ca^{2+} signal, attributable, in part at least, to LCR occurrence at different times during DD. Therefore, based on our experience in SAN cells and our previous work[13], in order to compare Ca^{2+} domain ignition onset among species, we empirically defined the LCR ensemble ignition onset as the time during DD when the integrated Ca^{2+} signal begins to rise from the background noise and reaches a value 1.5% of the peak value of the subsequent Ca^{2+} transient (see also Supplementary Figure S2). Other CaT measurements included: end of ignition (marked as time from baseline to the 3rd dCa/dtmax ($F/F0/ms^3$)) and restitution of AP-induced CaT, T90 (CaT duration from the peak to 90% of CaT decay, ms) (see Supplementary Figure S2).

Body mass (BM) and *in vivo* EKG parameters. BM and *in vivo* EKG RR cycle lengths (RR interval), EKG PR intervals (atrioventricular conduction times) and EKG QT intervals (ventricular depolarization and repolarization times) of the diverse species were taken from the literature[17,29-36].

To determine phylogenetic conservation of proteins that regulate pacemaker cell biophysical functions in Mammalian, Birds, Amphibians, Fishes, Insects, Flies and Worms, we used NCBI Ortholog web applet. Corresponding links provided for each compared protein in Supplementary Table S1. Alignments of protein sequences of mouse, guinea-pig rabbit and human proteins were performed with Clustal Omega V.1.2.2 (http://www.clustal.org/omega/) and their accession numbers provided in Supplementary Table S6. Protein sequences were obtained from NCBI database (https://www.ncbi.nlm.nih.gov/gene/) or from UNIPROT (https://www.uniprot.org/). When multiple isoforms were associated with one gene, we selected the longest available or specifically expressed in the heart (if available) for each species for comparison of Mammalian, Birds, Amphibians, Fishes, Insects, Flies and Worms phyla.

Data processing and statistical analysis. Vm (AP) and CaT parameters measured in SAN cells in vitro data were transformed to a natural logarithm and plotted as means or as medians of data in individual cells on double logarithmic plots versus means or medians of other Ca^{2+} LCR or Vm parameters or vs medians of species BM and EKG intervals *in vivo*. Least squares linear regression (no weighting) was applied to determine slopes and 95% confidence and prediction limits using Origin 9.0 software. Slope statistics were tested by ANOVA and t-tests for coefficients. Akaike weights and F-test were used

(Origin 9.0) to compare slope differences for multiple datasets; P<0.05 was considered statistically significant.

Figure legends

Figure 1. The coupled Ca^{2+} and current oscillator system that drives SAN cells automaticity. (**A**) Upper panel-2D image of an isolated, single human SAN cell loaded with Ca^{2+} indicator and recorded by a high speed 2D camera. Bright areas of fluorescence within the cell represent sub-cellular LCRs; lower panel-simultaneous recordings of Ca^{2+} signals and membrane potential from the same cell (redrawn from original traces [19]). **(B-D)** Upper panels-representative examples of confocal line-scan images and LCRs (indicated by white arrows on images) in single, spontaneously beating SAN cells; lower panels- AP-induced Ca^{2+} transients (CaT) from the same cells depicted in upper panels, isolated from (**B**) mouse, (**C**) guinea-pig, (**D**) rabbit, (**E**) human hearts and loaded with Ca^{2+} indicator (3-10μM, see methods).

Figure 2. Ignition phase onsets and AP cycle lengths across species are self-similar in Vm and Ca^{2+} domains. (**A**) Relationships of Ignition phase onset of the AP cycle in the Vm and (**B**) in the Ca^{2+} domain to AP cycle lengths in SAN cells (n=4-20 SAN cells per species, from 3-8 repetitions per species). Vm and Ca^{2+} domains parameters were measured in subsets of SAN pacemaker cells. Open symbols–transmembrane AP recordings via patch-clamp in Vm domain; closed symbols-AP-induced Ca^{2+} transient (CaT) and LCRs recordings via confocal microscopy. Linear regression of concatenated fit, no weighting; slopes are significantly different from zero ($p<0.05$). Outside dashed lines- 95% prediction band limit; pink - 95% confidence band.

Figure 3. End of ignition and AP cycle lengths across species are self-similar in Vm and Ca^{2+} domains. (**A**) Relationships of End of ignition of the AP cycle in the Vm and (**B**) in the Ca^{2+} domains to AP cycle lengths in SAN cells across species (n=4-20 SAN cells per species, from 3-8 repetition per species). Open symbols-transmembrane AP recordings via patch-clamp; closed symbols-CaT recordings via confocal microscopy. Linear regression of concatenated fit, no weighting; slopes are significantly different from zero ($p< 0.05$). Outside dashed lines-95% prediction band limit; pink-95% confidence band.

Figure 4. Restitution times and AP cycle lengths across species are self-similar in Vm and Ca^{2+} domains. (**A**) Relationships of Restitution times of the AP cycle in the Vm and (**B**) in the Ca^{2+} domains to AP cycle lengths in SAN cells (n=4-20 SAN cells per species, from 3-8 repetition per species). Open symbols-transmembrane AP recordings via patch-clamp; closed symbols-CaT recordings via confocal

microscopy. Linear regression of concatenated fit, no weighting; slopes are significantly different from zero ($p<0.05$). Outside dashed lines-95% prediction band limit; pink-95% confidence band.

Figure 5. Kinetics of ignition and restitution, and AP firing in Vm and Ca^{2+} domains in isolated SAN cells *in vitro* and EKG intervals *in vivo* are self-similar across species. (**A**) AP cycle lengths in SAN cells *in vitro* vs EKG RR intervals (cycle lengths) *in vivo*; (**B**) AP cycle lengths in SAN cells *in vitro* vs EKG PR intervals (atrioventricular conduction time) *in vivo*; (**C**) times to ignition onset in SAN cells *in vitro* vs EKG PR intervals in vivo; (**D**) times to APD90 and CaT90 in SAN cells *in vitro* vs EKG QT intervals (ventricular depolarization-repolarization times) *in vivo*. Open symbols-transmembrane AP (median values) recorded via patch-clamp; closed symbols CaT (median values) recorded via confocal microscopy (n=4-20 SAN cells per species, from 3-8 repetition per species). (**A-D**) Linear regression analysis without weighting of values; regression slopes are significantly different from zero ($p< 0.05$); *in vivo* EKG parameters are taken from published literature (see methods).

Figure 6. Kinetics of ignition, restitution and AP firing in Vm and Ca^{2+} domains in isolated SAN cells and body mass (BM) are self-similar across species. Median values of BM vs median values of (**A**) Ignition onset (ms), (**B**) End of ignition (ms), (**C**) Cycle lengths (ms) and (**D**) 90% of repolarization (ms) in SAN cells (n=4-20 SAN cells per species, from 3-8 repetition per species); BM values are taken from published literature, see methods). Open symbols-transmembrane AP recorded via patch-clamp; closed symbols CaT recorded via confocal microscopy. (A-D) Linear regression analysis without weighting of values; slopes are significantly different from zero ($p<0.05$). Slope differences between multiple datasets were compared by F-test and Akaike method (see methods, $p>0.05$). Outer lines: black-Ca^{2+} domain, red-Vm domain at 95% prediction band limit; pink - 95% confidence band. Predicted values from the equations in **A-D:** in VM domain (**A**)$=330.3\text{x}BM^{0.25\pm0.08}$; in Ca^{2+} domain (**A**) $=301.9\text{x}BM^{0.20\pm0.06}$; in Vm domain (**B**)$=156\text{x}BM^{0.31\pm0.06}$; in Ca^{2+} domain (**B**)$=60.3\text{x}BM^{0.20\pm0.27}$; in Vm domain (**C**)$=403.4\text{x}BM^{0.25\pm0.07}$; in Ca^{2+} domain (**C**)$=391.5\text{x}BM^{0.22\pm0.06}$; in Vm domain (**D**)$=204.4\text{x } BM^{0.26\pm0.06}$; in Ca^{2+} domain (**D**)$=119.1\text{x } BM^{0.24\pm0.06}$.

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Author contributions: S.T.S. performed all animal experiments, analyzed the data, wrote and edited the paper; K.T. performed and analyzed human SAN cells experiments; D.Y. modified the IDL program to measure the LCR ensemble at ignition onset; B.D.Z. isolated SAN cells; K.V.T. performed phylogenetic comparison across species; Y.Y. contributed to discussion and editing of the paper; E.G.L. conceptualized the project, interpreted, wrote and edited the manuscript; all authors commented on the manuscript.

Competing interests

The authors declare no competing interests.

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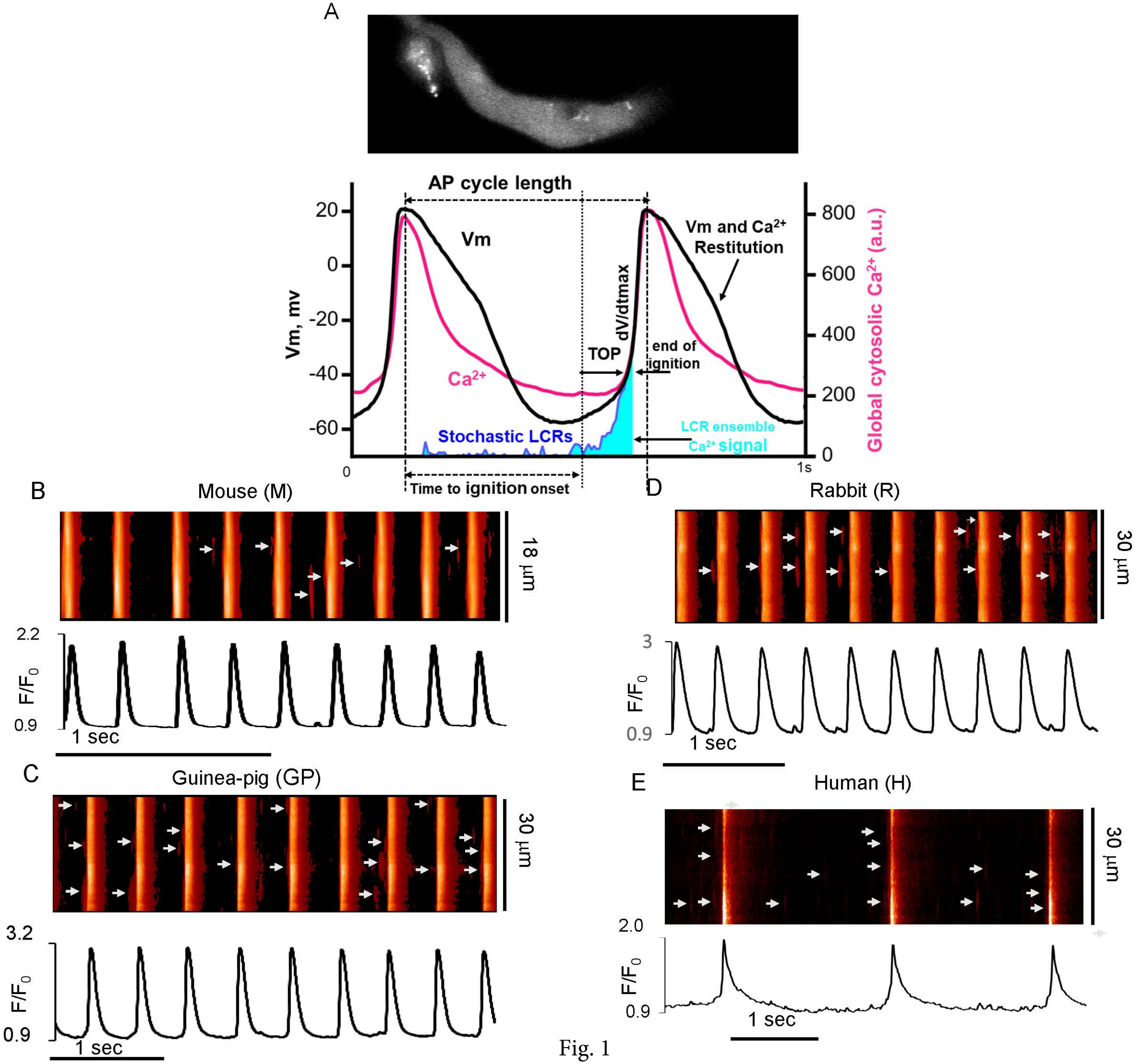
A
AP cycle length
Vm
Vm and Ca2+ Restitution
dV/dtmax
TOP
end of ignition
Ca2+
Stochastic LCRs
LCR ensemble Ca2+ signal
Time to ignition onset
Vm, mv
20
0
-20
-40
-60
0
1s
Global cytosolic Ca2+ (a.u.)
800
600
400
200
0
B
Mouse (M)
18 μm
2.2
F/F0
0.9
1 sec
C
Guinea-pig (GP)
30 μm
3.2
F/F0
0.9
1 sec
D
Rabbit (R)
30 μm
3
F/F0
0.9
1 sec
E
Human (H)
30 μm
2.0
F/F0
0.9
1 sec

Fig. 1

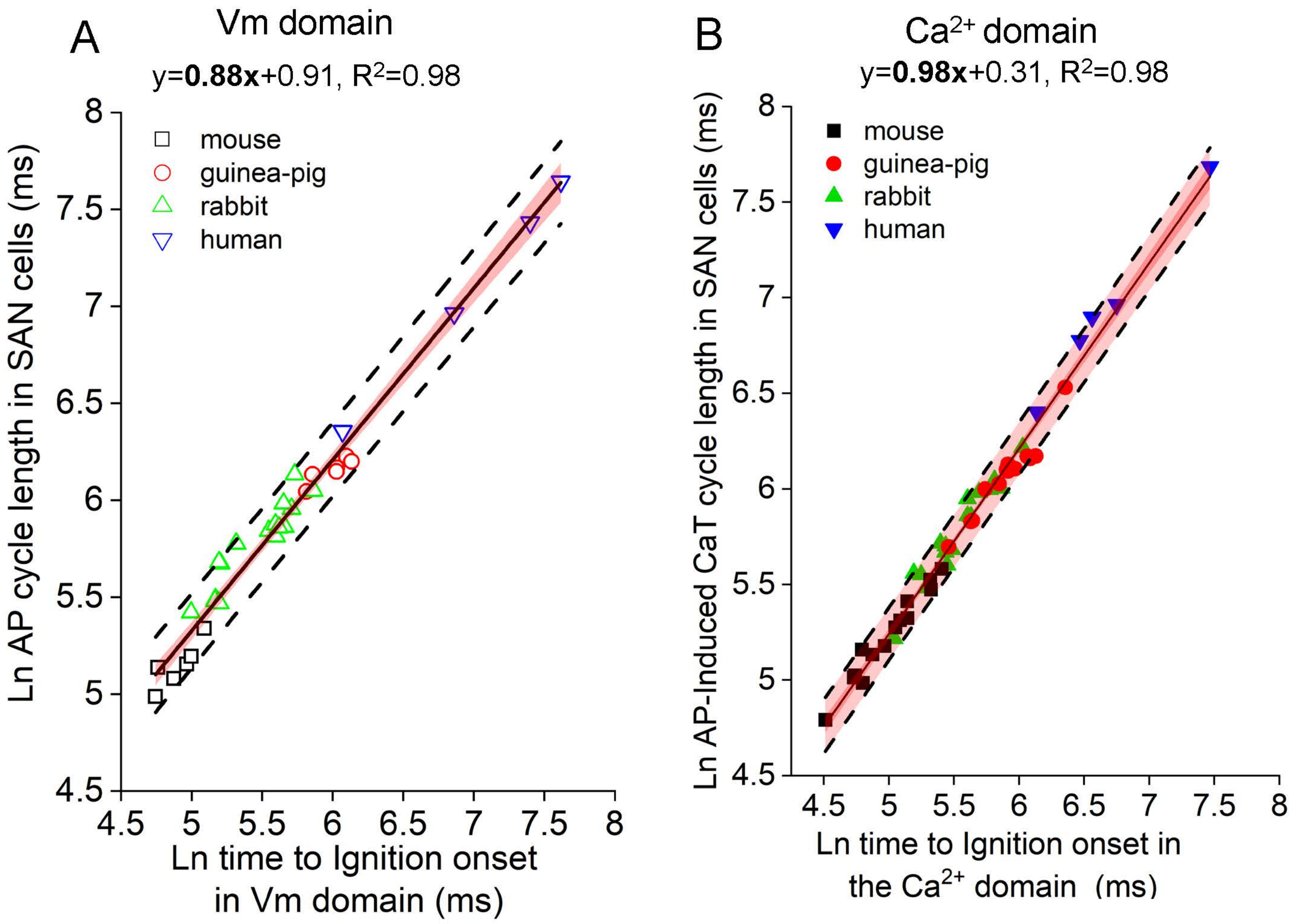
A
Vm domain
y=0.88x+0.91, R2=0.98
Ln AP cycle length in SAN cells (ms)
Ln time to Ignition onset in Vm domain (ms)
□ mouse
○ guinea-pig
△ rabbit
▽ human
4.5
5
5.5
6
6.5
7
7.5
8
B
Ca2+ domain
y=0.98x+0.31, R2=0.98
Ln AP-Induced CaT cycle length in SAN cells (ms)
Ln time to Ignition onset in the Ca2+ domain (ms)
■ mouse
● guinea-pig
▲ rabbit
▼ human

Fig. 2

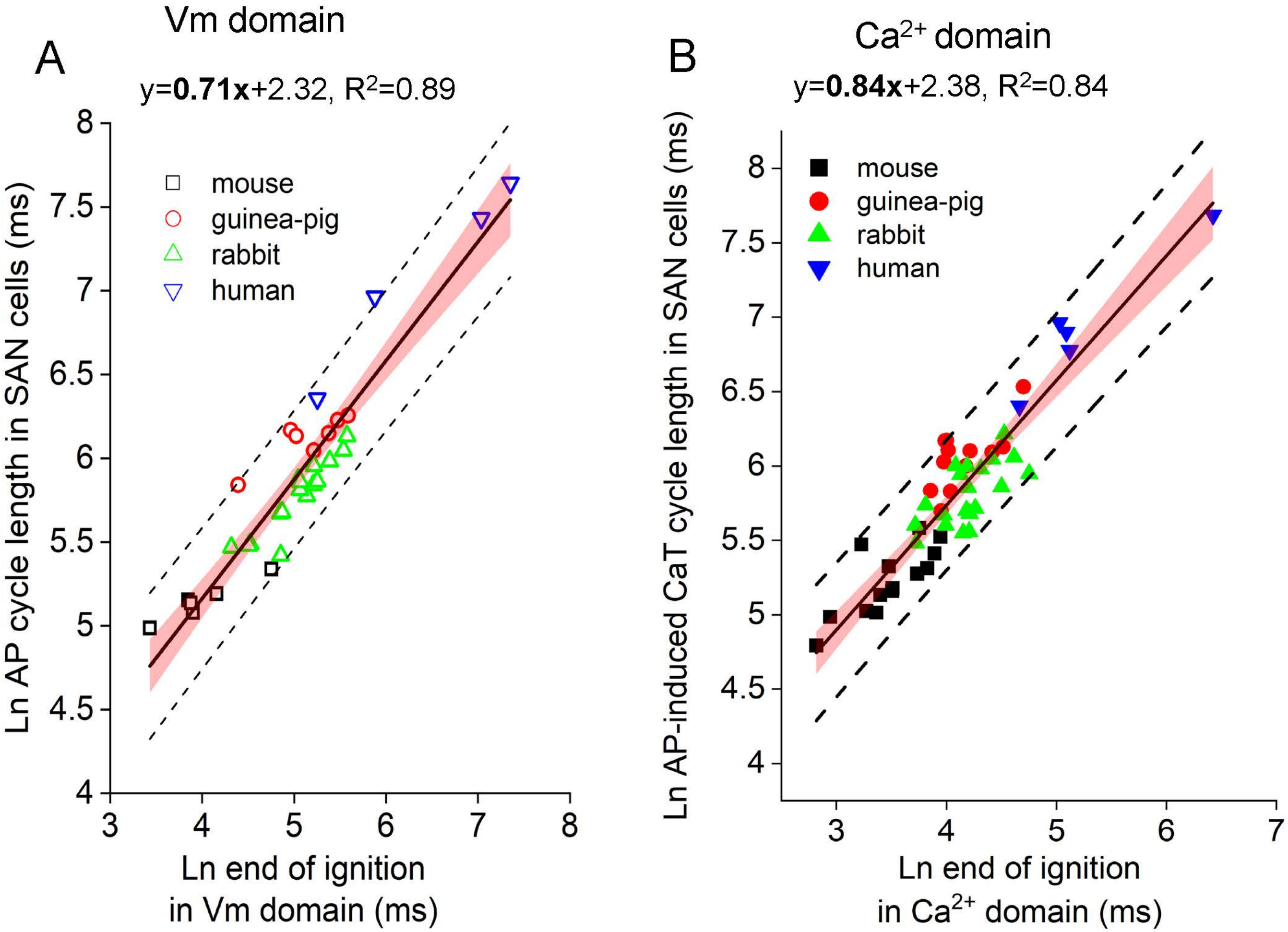
Vm domain
A
y=0.71x+2.32, R^2=0.89
mouse
guinea-pig
rabbit
human
Ln AP cycle length in SAN cells (ms)
Ln end of ignition in Vm domain (ms)
4
4.5
5
5.5
6
6.5
7
7.5
8
3
4
5
6
7
8
Ca2+ domain
B
y=0.84x+2.38, R^2=0.84
mouse
guinea-pig
rabbit
human
Ln AP-induced CaT cycle length in SAN cells (ms)
Ln end of ignition in Ca2+ domain (ms)
4
4.5
5
5.5
6
6.5
7
7.5
8
3
4
5
6
7

Fig. 3

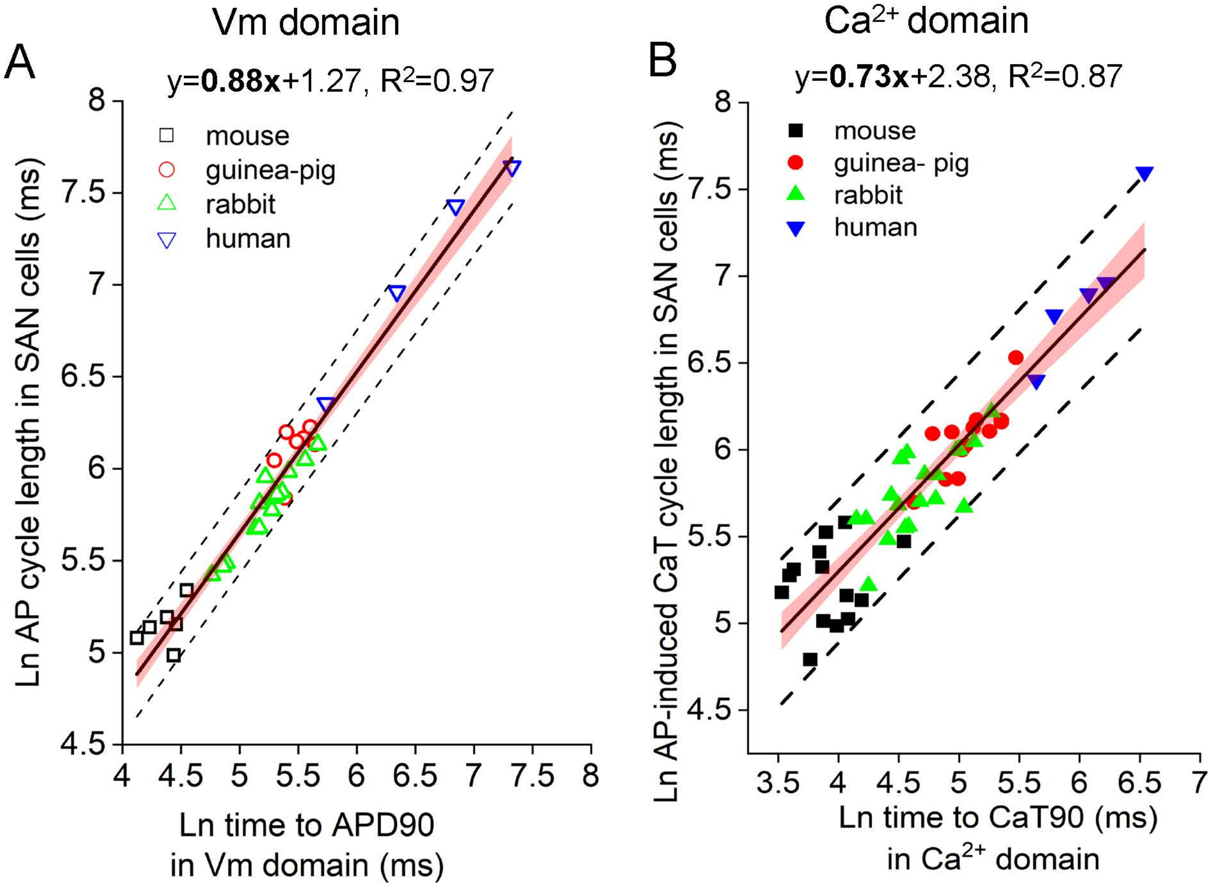
Vm domain
A
y=**0.88x**+1.27, R²=0.97
mouse
guinea-pig
rabbit
human
Ln AP cycle length in SAN cells (ms)
8
7.5
7
6.5
6
5.5
5
4.5
4
4.5
5
5.5
6
6.5
7
7.5
8
Ln time to APD90
in Vm domain (ms)
Ca²⁺ domain
B
y=**0.73x**+2.38, R²=0.87
mouse
guinea- pig
rabbit
human
Ln AP-induced CaT cycle length in SAN cells (ms)
8
7.5
7
6.5
6
5.5
5
4.5
3.5
4
4.5
5
5.5
6
6.5
7
Ln time to CaT90 (ms)
in Ca²⁺ domain

Fig. 4

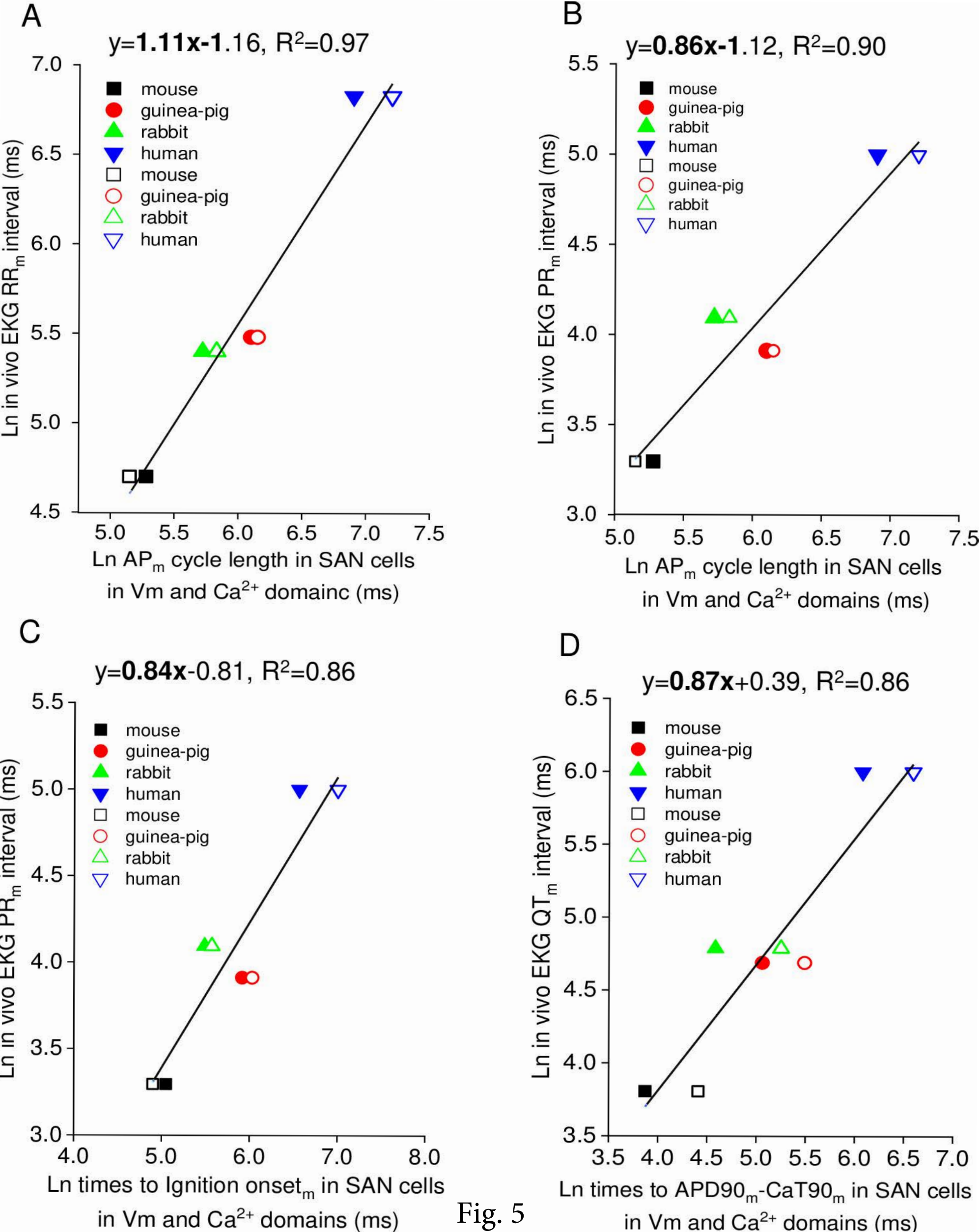
A
y=1.11x-1.16, R²=0.97
mouse
guinea-pig
rabbit
human
mouse
guinea-pig
rabbit
human
Ln in vivo EKG RRm interval (ms)
Ln APm cycle length in SAN cells in Vm and Ca2+ domainc (ms)
4.5
5.0
5.5
6.0
6.5
7.0
5.0
5.5
6.0
6.5
7.0
7.5
B
y=0.86x-1.12, R²=0.90
mouse
guinea-pig
rabbit
human
mouse
guinea-pig
rabbit
human
Ln in vivo EKG PRm interval (ms)
Ln APm cycle length in SAN cells in Vm and Ca2+ domains (ms)
3.0
3.5
4.0
4.5
5.0
5.5
5.0
5.5
6.0
6.5
7.0
7.5
C
y=0.84x-0.81, R²=0.86
mouse
guinea-pig
rabbit
human
mouse
guinea-pig
rabbit
human
Ln in vivo EKG PRm interval (ms)
Ln times to Ignition onsetm in SAN cells in Vm and Ca2+ domains (ms)
3.0
3.5
4.0
4.5
5.0
5.5
4.0
5.0
6.0
7.0
8.0
D
y=0.87x+0.39, R²=0.86
mouse
guinea-pig
rabbit
human
mouse
guinea-pig
rabbit
human
Ln in vivo EKG QTm interval (ms)
Ln times to APD90m-CaT90m in SAN cells in Vm and Ca2+ domains (ms)
3.5
4.0
4.5
5.0
5.5
6.0
6.5
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0

Fig. 5

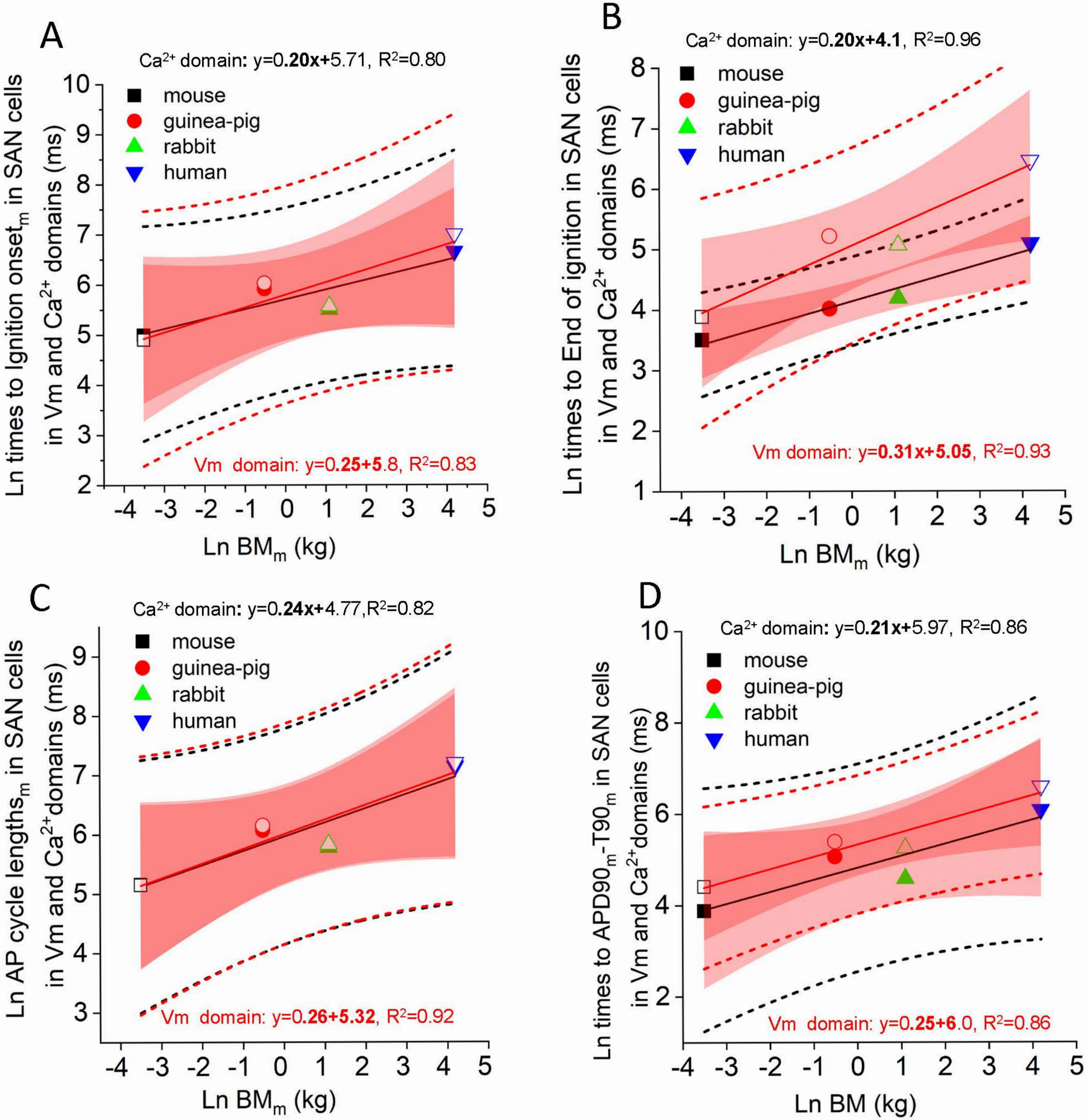
A
Ca^{2+} domain: y=0.20x+5.71, R^2=0.80
Ln times to Ignition $onset_m$ in SAN cells in Vm and Ca^{2+} domains (ms)
mouse
guinea-pig
rabbit
human
Vm domain: y=0.25+5.8, R^2=0.83
Ln BM_m (kg)
B
Ca^{2+} domain: y=0.20x+4.1, R^2=0.96
Ln times to End of ignition in SAN cells in Vm and Ca^{2+} domains (ms)
mouse
guinea-pig
rabbit
human
Vm domain: y=0.31x+5.05, R^2=0.93
Ln BM_m (kg)
C
Ca^{2+} domain: y=0.24x+4.77,R^2=0.82
Ln AP cycle $lengths_m$ in SAN cells in Vm and Ca^{2+}domains (ms)
mouse
guinea-pig
rabbit
human
Vm domain: y=0.26+5.32, R^2=0.92
Ln BM_m (kg)
D
Ca^{2+} domain: y=0.21x+5.97, R^2=0.86
Ln times to $APD90_m$-$T90_m$ in SAN cells in Vm and Ca^{2+}domains (ms)
mouse
guinea-pig
rabbit
human
Vm domain: y=0.25+6.0, R^2=0.86
Ln BM (kg)

Fig.6

Local calcium signals in pacemaker cells heart rate and body mass are self-similar from mice to humans

Syevda Tagirova (Sirenko), Kenta Tsutsui, Dongmei Yang, Bruce D. Ziman, Kirill V. Tarasov, Yael Yaniv, Edward G. Lakatta*

Short title: Self-similarity of local calcium signals in pacemaker cells and heart rate across species

Supplementary information

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Supplementary Figure S1. Restitution times and Ignition phase onset across species are self-similar in Vm and Ca^{2+} domains.

Supplementary Figure S2. Illustration and definition of the phase transition parameters in the Ca^{2+} domain.

Supplementary Table S1. Phylogeny of molecules that regulate cell pacemaker functions: mammals to worms.

Supplementary Table S2. Correlations among kinetic parameters **within** (**A**) Vm and (**B**) Ca^{2+} domains from mouse to human' in single, isolated SAN cells.

Supplementary Table S3. Correlations from mouse to human' among kinetic parameters **between** Vm and Ca^{2+} domains in single, isolated SAN cells.

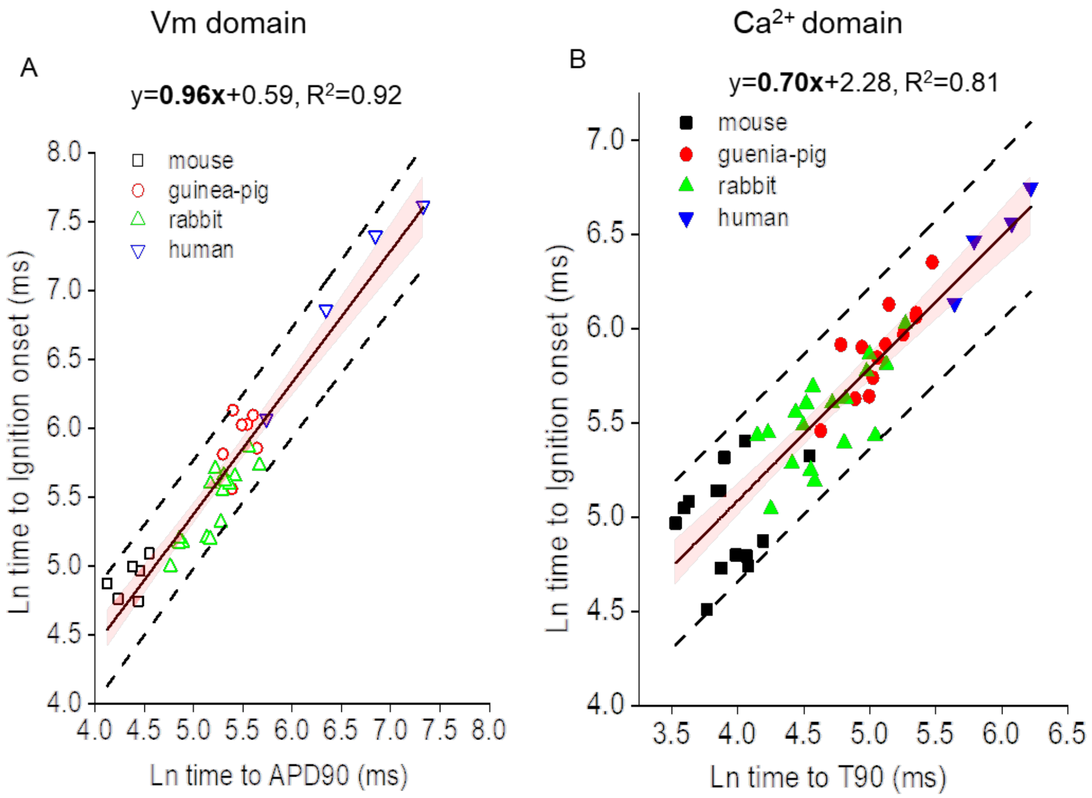
Supplementary Table S4. Correlations from mouse to human' between Vm and Ca^{2+} domains kinetic parameters in single SAN cells in vitro and EKG intervals in vivo.

Supplementary Table S5. Results of the linear fitting between Vm and Ca^{2+} domains parameters in single, isolated SAN cells in vitro and EKG intervals in vivo.

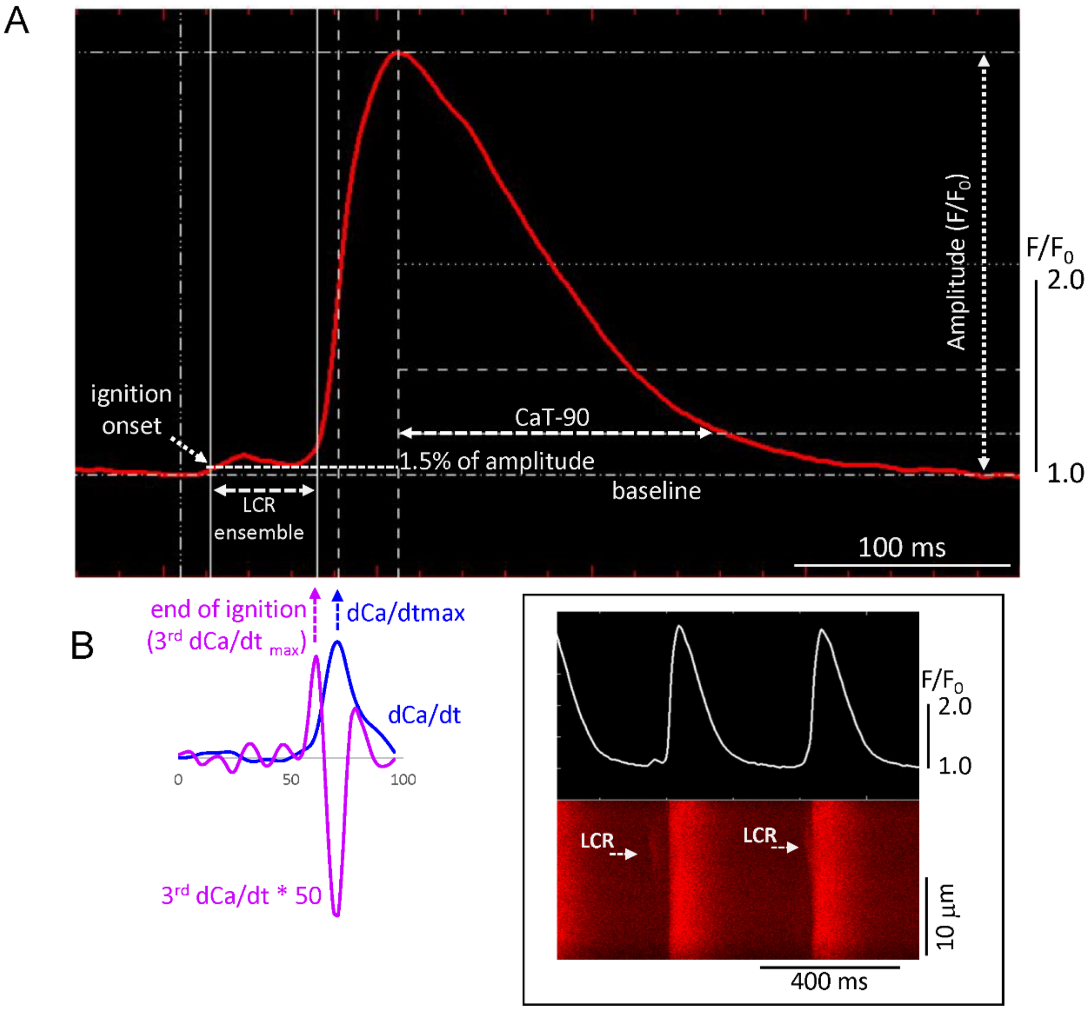
Supplementary Table S6. NCBI/Uniprot Accession IDs of sequences used for alignments.

Supplementary Table S7. Comparison of ion current channel density and channel proteins gene expression levels in SAN of different species.

Supplementary Alignments.pdf



Supplementary Figure S1. Restitution times and Ignition phase onset across species are self-similar in Vm and Ca^{2+} domains. (**A**) Relationships of Restitution times of the AP cycle in the Vm and (**B**) in the Ca^{2+} domains to Ignition phase onset in SAN cells (n=4-20 SAN cells per species, from 3-8 repetition per species). Open symbols-transmembrane AP recordings via patch-clamp; closed symbols-CaT recordings via confocal microscopy. Linear regression of concatenated fit, no weighting; slopes are significantly different from zero ($p<0.05$). Outside dashed lines-95% prediction band limit; pink-95% confidence band.



Supplementary Figure S2. Illustration and definition of the phase transition parameters in the Ca^{2+} domain. (A) Enlarged AP-induced Ca^{2+} transient (CaT) (2-d trace in the inset) demonstrate and defines the phase transition parameters measured with IDL (8.5) software. We defined the ignition onset of LCR ensemble at the time when the integrated Ca^{2+} signal begins to rise from the noise (background) and reached a 1.5% of the peak value of the subsequent Ca^{2+} transient (see also Methods). The inset shows the original confocal line-scan image and Ca^{2+} waveform in (**A**). (**B**) Time derivates of CaT (from baseline to CaT peak) in (A) used in our study to define the end of ignition phase and max rate of rise of CaT.

S1Table. Phylogeny of molecules that regulate cell pacemaker functions: mammals to worms.

Alias	Gene	Mammals	Birds	Amphibians	Fishes	Insects, Flies	Worms	Links to Orthologs	Genes with similar protein architectures
NCX1	SLC8A1	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/6546/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/6546/ortholog/similargenes/
Hcn2	HCN2	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/610/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/610/ortholog/similargenes/
Hcn4	HCN4	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/10021/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/10021/ortholog/similargenes/?scope=33208
Nav1.5	SCN5A	+	+					https://www.ncbi.nlm.nih.gov/gene/6331/ortholog/?scope=32524	https://www.ncbi.nlm.nih.gov/gene/6331/ortholog/similargenes/?scope=7568
Nav1.1	SCN1A	+	+	+	+	+		https://www.ncbi.nlm.nih.gov/gene/6323/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/6323/ortholog/similargenes/?scope=6960
Cav 1.2	CACNA1C	+	+	+	+			https://www.ncbi.nlm.nih.gov/gene/775/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/775/ortholog/?scope=117570
Cav1.3	CACNA1D	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/776/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/776/ortholog/similargenes/?scope=33208
Cav3.1	CACNA1G	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/8913/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/8913/ortholog/similargenes/
Kv 7.1	KCNQ1	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/3784/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/3784/ortholog/similargenes/?scope=33208
MinK	KCNE1	+	+	+	+			https://www.ncbi.nlm.nih.gov/gene/3753/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/3753/ortholog/similargenes/?scope=117570
HERG	KCNH2	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/3757/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/3757/ortholog/similargenes/?scope=2759
KCa1.1	KCNMA1	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/3778/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/3778/ortholog/similargenes/
KCa2.1	KCNN1	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/3780/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/3780/ortholog/similargenes/?scope=33213
KCa2.2	KCNN2	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/3781/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/3781/ortholog/similargenes/?scope=6157
KCa2.3	KCNN3	+	+	+	+			https://www.ncbi.nlm.nih.gov/gene/3782/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/3782/ortholog/similargenes/?scope=33208
Orai1	ORAI1	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/84876/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/84876/ortholog/similargenes/?scope=6072
Orai2	ORAI2	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/80228/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/80228/ortholog/similargenes/?scope=6072
Orai3	ORAI3	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/93129/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/93129/ortholog/similargenes/?scope=6072
Serca2a	Atp2a2	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/488/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/488/ortholog/similargenes/?scope=33208
RyR2	RyR2	+	+	+	+	+		https://www.ncbi.nlm.nih.gov/gene/6262/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/6262/ortholog/similargenes/?scope=33213
Pln	PLN	+	+	+	+			https://www.ncbi.nlm.nih.gov/gene/5350/ortholog/?scope=7898	https://www.ncbi.nlm.nih.gov/gene/5350/ortholog/similargenes/?scope=7776
Casq2	CASQ2	+	+	+	+			https://www.ncbi.nlm.nih.gov/gene/845/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/845/ortholog/similargenes/?scope=117570
IP3-kinase /	ITPKA	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/3706/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/3706/ortholog/similargenes/?scope=2759
FKBP12	FKBP1A	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/2280/ortholog/?scope=117570	https://www.ncbi.nlm.nih.gov/gene/2280/ortholog/similargenes/?scope=2759
Stim1	STIM1	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/6786/ortholog/similargenes/?scope	https://www.ncbi.nlm.nih.gov/gene/6786/ortholog/?scope=7776
Stim2	STIM2	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/57620/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/57620/ortholog/similargenes/?scope=6072
ADCY1	ADCY1	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/107/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/107/ortholog/similargenes/?scope=33208
ADCY8	ADCY8	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/114/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/114/ortholog/similargenes/?scope=33208
PDE4A	PDE4A	+	+	+	+	+	+	https://www.ncbi.nlm.nih.gov/gene/5141/ortholog/?scope=7776	https://www.ncbi.nlm.nih.gov/gene/5141/ortholog/similargenes/?scope=2759

Supplementary Table S2. Correlations among kinetic parameters **within** (**A**) Vm and (**B**) Ca^{2+} domains from   mouse to human’ in single, isolated SAN cells.

Vm domain parameters (ms)	**time to Ignition onset**	**end of ignition (time to TOP)**	**time to APD90**
	r^2	**r^2**	**r^2**
time to Ignition onset			
end of ignition (time to TOP)	**0.9**		
time to APD90	**1.0**	**0.9**	
Cycle length	**1.0**	**1.0**	**1.0**

(B)

Ca^{2+} domain parameters (ms)	**time to Ignition onset**	**end of ignition (time to 3rd dCa/dtmax)**	**time to T90**
	r^2	**r^2**	**r^2**
time to Ignition onset			
end of ignition (time to 3rd dCa/dtmax)	**0.9**		
time to T90	**0.8**	**0.7**	
Cycle length	**1.0**	**0.9**	**0.9**

A-B. Pearson correlations coefficients (r^2) of significant values; $p<0.05$, 2-tailed test; n=4-20 SAN cells per species.

Supplementary Table S3. Correlations from mouse to human' among kinetic parameters **between** Vm and Ca^{2+} domains in single, isolated SAN cells.

Ca^{2+} domain parameters (ms)	**Vm domain parameters (ms)**			
	time to APD90	**time to Ignition onset**	**end of ignition (time to TOP)**	**Cycle length**
time to T90	**1.0**	**1.0**	**1.0**	**1.0**
time to Ignition onset	**1.0**	**1.0**	**1.0**	**1.0**
end of ignition (time to 3rd dCa/dtmax)	**1.0**	**1.0**	**1.0**	**1.0**
Cycle length	**1.0**	**1.0**	**1.0**	**1.0**

Pearson correlations coefficients (r^2) of significant values; $p<0.05$, 2-tailed test; n=4-20 SAN cells per species.

Supplementary Table S4. Correlations from mouse to human' between Vm and Ca^{2+} domains kinetic parameters in single SAN cells in vitro and EKG intervals in vivo.

Vm and Ca^{2+} domains parameters (ms)	EKG Intervals (ms)		
	RR	PR	QT
Vm Cycle length	**1.0**	**1.0**	**1.0**
Vm time to APD90	**1.0**	**1.0**	**1.0**
Vm time to MDP	**1.0**	ns	ns
Vm time to Ignition onset	**1.0**	**1.0**	**1.0**
Vm end of ignition (time to TOP)	**1.0**	**1.0**	**1.0**
Ca^{2+} Cycle length	**1.0**	ns	**1.0**
Ca^{2+} time to T90	**1.0**	ns	**1.0**
Ca^{2+} time to Ignition onset	**1.0**	ns	ns
Ca2+ end of ignition (time to 3rd dCa/dtmax)	**1.0**	1.0	1.0

Pearson correlations coefficients (r^2) of significant values; $p<0.05$, 2-tailed test; n=4-20 SAN cells per species; in vivo EKG parameters are taken from published literature (see methods).

Supplementary Table S5. Results of the linear fitting between Vm and Ca^{2+} domains parameters *in vitro* of and *in vivo* EKG intervals.

	EKG intervals (ms)														
	RR					PR					QT				
Vm and Ca^{2+} domains (ms)	Equation	R	R-Square	Adj R-Square	SE of slope	Equation	R	R-Square	Adj R-Square	SE of slope	Equation	R	R-Square	Adj R-Square	SE of slope
Cycle length	y=1.11x-1.16	0.977	0.966	0.959	0.097	y=0.86x-1.12	0.949	0.901	0.884	0.116	y=1.12x-1.94	0.965	0.931	0.919	0.124
times to Ignition onset	y=1.10x-0.78	0.957	0.916	0.902	0.135	y=0.84x-0.81	0.925	0.856	0.832	0.141	y=1.10x-1.56	0.944	0.891	0.873	0.156
times to APD90-T90	y=0.60x+1.16	0.931	0.867	0.845	0.137	y=0.67x+0.63	0.911	0.830	0.802	0.123	y=0.87x+0.39	0.925	0.856	0.832	0.144
times to end of ignition	y=0.70x+2.34	0.812	0.660	0.603	0.204	y=0.55x+1.48	0.815	0.664	0.610	0.161	y=0.71x+1.49	0.820	0.671	0.620	0.203

Supplementary Table S6. NCBI/Uniprot Accession IDs of sequences used for alignments.

Symbol	mouse	guinea-pig	rabbit	human
SLC8A1	NP_035536	NP_001166490	NP_001164429	sp|P32418|NAC1_HUMAN
HCN2	O88703	H0WDP7	^	Q9UL51
HCN4	NP_001074661	XP_003462239	NP_001076176	sp|Q9Y3Q4|HCN4_HUMAN
SCN5A	Q9JJV9	H0V4Z8	G1STZ7	Q14524
SCN1A	A2APX8	H0UZ29	G1SSP8	P35498
CACNA1C	NP_033911	NP_001166394	NP_001129994	sp|Q13936|CAC1C_HUMAN
CACNA1D	NP_001289566	XP_005008320	XP_017199370	NP_000711.1
CACNA1G	NP_033913	XP_013004978	XP_008269518	sp|O43497|CAC1G_HUMAN
KCNQ1	P97414	O70344	Q9MYS6	P51787
KCNE1	P23299	Q60409	Q28705	P15382
KCNH2	O35219	Q8WNY2	H0VZT8	Q12809
KCNMA1	Q08460	A0A286XP95	Q9BG98	Q12791
KCNN1	Q9EQR3	H0W7E2	^	Q92952
KCNN2	P58390	H0UUD3	G1T862	Q9H2S1
KCNN3	P58391	H0VU03	A0A5F9C4T7	Q9UGI6
ORAI1	Q8BWG9	H0W6E9	G1TJL6	Q96D31
ORAI2	Q8BH10	A0A286Y0K4	G1U3B1	Q96SN7
ORAI3	Q6P8G8	A0A286XUS9	G1TRG3	Q9BRQ5
ATP2A2	NP_733765	XP_003462979	NP_001082790	NP_001103610
RyR2	NP_076357	XP_023422283	NP_001076226	sp|Q92736|RYR2_HUMAN
PLN	NP_001135399	XP_012998839	NP_001076090	sp|P26678|PPLA_HUMAN
CASQ2	O09161	A0A286Y396	P31235	O14958
ITPKA	Q8R071	H0UZF9	G1TMC6	P23677
FKBP1A	P26883	A0A286XID4	P62943	P62942
STIM1	P70302	A0A286Y154	G1T594	Q13586
STIM2	P83093	H0V0T4	G1T6V7	Q9P246
ADCY1	NP_033752	XP_005001973	XP_008260055	NP_066939
ADCY8	NP_033753	XP_003467396	XP_002710595	NP_001106
PDE4A	NP_899668	XP_003460919	^	P27815

^ *Not mapped to rabbit genome.*

Supplementary Table S7. Comparison of ion current channel density and channel proteins gene expression levels in SAN of different species.

Current/Gene	**Current Density (ratio)**				**Expression level (ratio)**			
Ignition	**M**	**R**	**RB**	**H**	**M**	**R**	**RB**	**H**
I_f/HCN4	5x vs H	1.8x vs H	3.3x vs H		7x vs H	2x vs H	8x vs H	
I_{NCX}/NCX1	– 4x vs RB		1x vs H		1.4x vs H	1x vs H	5x vs H	
I_{CaT}/Cav3.1	2x vs RB				16x vs H	17x vs H	1x vs H	
I_{CaL}/Cav1.3					1x vs H	1x vs H	4x vs H	
INa/Nav1.1-1.4					7.5 x H	2x vs H		
RyR					6x vs H	5x vs H	1x vs H	
SERCA					70 vs H	14x vs H	5x vs H	
End of Ignition								
I_{CaL}/Cav1.2	1x vs H	1x vs H	1x vs H		1x vs H	1x vs H	1x vs H	
Repolarizatiuon								
I_{kr} (activation)/hERG	1x vs RB	1x vs M			1x vs RB	1x vs M		
I_{ks}/KCNQ1								
I_{BK1}/KCNMA1								
$I_{SK1\text{-}3}$/KCNN1-3	1x vs RB							
SERCA$^{\&}$								

Data were collected from the literature from Li et al[1]*. and other studies*[2-7]*. M-mouse, R-rat, RB-rabbit, H-human. &see above (ignition). Values that were 1 or <1, we assigned as 1- no difference. Empty cells - no quantitative comparison was found.*

References

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**ADCY1**
-------------------------------------------------------------------------------
Consensus    MAGAPRGGGG-GGGGAGEPGGAERAAGPGGRRGLRACGEEFACPELEALFRGYTLRLEQA    59
ADCY1-H      ..........-................TSR.......D......................    59
ADCY1-R      ..........G.................................................    60
ADCY1-GP     ------------------------------------------------------------------
ADCY1-M      .......Q.--......................F..........................    58

Consensus    ATLKALAVLSLLAGALALAELLGAPGPAPGLAKGSHPVHCVLFLALLVVTNVRSLQVPQL   119
ADCY1-H      ............................................................   119
ADCY1-R      ............................................................   120
ADCY1-GP     ------------------------------------------------------------
ADCY1-M      ........................................I.....F..........S..   118

Consensus    QQVGQLALLFSLTFALLCCPFALGGPARGSAGAAXGPAXAEQGVWQLLLVTFVSYALLPV   179
ADCY1-H      ..................................G...T.....................   179
ADCY1-R      ...........................G.P....A...A.....................   180
ADCY1-GP     ------------------------------------------------------------
ADCY1-M      ........F...................S...G.M.STV.....................   178

Consensus    RSLLAIGFGLVVAASHLLVTATLVPAKRPRLWRTLGANALLFVGVNMYGVFVRILTERSQ   239
ADCY1-H      ............................................................   239
ADCY1-R      .....V....................R.................................   240
ADCY1-GP     ----------------------------------------------........V.....    14
ADCY1-M      .....................A....................F.................   238

Consensus    RKAFLQARSCIEDRLRLEDENEKQERLLMSLLPRNVAMEMKEDFLKPPERIFHKIYIQRH   299
ADCY1-H      ............................................................   299
ADCY1-R      ............................................................   300
ADCY1-GP     ........G...................................................    74
ADCY1-M      ........N...................................................   298

Consensus    DNVSILFADIVGFTGLASQCTAQELVKLLNELFGKFDELATENHCRRIKILGDCYYCVSG   359
ADCY1-H      ............................................................   359
ADCY1-R      ............................................................   360
ADCY1-GP     ............................................................   134
ADCY1-M      ............................................................   358

Consensus    LTQPKTDHAHCCVEMGLDMIDTITSVAEATEVDLNMRVGLHTGRVLCGVLGLRKWQYDVW   419
ADCY1-H      ............................................................   419
ADCY1-R      .....A..................------------------------------------   420
ADCY1-GP     ............................................................   194
ADCY1-M      ............................................................   418

Consensus    SNDVTLANVMEAAGLPGKVHITKTTLACLNGDYEVEPGHGHERNSFLKTHNIETFFIVPS   479
ADCY1-H      ......................................Y.....................   479
ADCY1-R      ------------------------------------------------------------   480
ADCY1-GP     ................................................A...........   254
ADCY1-M      ............................................T..R............   478

Consensus    HRRKIFPGLILSDIKPAKRMKFKTVCYLLVQLMHCRKMFKAEIPFSNVMTCEDDDKRRAL   539
ADCY1-H      ............................................................   539
ADCY1-R      ------------------------------------------------------------   540
ADCY1-GP     ....................R.......................................   314
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ADCY1-M         ............................................................   538

Consensus       RTASEKLRNRSSFSTNVVYTTPGTRVNRYISRLLEARQTELEMADLNFFTLKYKHVEREQ   599
ADCY1-H         ............................................................   599
ADCY1-R         ------------------------------------------------------------   600
ADCY1-GP        .............CA.......................P.......D.......QA...R   374
ADCY1-M         ............................................................   598

Consensus       KYHQLQDEYFTSAVVLALILAALFGLIYLLVIPQSVAVLLLLVFCICFLVACVLYLHITR   659
ADCY1-H         ................T.........V...IF....V.......................   659
ADCY1-R         ------------------------------------------------------------   660
ADCY1-GP        .........................................................V..   434
ADCY1-M         ............................................S.......T.......   658

Consensus       VQCFPGCLTIQIRTVLCVFIVVLIYSVAQGCVVGCLPWAWSSXSNSSLVVLASGGRRTVL   719
ADCY1-H         .................I........................KP.......S...Q..A.   719
ADCY1-R         ------------------------------------------------------------   720
ADCY1-GP        ..........R...........................S...R.................   494
ADCY1-M         ..............A...........................Q.........A.......   718

Consensus       PALPCESAHHALLCCLVGTLPLAIFLRVSSLPKMILLSGLTTSYILVLELSGYTKXGGGA   779
ADCY1-H         .T.....T.................F............................RT....   779
ADCY1-R         ------------------------------------------------------------   780
ADCY1-GP        ..................................................G....A....   554
ADCY1-M         .......................................................V....   778

Consensus       XSGRSYEPIMAILLFSCTLALHARQVDVRLRLDYLWAAQAEEERDDMERVKLDNKRILFN   839
ADCY1-H         V........V.......A.........I................E...K.....R.....   839
ADCY1-R         ------------------------------------------------------------   840
ADCY1-GP        I...........................................................   614
ADCY1-M         L...........................................................   838

Consensus       LLPAHVAQHFLMSNPRNMDLYYQSYSQVGVMFASIPNFNDFYIELDGNNMGVECLRLLNE   899
ADCY1-H         ............................................................   899
ADCY1-R         ------------------------------------------------------------   900
ADCY1-GP        ............................................................   674
ADCY1-M         ............................................................   898

Consensus       IIADFDELMDKDFYKDLEKIKTIGSTYMAAVGLAPTSGTRAKKSISSHLCTLADFAIEMF   959
ADCY1-H         .........E......I......................K.........S..........   959
ADCY1-R         ------------------------------------------------------------   960
ADCY1-GP        ............................................................   734
ADCY1-M         ....................................A....................D..   958

Consensus       DVLDEINYQSYNDFVLRVGINVGPVVAGVIGARRPQYDIWGNTVNVASRMDSTGVQGRIQ  1019
ADCY1-H         ............................................................  1019
ADCY1-R         ------------------------------------------------------------  1020
ADCY1-GP        ............................................................   794
ADCY1-M         ............................................................  1018

Consensus       VTEEVHRLLRRCPYHFVCRGKVSVKGKGEMLTYFLEGRTDGNGSHGRXXXLERRMCPYGR  1079
ADCY1-H         ............................................QI.SLG.D.K...F..  1079
ADCY1-R         ------------------------------------------------------------  1080
ADCY1-GP        ..........K................................G...PMH....VYS..G   854
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ADCY1-M      .........K..S.Q...........................S....TFR..........  1078

Consensus    AGGQARRPPLCPAPGPPVRAGLPPASPGQYLPSTAAGKEA                      1119
ADCY1-H      ..L.G....V..M..VS.......H........A......                      1119
ADCY1-R      ----------------------------------------                       384
ADCY1-GP     ..........G.................P.P.A....R..                       894
ADCY1-M      G............A.....P.....PTS...S........                      1118


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**ADCY8**
-------------------------------------------------------------------------------
Consensus    MELSDVRCLSGSEELYTIHPTPPAGDGGSGSRPQRLLWQTAVRHITEQRFIHGHRGGGGG    60
ADCY8-H      .........T.................R.A...........................S.S    60
ADCY8-M      ......H...........Q.......D.................................    60
ADCY8-GP     ..........................................................-.    59
ADCY8-R      .......F....................................................    60

Consensus    GSGGSXKASNPAGGGPNHHAPQLSGDSALPLYSLGPGERAHSTGGTKVFPERSGSGSASG   120
ADCY8-H      .....G...D.................................C................   120
ADCY8-M      .--V.R.......S..........S..V.............N..................   118
ADCY8-GP     .....R.....................E................................   119
ADCY8-R      .....G.G.....C.S.........E...................S..............   120

Consensus    SGGGGDLGFLHLDCAPSNSDFFLNGGYSYRGVIFPTLRNSFKSRDLERLYQRYFLGQRRK   180
ADCY8-H      ............................................................   180
ADCY8-M      ............................................................   178
ADCY8-GP     ...............................................H............   179
ADCY8-R      ............................................................   180

Consensus    SEVVMNVLDVLTKLTLLVLHLSLASAPMDPLKGILLGFFTGIEVVICALVVVRKDTTSHT   240
ADCY8-H      ............................................................   240
ADCY8-M      .......................................................N....   238
ADCY8-GP     ............................................................   239
ADCY8-R      ............................................................   240

Consensus    YLQYSGVVTWVAMTTQILAAGLGYGLLGDGIGYVLFTLFATYSMLPLPLTWAILAGLGTS   300
ADCY8-H      ............................................................   300
ADCY8-M      ............................................................   298
ADCY8-GP     ......L.....................................................   299
ADCY8-R      ............................................................   300

Consensus    LLQVVLQVVIPRLAVISINQVVAQAVLFMCMNTAGIFISYLSDRAQRQAFLETRRCVEAR   360
ADCY8-H      ....I.......................................................   360
ADCY8-M      ....T...L......F.....L..V...................................   358
ADCY8-GP     ............................................................   359
ADCY8-R      ............................................................   360

Consensus    LRLETENQRQERLVLSVLPRFVVLEMINDMTNVEDEHLQHQFHRIYIHRYENVSILFADV   420
ADCY8-H      ............................................................   420
ADCY8-M      ............................................................   418
ADCY8-GP     ............................................................   419
ADCY8-R      ............................................................   420
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Consensus     KGFTNLSTTLSAQELVRMLNELFARFDRLAHEHHCLRIKILGDCYYCVSGLPEPRQDHAH    480
ADCY8-H       ............................................................    480
ADCY8-M       .......................................................R....    478
ADCY8-GP      ............................................................    479
ADCY8-R       ............................................................    480

Consensus     CCVEMGLSMIKTIRYVRSRTKHDVDMRIGIHSGSVLCGVLGLRKWQFDVWSWDVDIANKL    540
ADCY8-H       ............................................................    540
ADCY8-M       ..............F.............................................    538
ADCY8-GP      ............................................................    539
ADCY8-R       ............................................................    540

Consensus     ESGGIPGRIHISKATLDCLNGDYNVEEGHGKERNEFLRKHNIETYLIKQPEESLLSLPED    600
ADCY8-H       ...................................................D........    600
ADCY8-M       .......................................................C....    598
ADCY8-GP      ............................................................    599
ADCY8-R       ............................................................    600

Consensus     IVKESVSSSDRRNSGATFTEGSWSPELPFDNIVGKQNTLAALTRNSINLLPNHLAQALHV    660
ADCY8-H       ............................................................    660
ADCY8-M       .......C....................................................    658
ADCY8-GP      ............................................................    659
ADCY8-R       .......P....................................................    660

Consensus     QSGPEEINKRIEHTIDLRSGDKLRREHIKPFSLMFKDSSLEHKYSQMRDEVFKSNLVCAF    720
ADCY8-H       ............................................................    720
ADCY8-M       ............................................................    718
ADCY8-GP      ............................................................    719
ADCY8-R       ............................................................    720

Consensus     IVLLFITAIQSLLPSSRVMPMTIQFSILIMLHSALVLITTAEDYKCLPLILRKTCCWINE    780
ADCY8-H       ............................................................    780
ADCY8-M       .................L..........................................    778
ADCY8-GP      ......................V..........T..........................    779
ADCY8-R       .......T.........................................V..........    780

Consensus     TYLARNVIIFASILINFLGAVLNILWCDFDKSIPLKNLTFNSSAVFTDICSYPEYFVFTG    840
ADCY8-H       ....................I.......................................    840
ADCY8-M       ............................................................    838
ADCY8-GP      ............................................................    839
ADCY8-R       N...........................................................    840

Consensus     VLAMVTCAVFLRLNSVLKLAVLLIMIAIYALLTETIYAGLFLRYDNLNHSGEDFLGTKEA    900
ADCY8-H       ...................................V.......................V    900
ADCY8-M       ..........................................S.................    898
ADCY8-GP      ......................................D............K........    899
ADCY8-R       ............................................................    900

Consensus     SLLLMAMFLLAVFYHGQQLEYTARLDFLWRVQAKEEINEMKELREHNENMLRNILPSHVA    960
ADCY8-H       ............................................................    960
ADCY8-M       ............................................................    958
ADCY8-GP      ............................................................    959
ADCY8-R       ............................................................    960
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Consensus    RHFLEKDRDNEELYSQSYDAVGVMFASIPGFADFYSQTEMNNQGVECLRLLNEIIADFDE  1020
ADCY8-H      ............................................................  1020
ADCY8-M      ............................................................  1018
ADCY8-GP     ............................................................  1019
ADCY8-R      ............................................................  1020

Consensus    LLGEDRFQDIEKIKTIGSTYMAVSGLSPEKQQCEDKWGHLCALADFSLALTESIQEINKH  1080
ADCY8-H      ............................................................  1080
ADCY8-M      ............................................................  1078
ADCY8-GP     ..................................................A.........  1079
ADCY8-R      ............................................................  1080

Consensus    SFNNFELRIGISHGSVVAGVIGAKKPQYDIWGKTVNLASRMDSTGVSGRIQVPEETYLIL  1140
ADCY8-H      ............................................................  1140
ADCY8-M      ............................................................  1138
ADCY8-GP     ............................................................  1139
ADCY8-R      ............................................................  1140

Consensus    KDQGFAFDYRGEIYVKGISEQEGKIKTYFLLGRVQPNPFILPPRRLPGQYSLAAVVLGLV  1200
ADCY8-H      ............................................................  1200
ADCY8-M      ............................................................  1198
ADCY8-GP     ............................................................  1199
ADCY8-R      ............................................................  1200

Consensus    QSLNRQRQKQLLNENNNTGIIKGHYNRRTLLTPSGPEPGAQAEGTDKSDLP           1251
ADCY8-H      ...............................S...T...............           1251
ADCY8-M      ...............S.S....S............................           1249
ADCY8-GP     .....................................S.......E.....           1250
ADCY8-R      .................................T.................           1251


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**Atp2a2**
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Consensus    MENAHTKTVEEVLGHFGVNESTGLSLEQVKKLKERWGSNELPAEEGKTLLELVIEQFEDL    60
ATP2A2-H     ............................................................    60
ATP2A2-M     ............................................................    60
ATP2A2-R     ............................................................    60
ATP2A2-GP    ............................................................    60

Consensus    LVRILLLAACISFVLAWFEEGEETITAFVEPFVILLILVANAIVGVWQERNAENAIEALK   120
ATP2A2-H     ............................................................   120
ATP2A2-M     ............................................................   120
ATP2A2-R     ............................................................   120
ATP2A2-GP    ............................................................   120

Consensus    EYEPEMGKVYRQDRKSVQRIKAKDIVPGDIVEIAVGDKVPADIRLTSIKSTTLRVDQSIL   180
ATP2A2-H     ............................................................   180
ATP2A2-M     ............................................................   180
ATP2A2-R     ............................................................   180
ATP2A2-GP    ............................................................   180

Consensus    TGESVSVIKHTDPVPDPRAVNQDKKNMLFSGTNIAAGKAMGVVVATGVNTEIGKIRDEMV   240
ATP2A2-H     ............................................................   240
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ATP2A2-M      ............................................................   240
ATP2A2-R      ............................................................   240
ATP2A2-GP     ......................................V.....................   240

Consensus     ATEQERTPLQQKLDEFGEQLSKVISLICIAVWIINIGHFNDPVHGGSWIRGAIYYFKIAV   300
ATP2A2-H      ............................................................   300
ATP2A2-M      ............................................................   300
ATP2A2-R      ............................................................   300
ATP2A2-GP     ............................................................   300

Consensus     ALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTTNQ   360
ATP2A2-H      ............................................................   360
ATP2A2-M      ............................................................   360
ATP2A2-R      ............................................................   360
ATP2A2-GP     ............................................................   360

Consensus     MSVCRMFILDKVEGDTCSLNEFTITGSTYAPIGEVHKDDKPVKCHQYDGLVELATICALC   420
ATP2A2-H      ......................S............Q........................   420
ATP2A2-M      ..........R...............................N.................   420
ATP2A2-R      ............D...............................................   420
ATP2A2-GP     ...............................M.........I..................   420

Consensus     NDSALDYNEAKGVYEKVGEATETALTCLVEKMNVFDTELKGLSKIERANACNSVIKQLMK   480
ATP2A2-H      ............................................................   480
ATP2A2-M      ............................................................   480
ATP2A2-R      ............................................................   480
ATP2A2-GP     .................................................V..........   480

Consensus     KEFTLEFSRDRKSMSVYCTPNKPSRTSMSKMFVKGAPEGVIDRCTHIRVGSTKVPMTPGV   540
ATP2A2-H      ............................................................   540
ATP2A2-M      .........................................................S..   540
ATP2A2-R      .........................................................A..   540
ATP2A2-GP     ......................................................L.....   540

Consensus     KQKIMSVIREWGSGSDTLRCLALATHDNPLRREEMHLEDSANFIKYETNLTFVGCVGMLD   600
ATP2A2-H      ..............................K.............................   600
ATP2A2-M      ............................................................   600
ATP2A2-R      ............................................................   600
ATP2A2-GP     ............................................................   600

Consensus     PPRIEVASSVKLCRQAGIRVIMITGDNKGTAVAICRRIGIFGQDEDVTSKAFTGREFDEL   660
ATP2A2-H      ............................................................   660
ATP2A2-M      ............................................................   660
ATP2A2-R      ...........................................E....A...........   660
ATP2A2-GP     ............................................................   660

Consensus     XPSAQRDACLNARCFARVEPSHKSKIVEFLQSFDEITAMTGDGVNDAPALKKAEIGIAMG   720
ATP2A2-H      S...................................................S.......   720
ATP2A2-M      N...........................................................   720
ATP2A2-R      N...........................................................   720
ATP2A2-GP     S...........................................................   720

Consensus     SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNMKQFIRYLISSNVGEVVCIFLTAAL   780
ATP2A2-H      ............................................................   780
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ATP2A2-M     ............................................................  780
ATP2A2-R     ............................................................  780
ATP2A2-GP    ............................................................  780

Consensus    GFPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMNKPPRNPKEPLISGWLFFRYLAIG  840
ATP2A2-H     ............................................................  840
ATP2A2-M     ............................................................  840
ATP2A2-R     ............................................................  840
ATP2A2-GP    ............................................................  840

Consensus    CYVGAATVGAAAWWFIAADGGPRVSFYQLSHFLQCKEDNPDFEGVDCAIFESPYPMTMAL  900
ATP2A2-H     ..........................................D.................  900
ATP2A2-M     ............................................................  900
ATP2A2-R     ............................................................  900
ATP2A2-GP    ................................................V...........  900

Consensus    SVLVTIEMCNALNSLSENQSLLRMPPWENIWLVGSICLSMSLHFLILYVEPLPLIFQITP  960
ATP2A2-H     ............................................................  960
ATP2A2-M     ............................................................  960
ATP2A2-R     ............................................................  960
ATP2A2-GP    ............................................................  960

Consensus    LNXTQWLMVLKISLPVILMDETLKFVARNYLE-PGKECVQPATK-SCSLSACTDGISWPF 1018
ATP2A2-H     ..L.............................Q...........S............... 1020
ATP2A2-M     ..V.............................-...........-...F........... 1018
ATP2A2-R     ..V.............................-.........PQ-....W...E.V.... 1018
ATP2A2-GP    ..L.............................PAIL.----------------------- 1020

Consensus    VLLIMPLVXWVYSTDTNFSDMFWS                                     1042
ATP2A2-H     ........V...............                                     1044
ATP2A2-M     ........I...............                                     1042
ATP2A2-R     ....V...M...........LL..                                     1042
ATP2A2-GP    ------------------------                                      997


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**CACNA1C**
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Consensus            MXRALVQPXTPAYQPLPSHLSAETEXXXKGTVVHEAQLNCFYISPGGSNYGSPRPAHANM    60
CACNA1C-H            ------------------------------M.NENTRMYIPEENHQ..............    30
CACNA1C-M            .I..F...S..P....S..S.E...RKF..K.............................    60
CACNA1C-GP           -MVP....T....R........D..VRGR..L...........................I    59
CACNA1C-R            .L......A................STC...........H....................    60

Consensus            NANAAAGLAPEHIPTPGAALSWQAAIDAARQAKLMGSAGNATISTVSSTQRKRQQYGKPK   120
CACNA1C-H            ............................................................    90
CACNA1C-M            ............................................................   120
CACNA1C-GP           ............................G...........T...................   119
CACNA1C-R            ............................................................   120

Consensus            KQGXTTATRPPRALLCLTLKNPIRRACISIVEWKPFEIIILLTIFANCVALAIYIPFPED   180
CACNA1C-H            ...S........................................................   150
CACNA1C-M            ...G........................................................   180
CACNA1C-GP           ..SG........................................................   179
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CACNA1C-R               ...S........................................................  180

Consensus               DSNATNSNLERVEYLFLIIFTVEAFLKVIAYGLLFHPNAYLRNGWNLLDFIIVVVGLFSA  240
CACNA1C-H               ............................................................  210
CACNA1C-M               ............................................................  240
CACNA1C-GP              ............................................................  239
CACNA1C-R               ............................................................  240

Consensus               ILEQATKADGANALGGKGAGFDVKALRAFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLH  300
CACNA1C-H               ............................................................  270
CACNA1C-M               ............................................................  300
CACNA1C-GP              ............................................................  299
CACNA1C-R               ............................................................  300

Consensus               IALLVLFVIIIYAIIGLELFMGKMHKTCYNQEGIADVPAEXDPSPCALETGHGRQCQNGT  360
CACNA1C-H               ........................................D...................  330
CACNA1C-M               ..................................I.....E...................  360
CACNA1C-GP              T.................................T.....E........S..........  359
CACNA1C-R               .................................V......D...................  360

Consensus               VCKPGWDGPKHGITNFDNFAFAMLTVFQCITMEGWTDVLYWMQDAMGYELPWVYFVSLVI  420
CACNA1C-H               .........................................VN..V.RDW..I...T.I.  390
CACNA1C-M               ............................................................  420
CACNA1C-GP              ............................................................  419
CACNA1C-R               ............................................................  420

Consensus               FGSFFVLNLVLGVLSGEFSKEREKAKARGDFQKLREKQQLEEDLKGYLDWITQAEDIDPE  480
CACNA1C-H               I...........................................................  450
CACNA1C-M               ............................................................  480
CACNA1C-GP              ............................................................  479
CACNA1C-R               ............................................................  480

Consensus               NEDEGMDEEKPRNMSMPTSETESVNTENVAGGDIEGENCGARLAHRISKSKFSRYWRRWN  540
CACNA1C-H               ............................................................  510
CACNA1C-M               ........D...................................................  540
CACNA1C-GP              .....V......................................................  539
CACNA1C-R               ............................................................  540

Consensus               RFCRRKCRAAVKSNVFYWLVIFLVFLNTLTIASEHYNQPHWLTEVQDTANKALLALFTAE  600
CACNA1C-H               .......................................N....................  570
CACNA1C-M               ............................................................  600
CACNA1C-GP              ............................................................  599
CACNA1C-R               ............................................................  600

Consensus               MLLKMYSLGLQAYFVSLFNRFDCFIVCGGILETILVETKIMSPLGISVLRCVRLLRIFKI  660
CACNA1C-H               ........................V...................................  630
CACNA1C-M               ............................................................  660
CACNA1C-GP              ....................L.......................................  659
CACNA1C-R               .......................................V....................  660

Consensus               TRYWNSLSNLVASLLNSVRSIASLLLLLFLFIIIFSLLGMQLFGGKFNFDEMQTRRSTFD  720
CACNA1C-H               ............................................................  690
CACNA1C-M               ............................................................  720
CACNA1C-GP              ....................................................R.......  719
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CACNA1C-R           ............................................................   720

Consensus           NFPQSLLTVFQILTGEDWNSVMYDGIMAYGGPSFPGMLVCIYFIILFICGNYILLNVFLA   780
CACNA1C-H           ............................................................   750
CACNA1C-M           ............................................................   780
CACNA1C-GP          ............................................................   779
CACNA1C-R           ............................................................   780

Consensus           IAVDNLADAESLTSAQKEEEEEKERKKLARTASPEKKQEVVEKPAVEESKEEKIELKSIT   840
CACNA1C-H           .......................................L......G.............   810
CACNA1C-M           ........................................M...................   840
CACNA1C-GP          ................................................T...........   839
CACNA1C-R           .........................................G...L..A...........   840

Consensus           ADGESPPTTKINMDDLQPNENEDKSPYPNPXTXGEEDEEEPEMPVGPRPRPLSELHLKEK   900
CACNA1C-H           .......A......................E.T...........................   870
CACNA1C-M           ..................S.......HS..D.A...........................   900
CACNA1C-GP          ..............................DAA...........................   899
CACNA1C-R           ....................S.........E.T...........................   900

Consensus           AVPMPEASAFFIFSPNNRFRLQCHRIVNDTIFTNLILFFILLSSISLAAEDPVQHTSFRN   960
CACNA1C-H           ..............S.............................................   930
CACNA1C-M           ............................................................   960
CACNA1C-GP          ............................................................   959
CACNA1C-R           ............................................................   960

Consensus           HILFYFDIVFTT--------------------IFTJEIXLKMTAYGAFLHKGSFCRNYFN  1000
CACNA1C-H           ............IFTIEIALKILGNADYVFTS...L..I.....................   990
CACNA1C-M           ...GNA.Y...S--------------------...L..I.....................  1000
CACNA1C-GP          ............--------------------...I..A.....................   999
CACNA1C-R           ............--------------------...I..A.....................  1000

Consensus           ILDLLVVSVSLISFGIQSSAINVVKILRVLRVLRPLRAINRAKGLKHVVQCVFVAIRTIG  1060
CACNA1C-H           ............................................................  1050
CACNA1C-M           ............................................................  1060
CACNA1C-GP          ............................................................  1059
CACNA1C-R           ............................................................  1060

Consensus           NIVIVTTLLQFMFACIGVQLFKGKLYTCSDSSKQTEAECKGNYITYKDGEVDHPIIQPRS  1120
CACNA1C-H           ............................................................  1110
CACNA1C-M           ............................................................  1120
CACNA1C-GP          ....................................................Q.......  1119
CACNA1C-R           ............................................................  1120

Consensus           WENSKFDFDNVLAAMMALFTVSTFEGWPELLYRSIDSHTEDKGPIYNYRVEISIFFIIYI  1180
CACNA1C-H           ............................................................  1170
CACNA1C-M           ............................................................  1180
CACNA1C-GP          ............................................................  1179
CACNA1C-R           ............................................................  1180

Consensus           IIIAFFMMNIFVGFVIVTFQEQGEQEYKNCELDKNQRQCVEYALKARPLRRYIPKNQHQY  1240
CACNA1C-H           ............................................................  1230
CACNA1C-M           ............................................................  1240
CACNA1C-GP          ............................................................  1239
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CACNA1C-R        ............................................................ 1240

Consensus        KVWYVVNSTYFEYLMFVLILLNTICLAMQHYGQSCLFKIAMNILNMLFTGLFTVEMILKL 1300
CACNA1C-H        ............................................................ 1290
CACNA1C-M        ............................................................ 1300
CACNA1C-GP       ............................................................ 1299
CACNA1C-R        ............................................................ 1300

Consensus        IAFKPKGYFSDPWNVFDFLIVIGSIIDVILSE---------------------------- 1332
CACNA1C-H        ................................TNHYFCDAWNTFDALIVVGSIVDIAITE 1350
CACNA1C-M        ................................---------------------------- 1332
CACNA1C-GP       ......H..C.A..T..A...V...V.IAIT.---------------------------- 1331
CACNA1C-R        ................................---------------------------- 1332

Consensus        XNPAEHTQCSPSMNAEENSRISITFFRLFRVMRLVKLLSRGEGIRTLLWTFIKSFQALPY 1392
CACNA1C-H        V........................................................... 1410
CACNA1C-M        T............S.............................................. 1392
CACNA1C-GP       V........................................................... 1391
CACNA1C-R        T........................................................... 1392

Consensus        VALLIVMLFFIYAVIGMQVFGKIALNDTTEINRNNNFQTFPQAVLLLFRCATGEAWQDIM 1452
CACNA1C-H        ............................................................ 1470
CACNA1C-M        ............................................................ 1452
CACNA1C-GP       ............................................................ 1451
CACNA1C-R        ............................................................ 1452

Consensus        LACMPGKKCAPESEPSNSTEGETPCGSSFAVFYFISFYMLCAFLIINLFVAVIMDNFDYL 1512
CACNA1C-H        ............................................................ 1530
CACNA1C-M        ............................................................ 1512
CACNA1C-GP       .............D......................................V....... 1511
CACNA1C-R        ...............H............................................ 1512

Consensus        TRDWSILGPHHLDEFKRIWAEYDPEAKGRIKHLDVVTLLRRIQPPLGFGKLCPHRVACKR 1572
CACNA1C-H        ............................................................ 1590
CACNA1C-M        ............................................................ 1572
CACNA1C-GP       ............................................................ 1571
CACNA1C-R        ............................................................ 1572

Consensus        LVSMNMPLNSDGTVMFNATLFALVRTALRIKTEGNLEQANEELRAIIKKIWKRTSMKLLD 1632
CACNA1C-H        ............................................................ 1650
CACNA1C-M        ............................................................ 1632
CACNA1C-GP       .............A.............................................. 1631
CACNA1C-R        ............................................................ 1632

Consensus        QVVPPAGDDEVTVGKFYATFLIQEYFRKFKKRKEQGLVGKPSQRNALSLQAGLRTLHDIG 1692
CACNA1C-H        ............................................................ 1710
CACNA1C-M        ............................................................ 1692
CACNA1C-GP       ............................................................ 1691
CACNA1C-R        ............................................................ 1692

Consensus        PEIRRAISGDLTAEEELDKAMKEAVSAASEDDIFRRAGGLFGNHVSYYQSDSRSAFPQTF 1752
CACNA1C-H        ...................................................G........ 1770
CACNA1C-M        .............................................T.......GN..... 1752
CACNA1C-GP       ..................................G...................T..... 1751
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CACNA1C-R             ............................................................  1752

Consensus             TTQRPLHINKAGNNQGDTESPSHEKLVDSTFTPSSYSSTGSNANINNANNTALGRXPXPA  1812
CACNA1C-H             ............SS.........................................L.R..  1830
CACNA1C-M             A.........T....A.......................................F.H..  1812
CACNA1C-GP            .......................................................F.H..  1811
CACNA1C-R             ........S..............................................L.R..  1812

Consensus             GYPSTVSTVEGHGPPLSPAVRXQEAAWKLSS-----------------------------  1843
CACNA1C-H             ...................I.V..V......NRERHVPMCEDLELRRDSGSAGTQAHCLL  1890
CACNA1C-M             ..S..................V.........-----------------------------  1843
CACNA1C-GP            ............R..S...TWA...TR..GA-----------------------------  1842
CACNA1C-R             .............S.......A.........-----------------------------  1843

Consensus             ------KRCHSRESQIAMXCQEEXSQDETYDVRMNEDAEYCSEPSLLSTEMLSYQDDENR  1897
CACNA1C-H             LRKANPS........A..AG...T......E.K..H.T.A....................  1950
CACNA1C-M             ------.........G.TVN..-IFP...RS...S.E............D.F...E..H.  1896
CACNA1C-GP            ------M..........VV....P...K....EL.K..................K.....  1896
CACNA1C-R             ------.....Q......A...GA...DN....IG....C....................  1897

Consensus             QLTPPEEDKRDIRPSPKXGFLRSASLGRRASFHLECLKRQKBQGGDISQKTVLPLHLVHH  1957
CACNA1C-H             ...L.........Q...R.......................DR.................  2010
CACNA1C-M             ...C......E.Q....RS......................D.........A........  1956
CACNA1C-GP            .........G.T.....K.......................NH.................  1956
CACNA1C-R             ..A....E.....L...K.......................N..................  1957

Consensus             QALAVAGLSPLLQRSHSPTSFPRPCATPPATPGSRGWPPQPIPTLRLEGAESSEKLNSSF  2017
CACNA1C-H             ..................A.....F................V.......V..........  2070
CACNA1C-M             ...................T.....P...V......R.LR....................  2016
CACNA1C-GP            ...................AI..................K............C.......  2016
CACNA1C-R             ....................L.............................D.........  2017

Consensus             PSIHCXSWSEEXXPCGGGSSAARRARPVSLXVPSQAGAPGRQFHGSASSLVEAVLISEGL  2077
CACNA1C-H             .....G..A.T-T.G.........V.....M.............................  2129
CACNA1C-M             .....S.....TTA.S.S..M.........T.............................  2076
CACNA1C-GP            .....S.....PS.................M...................A.........  2076
CACNA1C-R             .....G...G.NS..R.D............T.......Q.....................  2077

Consensus             GQFAQDPKFIEVTTQELADACDMTIEEMENAADNILSGGAPQSPNGTLLPFVNCRDPGQD  2137
CACNA1C-H             .............................S................A.........A...  2189
CACNA1C-M             ........................................Q...................  2136
CACNA1C-GP            .........................G..................................  2136
CACNA1C-R             ......................L..........D......R............R....R.  2137

Consensus             RAGGXE-DXXCACALGRGXSEEXLADSRVYVSSL                            2170
CACNA1C-H             ....E.-.AG.VR.R..-P...E.Q.........                            2221
CACNA1C-M             ..VAP.-.ES..Y.....R...A.....S...N.                            2169
CACNA1C-GP            ....D.D-EG........W...E......H.R..                            2169
CACNA1C-R             ...QN.Q.ASG...P.C.Q...A...R.AG....                            2171


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**CACNA1D**
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Consensus     MMMMMMMKKMQHQRQQQADHANEANYARGTRLPLSGEGPTSQPNSSKQTVLSWQAAIDAA    60
CACNA1D-GP    .............................S..............................    60
CACNA1D-R     ............................................................    60
CACNA1D-M     ...............H.E...............I..........................    60
CACNA1D-H     ............................................................    60

Consensus     RQAKAAQTMSTSAPPPVGSLSQRKRQQYAKSKKQGNSSNSRPARALFCLSLNNPIRRACI   120
CACNA1D-GP    ............................................................   120
CACNA1D-R     ...................................S........................   120
CACNA1D-M     ............................................................   120
CACNA1D-H     ............................................................   120

Consensus     SIVEWKPFDIFILLAIFANCVALAIYIPFPEDDSNSTNHNLEKVEYAFLIIFTVETFLKI   180
CACNA1D-GP    ............................................................   180
CACNA1D-R     ............................................................   180
CACNA1D-M     ............................................................   180
CACNA1D-H     ............................................................   180

Consensus     IAYGLLLHPNAYVRNGWNLLDFVIVIVGLFSVILEQLTKETEGGNHSSGKSGGFDVKALR   240
CACNA1D-GP    ............................................................   240
CACNA1D-R     ............................................S...............   240
CACNA1D-M     ............................................................   240
CACNA1D-H     ............................................................   240

Consensus     AFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFIGKMHKT   300
CACNA1D-GP    ............................................................   300
CACNA1D-R     ............................................................   300
CACNA1D-M     ............................................................   300
CACNA1D-H     ............................................................   300

Consensus     CFFADSDIVAEEDPAPCAFSGNGRQCTANGTECRSGWVGPNGGITNFDNFAFAMLTVFQC   360
CACNA1D-GP    ............................................................   360
CACNA1D-R     ............................................................   360
CACNA1D-M     ............................................................   360
CACNA1D-H     ............................................................   360

Consensus     ITMEGWTDVLYWVNDAIGWEWPWVYFVSLIILGSFFVLNLVLGVLSGEFSKEREKAKARG   420
CACNA1D-GP    ............................................................   420
CACNA1D-R     ............................................................   420
CACNA1D-M     ............................................................   420
CACNA1D-H     ............................................................   420

Consensus     DFQKLREKQQLEEDLKGYLDWITQAEDIDPENEEEGGEEGKRNTSMPTSETESVNTENVS   480
CACNA1D-GP    ............................................................   480
CACNA1D-R     ............................................................   480
CACNA1D-M     ............................................................   480
CACNA1D-H     ............................................................   480

Consensus     GEGETQGCCGSLWCWWXRRGAAKXGPSGCRRWGQAISKSKLSRRWRRWNRFXRRRCRAAV   540
CACNA1D-GP    .....K...R......K......T...........................S........   540
CACNA1D-R     ................R.....TA...........................S........   540
CACNA1D-M     ..........T.....K......T...........................N........   540
CACNA1D-H     ....NR..........R......A...........................N........   540
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Consensus     KSVTFYWLVIVLVFLNTLTISSEHYNQPDWLTQIQDIANKVLLALFTCEMLVKMYSLGLQ   600
CACNA1D-GP    ...................................................I........   600
CACNA1D-R     ............................................................   600
CACNA1D-M     ............................................................   600
CACNA1D-H     ............................................................   600

Consensus     AYFVSLFNRFDCFVVCGGITETILVELEIMSPLGISVFRCVRLLRIFKVTRHWTSLSNLV   660
CACNA1D-GP    ............................................................   660
CACNA1D-R     ............................................................   660
CACNA1D-M     ............................L.....V.........................   660
CACNA1D-H     ............................................................   660

Consensus     ASLLNSMKSIASLLLLLFLFIIIFSLLGMQLFGGKFNFDETQTKRSTFDNFPQALLTVFQ   720
CACNA1D-GP    ...................................................S........   720
CACNA1D-R     ............................................................   720
CACNA1D-M     ............................................................   720
CACNA1D-H     ............................................................   720

Consensus     ILTGEDWNAVMYDGIMAYGGPSSSGMIVCIYFIILFICGNYILLNVFLAIAVDNLADAES   780
CACNA1D-GP    ............................................................   780
CACNA1D-R     ............................................................   780
CACNA1D-M     ............................................................   780
CACNA1D-H     ............................................................   780

Consensus     LNTAQKEEAEEKERKKIARKESLENKKNNKPEVNQIANSDNKVTIDDYREEDEDKDPYPP   840
CACNA1D-GP    ............................................................   840
CACNA1D-R     ............................S..........E....................   840
CACNA1D-M     ................................................Q.DA........   840
CACNA1D-H     ............................................................   840

Consensus     CDVPVGEEEEEEEEDEPEVPAGPRPRRISELNMKEKIAPIPEGSAFFILSKTNPIRVGCH   900
CACNA1D-GP    ............................................................   900
CACNA1D-R     ......................................................V.....   900
CACNA1D-M     ............................................................   900
CACNA1D-H     ............................................................   900

Consensus     KLINHHIFTNLILVFIMLSSAALAAEDPIRSHSFRNTILGYFDYAFTAIFTVEILLKMTT   960
CACNA1D-GP    ............................................................   960
CACNA1D-R     .......................PP.......P...........................   960
CACNA1D-M     ............................................................   960
CACNA1D-H     ............................................................   960

Consensus     FGAFLHKGAFCRNYFNLLDMLVVGVSLVSFGIQSSAISVVKILRVLRVLRPLRAINRAKG  1020
CACNA1D-GP    ............................................................  1020
CACNA1D-R     ............................................................  1020
CACNA1D-M     ............................................................  1020
CACNA1D-H     ............................................................  1020

Consensus     LKHVVQCVFVAIRTIGNIMIVTTLLQFMFACIGVQLFKGKFYRCTDEAKSNPEECRGLFI  1080
CACNA1D-GP    ............................................................  1080
CACNA1D-R     ............................................................  1080
CACNA1D-M     ............................................................  1080
CACNA1D-H     ............................................................  1080
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Consensus     LYKDGDVDSPVVRERIWQNSDFNFDNVLSAMMALFTVSTFEGWPALLYKAIDSNGENXGP  1140
CACNA1D-GP    ..........M..............................................I..  1140
CACNA1D-R     .........................................................V..  1140
CACNA1D-M     .........................................................V..  1140
CACNA1D-H     .........................................................I..  1140

Consensus     VYNXRVEISIFFIIYIIIVAFFMMNIFVGFVIVTFQEQGEKEYKNCELDKNQRQCVEYAL  1200
CACNA1D-GP    ...Y........................................................  1200
CACNA1D-R     ...H........................................................  1200
CACNA1D-M     ...Y........................................................  1200
CACNA1D-H     I..H........................................................  1200

Consensus     KARPLRRYIPKNPYQYKFWYVVNSSPFEYMMFVLIMLNTLCLAMQHYEQSKMFNDAMDIL  1260
CACNA1D-GP    ............................................................  1260
CACNA1D-R     ............................................................  1260
CACNA1D-M     ............................................................  1260
CACNA1D-H     ............................................................  1260

Consensus     NMVFTGVFTVEMVLKVIAFKPKGYFSDAWNTFDSLIVIGSIIDVALSEADPTESENIPVP  1320
CACNA1D-GP    ......................................................D.....  1320
CACNA1D-R     ........................................................A...  1320
CACNA1D-M     ...................................................S...T..L.  1320
CACNA1D-H     ........................................................V...  1320

Consensus     TATPGNSEESNRISITFFRLFRVMRLVKLLSRGEGIRTLLWTFIKSFQALPYVALLIAML  1380
CACNA1D-GP    ............................................................  1380
CACNA1D-R     A...........................................................  1380
CACNA1D-M     ............................................................  1380
CACNA1D-H     ............................................................  1380

Consensus     FFIYAVIGMQMFGKVAMRDNNQINRNNNFQTFPQAVLLLFRCATGEAWQEIMLACLPGKL  1440
CACNA1D-GP    ............................................................  1440
CACNA1D-R     ............................................................  1440
CACNA1D-M     ............................................................  1440
CACNA1D-H     ............................................................  1440

Consensus     CDPESDYNPGEEYTCGSNFAIVYFISFYMLCAFLIINLFVAVIMDNFDYLTRDWSILGPH  1500
CACNA1D-GP    ............................................................  1500
CACNA1D-R     .......S................V...................................  1500
CACNA1D-M     ...D........................................................  1500
CACNA1D-H     ............................................................  1500

Consensus     HLDEFKRIWSEYDPEAKGRIKHLDVVTLLRRIQPPLGFGKLCPHRVACKRLVAMNMPLNS  1560
CACNA1D-GP    ............................................................  1560
CACNA1D-R     ............................................................  1560
CACNA1D-M     ............................................................  1560
CACNA1D-H     ............................................................  1560

Consensus     DGTVMFNATLFALVRTALKIKTEGNLEQANEELRAVIKKIWKKTSMKLLDQVVPPAGDDE  1620
CACNA1D-GP    ............................................................  1620
CACNA1D-R     ............................................................  1620
CACNA1D-M     ............................................................  1620
CACNA1D-H     ............................................................  1620
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Consensus     VTVGKFYATFLIQDYFRKFKKRKEQGLVGKYPAKNTTIALQAGLRTLHDIGPEIRRAISC  1680
CACNA1D-GP    ............................................................  1680
CACNA1D-R     ..............................H.............................  1680
CACNA1D-M     ............................................................  1680
CACNA1D-H     ............................................................  1680

Consensus     DLQDDEPEETKREEEXDVFKRNGALLGNHVNHVNSDRRDSLQQTNTTHRPLHVQRPSIPP  1740
CACNA1D-GP    ...............D----........................................  1736
CACNA1D-R     .........A...-.E.M....................E..................V..  1739
CACNA1D-M     ........DS.P-..E.........................................M..  1739
CACNA1D-H     ...............D............................................  1740

Consensus     ASDTEKPLFPPAGNSVCHNHHNHNSIGKQVPTSTNANLNNANMSKAAHGKRPSIGNLEHV  1800
CACNA1D-GP    ............................................................  1796
CACNA1D-R     .R.....................S.....L.......................L....L.  1799
CACNA1D-M     ...............G.............A....................P.........  1799
CACNA1D-H     ............................................................  1800

Consensus     SENGHHSSHKHDREPQRRSSXKRTRYYETYIRSDSGDEQXPTICREDPEIHGYFRDPRCL  1860
CACNA1D-GP    .................W..I..................F...........S.....C.V  1856
CACNA1D-R     ...............P..C.V..................L.......L..D........P  1859
CACNA1D-M     .....Y.-C.....L.....I............E.....F....................  1858
CACNA1D-H     ....................V..................L.................H..  1860

Consensus     GEQEYFSSEECYEXDSSPTWSRQNYGYYXRYPGSTMDFERPRGYHHPQGFLEDDDSPVXY  1920
CACNA1D-GP    .............E...........S..N.............................G.  1916
CACNA1D-R     .............E.....G..HSC...S..A...L.L........S....D.E..A.C.  1919
CACNA1D-M     ...........C.D...........N..N.....S......................TG.  1918
CACNA1D-H     .............D..............S....RNI.S....................C.  1920

Consensus     DSRRSPRRRLLPPTPPSHRRSSFNFECLRRQSSQEEVPPSPALPHRTALPLHLMQQQIMA  1980
CACNA1D-GP    ................P..................SS....S..................  1976
CACNA1D-R     ...............TA.....................L.....................  1979
CACNA1D-M     ..................................DD.L........A.............  1978
CACNA1D-H     ...............A......................S..IF.................  1980

Consensus     VAGLDSSKAQKYSPSHSTRSWATPPATPPYXDWTPCYTPLIQVERSESLDQVNGSLPSLH  2040
CACNA1D-GP    .........P....................Q.............................  2036
CACNA1D-R     .....P.R.-Q...................Q..................E..........  2038
CACNA1D-M     ..............................R..S.........D....M...........  2038
CACNA1D-H     ..............................R.............Q..A............  2040

Consensus     RSSWYTDEPDISYRTFTPASLTVPSSFRNKNSDKQRSADSLVEAVLISEGLGRYARDPKF  2100
CACNA1D-GP    ............................................................  2096
CACNA1D-R     ...........A............C.....D.............................  2098
CACNA1D-M     ............................................................  2098
CACNA1D-H     ............................................................  2100

Consensus     VSATKHEIADACDLTIDEMESAASTLLNGXVCPRANGDMGPVSHRQDYELQDFGPGYSDE  2160
CACNA1D-GP    .............................ST.........L..R................  2156
CACNA1D-R     .....Y.....................C.NA.......L...PQ..G.............  2158
CACNA1D-M     .............................S...........I..................  2158
CACNA1D-H     .............................N.R......V..L..................  2160
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Consensus    EPDPGRXEEDLADEMICITTL                                            2181
CACNA1D-GP   ......D..............                                            2177
CACNA1D-R    ......E..............                                            2179
CACNA1D-M    ......E..............                                            2179
CACNA1D-H    ......D..............                                            2181


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**CACNA1F**
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Consensus  MSESEGGKDTTPEPSPANGAGPGPEWGLCPGPPAVEGDXSGASGLGTPRRRTQHSKHKTV     60
CACNA1F-M  .....V.............T.............T.GT.T...............N.....     60
CACNA1F-GP .........A..D.........................-...........K.......M.     59
CACNA1F-H  .....................................ES.........K..N........     60
CACNA1F-R  ------------------------------------------------------------

Consensus  AVASAQRSPRALFCLTLANPLRRSCISIVEWKPFDILILLTIFANCVALGVYIPFPEDDS    120
CACNA1F-M  .................T..I.......................................    120
CACNA1F-GP ............................................................    119
CACNA1F-H  ............................................................    120
CACNA1F-R  ------------------------------------------------------------

Consensus  NTANHNLEQVEYVFLVIFTVETVLKIVAYGLVLHPSAYIRNGWNLLDFIIVVVGLFSVLL    180
CACNA1F-M  ............................................................    180
CACNA1F-GP ..........................................................P.    179
CACNA1F-H  ............................................................    180
CACNA1F-R  -----------------------------------------------------------M      1

Consensus  EQGPGRPGDAPHTGGKPGGFDVKALRAFRVLRPLRLVSGVPSLHIVLNSIMKALVPLLHI    240
CACNA1F-M  ..............................................V.............    240
CACNA1F-GP ............................................................    239
CACNA1F-H  ............................................................    240
CACNA1F-R  SESE.GK.ESSF------APLQTLRA............E.....................     55

Consensus  ALLVLFVIIIYAIIGLELFLGRMHKTCYFLGSDXEAEEDPSPCASSGSGRACTLNQTECR    300
CACNA1F-M  .................................M................S....H....    300
CACNA1F-GP .................................V...................M......    299
CACNA1F-H  .................................M..........................    300
CACNA1F-R  .................................V..........................    115

Consensus  GRWPGPNGGITNFDNFFFAMLTVFQCITMEGWTDVLYWMQDAMGYELPWVYFVSLVIFGS    360
CACNA1F-M  ............................................................    360
CACNA1F-GP ............................................................    359
CACNA1F-H  ..........................V.................................    360
CACNA1F-R  .................................................L..........    175

Consensus  FFVLNLVLGVLSGEFSKEREKAKARGDFQKLREKQQMEEDLRGYLDWITQAEELDLEDPS    420
CACNA1F-M  ........................................................H...    420
CACNA1F-GP .........................................Q......M...........    419
CACNA1F-H  ..............................Q........................M....    420
CACNA1F-R  ....................................L.......................    235

Consensus  ADGNLGSMAEEGRAGHRPQLAELTNRRRGRLRWFSHSTRSTHSTSSHASLPASDTGSMTE    480
CACNA1F-M  V....A.L............S......................................D    480
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CACNA1F-GP T...........................................................   479
CACNA1F-H  ..D.........................................................   480
CACNA1F-R  ...AS..VT...............S.................................A.   295

Consensus  TPGDEDEEEGALASCTRCLNKIMKTRVCRRFRRANRXLRARCRRAVKSNACYWAVLLLVF   540
CACNA1F-M  ..........TM..............I..H......G.......................   540
CACNA1F-GP ...E................................S...Y...................   539
CACNA1F-H  .Q............................L.....V.......................   540
CACNA1F-R  .A...........G...........K----------------------------------   321

Consensus  LNTLTIASEHHGQPVWLTQTQEYANKVLLCLFTVEMLLKLYGLGPSVYVSSFFNRFDCFV   600
CACNA1F-M  ..............L..................................A..........   600
CACNA1F-GP .....................GEPPSLSA-------------------------------   568
CACNA1F-H  ...................I..........................A.............   600
CACNA1F-R  ---------------------V......................................   360

Consensus  VCGGILETTLVEVGAMQPLGISVLRCVRLLRIFKVTRHWASLSNLVASLLNSMKSIASLL   660
CACNA1F-M  ............................................................   660
CACNA1F-GP -----------------------.SHSP..---P--------------------------   576
CACNA1F-H  ............................................................   660
CACNA1F-R  ............................................................   420

Consensus  LLLFLFIIIFSLLGMQLFGGKFNFDQTHTKRSTFDTFPQALLTVFQILTGEDWNVVMYDG   720
CACNA1F-M  ............................................................   720
CACNA1F-GP ------------------------------------L.PH.-------.-----------   582
CACNA1F-H  ............................................................   720
CACNA1F-R  ............................................................   480

Consensus  IMAYGGPFFPGMLVCVYFIILFICGNYILLNVFLAIAVDNLASGDAGTAKDKGREKSSEG   780
CACNA1F-M  ............................................................   780
CACNA1F-GP -------------------------------------------SRQSAPMSSY...GG..   599
CACNA1F-H  ...............I.....................................G...N.K   780
CACNA1F-R  ...........................................................S   540

Consensus  NLPQENGVLVPGGEKEEEEGARSEGAXM--EE---EEEEEEEEEEEEEEGGAGHVELLQE   835
CACNA1F-M  .P.K..K.......N.DAK.......APGM..EEE..............N..........   840
CACNA1F-GP .A........MP.V...--------------.---................V..T.....   642
CACNA1F-H  D.....EG....V.........R...D.--..---..............E...G......   835
CACNA1F-R  .....................K....G.--..---.....---..........R......   592

Consensus  VVPKEKVVPIPEGSAFFCLSQTNPLRKACHTLIHHHIFTNLILVFIILSSVSLAAEDPIR   895
CACNA1F-M  .......................................S....................   900
CACNA1F-GP ............................................................   702
CACNA1F-H  ...........................G........V.......................   895
CACNA1F-R  ............................................................   652

Consensus  AHSFRNHILGYFDYAFTSIFTVEILLKMTVFGAFLHRGSFCRSWFNLLDLLVVSVSLISF   955
CACNA1F-M  ............................................................   960
CACNA1F-GP ............................................................   762
CACNA1F-H  ..............................................M.............   955
CACNA1F-R  ............................................................   712

Consensus  GIHSSAISVVKILRVLRVLRPLRAINRAKGLKHVVQCVFVAIRTIGNIMIVTTLLQFMFA  1015
CACNA1F-M  ............................................................  1020
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CACNA1F-GP ............................................................   822
CACNA1F-H  ............................................................  1015
CACNA1F-R  ............................................................   772

Consensus  CIGVQLFKGKFYSCTDEAKHTPKECKGSFLXYPDGDVSRPLVRERLWVNSDFNFDNVLSA  1075
CACNA1F-M  .....................L..S.....I.............................  1080
CACNA1F-GP ..............................I.............................   882
CACNA1F-H  ............T.........Q.......V.............................  1075
CACNA1F-R  ..............................V.............................   832

Consensus  MMALFTVSTFEGWPALLYKAIDAHAEDEGPIYNYHVEISVFFIVYIIIIAFFMMNIFVGF  1135
CACNA1F-M  .......................N....................................  1140
CACNA1F-GP ............................................................   942
CACNA1F-H  .......................Y...H......R.........................  1135
CACNA1F-R  ............................................................   892

Consensus  VIITFRAQGEQEYQNCELDKNQRQCVEYALKAQPLRRYIPKNPHQYRVWATVNSAAFEYL  1195
CACNA1F-M  ......................................................R.....  1200
CACNA1F-GP ............................................................  1002
CACNA1F-H  ............................................................  1195
CACNA1F-R  ............................................................   952

Consensus  MFLLILLNTVALAMQHYEQTAPFNYAMDILNMVFTGLFTIEMVLKIIAFKPKHYFXDAWN  1255
CACNA1F-M  .......................................................A....  1260
CACNA1F-GP .......................................................A....  1062
CACNA1F-H  .......................................................T....  1255
CACNA1F-R  .......................................................T....  1012

Consensus  TFDALIVVGSXVDIAVTEVNNGGHLGESSEDSSRISITFFRLFRVMRLVKLLSKGEGIRT  1315
CACNA1F-M  ..........V....................T............................  1320
CACNA1F-GP ..........I.................................................  1122
CACNA1F-H  ..........I.................................................  1315
CACNA1F-R  ..........V.................................................  1072

Consensus  LLWTFIKSFQALPYVALLIAMIFFIYAVIGMQMFGKVALQDGTQINRNNNFQTFPQAVLL  1375
CACNA1F-M  ...................................L........................  1380
CACNA1F-GP ............................................................  1182
CACNA1F-H  ............................................................  1375
CACNA1F-R  ............................................................  1132

Consensus  LFRCATGEAWQEIMLASLPGNRCDPESDFGPGEEFTCGSNFAIAYFISFFMLCAFLIINL  1435
CACNA1F-M  .......................................S...V................  1440
CACNA1F-GP ............................................................  1242
CACNA1F-H  ............................................................  1435
CACNA1F-R  ....................S.......................................  1192

Consensus  FVAVIMDNFDYLTRDWSILGPHHLDEFKRIWSEYDPGAKGRIKHLDVVALLRRIQPPLGF  1495
CACNA1F-M  ............................................................  1500
CACNA1F-GP ............................................................  1302
CACNA1F-H  ............................................................  1495
CACNA1F-R  ............................................................  1252

Consensus  GKLCPHRVACKRLVAMNVPLNSDGTVTFNATLFALVRTSLKIKTEGNLEQANQELRMVIK  1555
CACNA1F-M  ................................................D...........  1560
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CACNA1F-GP ............................................................  1362
CACNA1F-H  .................M......................................I...  1555
CACNA1F-R  .....................A......................................  1312

Consensus  KIWKRIKQKLLDEVIPPPDEEEVTVGKFYATFLIQDYFRKFRRRKEKGLLGAEAPSSTSS  1615
CACNA1F-M  ...................................................R...T....  1620
CACNA1F-GP ............................................................  1422
CACNA1F-H  .....M.............................................ND.AP....  1615
CACNA1F-R  ..............L.-...........................................  1371

Consensus  XLQAGLRSLQDLGPEIRQALTCDTEEEEEE---EGQEEXEEEXEKDPETYKAPMDSQPSS  1672
CACNA1F-M  A....................YV.......EEAV...AE...A.NN..P..DSI....Q.  1680
CACNA1F-GP V......................S......---D.K..V.DKT..............S..  1479
CACNA1F-H  A..............M.............----....GV...D...L..N..T.V....A  1671
CACNA1F-R  V.............................---...A.E...P......H...V....P.  1428

Consensus  RRGSRISVSLPVGDRLPDSLSXGPSDDDXGAPNSRQPSVPQAGSHXHRRSSGVFMFTIPE  1732
CACNA1F-M  .WN.........KEK......T......GL.........I....QP..............  1740
CACNA1F-GP ..S........L...V...P.P....E.R.D..P.E.N...P...K..............  1539
CACNA1F-H  ....G................F......R.T.T.S.........NT...G..ALI.....  1731
CACNA1F-R  ...........T...P....TL......G....T....AS.....S...D..........  1488

Consensus  EGSXQXKGTXGQDKQDEXEEXPDRLSYLDEQAGTPPCXVLLPPHRPQRYVNGHHAPRRRL  1792
CACNA1F-M  ...I.L...Q...N.N.EQ.L..WTPD..RAGRDSFEPSPFTTSLV.QH....MS-TPTF  1799
CACNA1F-GP .E.DKH-----------MTLFLH..Y...........S......................  1588
CACNA1F-H  ..NS.P...K..N....D..V................S.......A...MD..LV.....  1791
CACNA1F-R  ...P.FQ..SR......Q..AA.Q..FV...T....HPL.P..Q................  1548

Consensus  LPPTPAGRKPSFTIQCLQRQGSCEDLPIPGTYHRGRNSGPSRAQGSWATPPQRGRLLYAP  1852
CACNA1F-M  AA.HACRSE..........L................T...........A...K.......  1859
CACNA1F-GP .....T.Q...........................QKL......................  1648
CACNA1F-H  ........................................N...................  1851
CACNA1F-R  ......A.....................................................  1608

Consensus  LLLVEEGAAGEGYLGKSSGPLRTFTCLHVPGTHSBPSHGKRGSADSLVEAVLISEGLGLF  1912
CACNA1F-M  ......STV.......LG.........Q...A.PN...R.....................  1919
CACNA1F-GP ..........K.......SA.H..A.........D..YS.....................  1708
CACNA1F-H  ...............R..................D.........................  1911
CACNA1F-R  ................A.R...............N.G.......................  1668

Consensus  ARDPRFVALAKQEIADACRLTLDEMDSAASDLLAQGTSSLYSDEESILSRFDXEDLGDEM  1972
CACNA1F-M  .Q................H................R.I..............E.......  1979
CACNA1F-GP ...............................................F.H..D.......  1768
CACNA1F-H  ..........................N.........................E.......  1971
CACNA1F-R  ....................................S.............L.D.......  1728

Consensus  ACVHAL                                                        1978
CACNA1F-M  ......                                                        1985
CACNA1F-GP ......                                                        1774
CACNA1F-H  ......                                                        1977
CACNA1F-R  ..I...                                                        1734
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**CACNA1G**
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Consensus    MDEEEDGAGAEESGQPRSFXRLNDLSGAGGRPGPGSAEKDPGSADSEAEGLPYPALAPVV    60
CACNA1G-M    ...................TQ..........Q....T.......................    60
CACNA1G-GP   -MD......T......Q.AL........................................    59
CACNA1G-R    ------------------------------------------------------------
CACNA1G-H    ...................M........................................    60

Consensus    FFYLSQDSRPRSWCLRTVCNPWFERISMLVILLNCVTLGMFRPCEDIACDSQRCRILQAF   120
CACNA1G-M    .........................V..................................   120
CACNA1G-GP   .........................................Q..................   119
CACNA1G-R    ---------------------------.................................    33
CACNA1G-H    ............................................................   120

Consensus    DDFIFAFFAVEMVVKMVALGIFGKKCYLGDTWNRLDFFIVIAGMLEYSLDLQNVSFSAVR   180
CACNA1G-M    ............................................................   180
CACNA1G-GP   ............................................................   179
CACNA1G-R    ............................................................    93
CACNA1G-H    ............................................................   180

Consensus    TVRVLRPLRAINRVPSMRILVTLLLDTLPMLGNVLLLCFFVFFIFGIVGVQLWAGLLRNR   240
CACNA1G-M    ............................................................   240
CACNA1G-GP   ............................................................   239
CACNA1G-R    ............................................................   153
CACNA1G-H    ............................................................   240

Consensus    CFLPENFSLPLSVDLEXYYQTENEDESPFICSQPRENGMRSCRSVPTLRGXGGGGPPCGL   300
CACNA1G-M    ................P.................................E.........   300
CACNA1G-GP   ................P.................................E.........   299
CACNA1G-R    ................R.................................D.........   213
CACNA1G-H    ................R.................................D.........   300

Consensus    DYEAYNSSSNTTCVNWNQYYTNCSAGEHNPFKGAINFDNIGYAWIAIFQVITLEGWVDIM   360
CACNA1G-M    ............................................................   360
CACNA1G-GP   ............................................................   359
CACNA1G-R    ............................................................   273
CACNA1G-H    ............................................................   360

Consensus    YFVMDAHSFYNFIYFILLIIVGSFFMINLCLVVIATQFSETKQRESQLMREQRVRFLSNA   420
CACNA1G-M    ............................................................   420
CACNA1G-GP   .............................................N..............   419
CACNA1G-R    ............................................................   333
CACNA1G-H    ............................................................   420

Consensus    STLASFSEPGSCYEELLKYLVYILRKAARRLAQVSRAXGVRAGLLSSPXXLGGQEPQPSS   480
CACNA1G-M    .....................................V..........VAR........G   480
CACNA1G-GP   ................................RL...A..........VA..........   479
CACNA1G-R    .....................................V..........AP..S....A..   393
CACNA1G-H    .....................................A...V......AP.....T....   480

Consensus    SCSRSHRRLSVHHLVH-HHHHHHHHYHLGNGTLRAPRASPEIQDRDANGSRRLMLPPPST   539
CACNA1G-M    ................-.................V................W........   539
CACNA1G-GP   ....AR.H........H.........................R.K...............   539
CACNA1G-R    ................-.......................................A...   452
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CACNA1G-H     ................-...........................................   539

Consensus     PTLSGXP-PGGAESVHSFYHADCHLEPVRCQAPPPRSPSEASGRTVGSGKVYPTVHTSPP   598
CACNA1G-M     ..P..G.-.R..................................................   598
CACNA1G-GP    ...ARA.-..................................A.................   598
CACNA1G-R     .....G.A....................................................   512
CACNA1G-H     .A...A.-....................................................   598

Consensus     PEMLKEKALVEVAPSSGPPTLTSLNIPPGPYSSMHKLLETQSTGXCXSSCKISSPCXKAD   658
CACNA1G-M     .....D.........P.......F......F.............A.H.........S...   658
CACNA1G-GP    ............G.....L..P......................T.HG...F....S...   658
CACNA1G-R     ............................................T.Q.........L...   572
CACNA1G-H     ..T..........A..............................A.Q.........L...   658

Consensus     SGACGPDSCPYCARAGAGEVELADREMPDSDSEAVYEFTQDAQHSDLRDPHSRRXRSLGP   718
CACNA1G-M     ..............T....P.S..H..........................R..RP....   718
CACNA1G-GP    .............QP.T..L.PG.Q.............................Q.T..V   718
CACNA1G-R     R...............S........................V.Q.......G..R..Q.C   632
CACNA1G-H     ......................................................Q.....   718

Consensus     DAEPSXVLAFWRLICDTFRKIVDSKYFGRGIMIAILVNTLSMGIEYHEQPEELTNALEIS   778
CACNA1G-M     .....S......................................................   778
CACNA1G-GP    .....P......................................................   778
CACNA1G-R     .....P......................................................   692
CACNA1G-H     .....S......................................................   778

Consensus     NIVFTSLFALEMLLKLLVYGPFGYIKNPYNIFDGVIVVISVWEIVGQQGGGLSVLRTFRL   838
CACNA1G-M     ............................................................   838
CACNA1G-GP    ............................................................   838
CACNA1G-R     ............................................................   752
CACNA1G-H     ............................................................   838

Consensus     MRVLKLVRFLPALQRQLVVLMKTMDNVATFCMLLMLFIFIFSILGMHLFGCKFASERDGD   898
CACNA1G-M     ............................................................   898
CACNA1G-GP    ............................................................   898
CACNA1G-R     ............................................................   812
CACNA1G-H     ............................................................   898

Consensus     TLPDRKNFDSLLWAIVTVFQILTQEDWNKVLYNGMASTSSWAALYFIALMTFGNYVLFNL   958
CACNA1G-M     ............................................................   958
CACNA1G-GP    ............................................................   958
CACNA1G-R     ............................................................   872
CACNA1G-H     ............................................................   958

Consensus     LVAILVEGFQAEEISKREDXSGQLSCIQLPVBSQGGDATKSESEPDFFSPSXDGDGDRKK  1018
CACNA1G-M     ..............G....T...........N...................V........  1018
CACNA1G-GP    ...................A...........D..............C....V...R.G..  1018
CACNA1G-R     ...................T...........N...................L........   932
CACNA1G-H     ...................A...........D......N............L........  1018

Consensus     RLALVSLGEHPELRKSLLPPLIIHTAATPMSLPKSSSTGLGEALGXGSRRTSSSGSAEPG  1078
CACNA1G-M     .....A....S............................V.....S..............  1078
CACNA1G-GP    .......AQ.................................VP.S..C...........  1078
CACNA1G-R     H..................................N.........PS.............   992
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CACNA1G-H    C..................................T.........PA.............  1078

Consensus    AA-HEMKSPPSARSSPHSPWSAASSWTSRRSSRNSLGRAPSLKRRSPSGERRSLLSGEGX  1137
CACNA1G-M    T.H........................................................Q  1138
CACNA1G-GP   ..-........T...............................................R  1137
CACNA1G-R    V.-........................................................R  1051
CACNA1G-H    ..-........................................................Q  1137

Consensus    ESQDEEESSEEERASPAGSDHRHRGSLEREAKSSFDLPDTLQVPGLHRTASGRSSASEHQ  1197
CACNA1G-M    ...........D................................................  1198
CACNA1G-GP   .....D.......T........P............................S........  1197
CACNA1G-R    ......-.............R.......................................  1110
CACNA1G-H    .....................................................G......  1197

Consensus    DCNGKSASGRLARALRPDDPPLDGDDGDDEGNLSKGERIRAWXRARLPACCRERDSWSAY  1257
CACNA1G-M    .............T..A.....................L...V.................  1258
CACNA1G-GP   ..........................--..............I.................  1255
CACNA1G-R    ..........................................V............A....  1170
CACNA1G-H    ..........................A...........V...I........L........  1257

Consensus    IFPPQSRFRLLCHRIITHKMFDHVVLVIIFLNCITIAMERPKIDPHSAERIFLTLSNYIF  1317
CACNA1G-M    ............................................................  1318
CACNA1G-GP   ............................................................  1315
CACNA1G-R    ............................................................  1230
CACNA1G-H    ............................................................  1317

Consensus    TAVFLAEMTVKVVALGWCFGEQAYLRSSWNVLDGLLVLISVIDILVSMVSDSGTKILGML  1377
CACNA1G-M    ............................................................  1378
CACNA1G-GP   ............................................................  1375
CACNA1G-R    ............................................................  1290
CACNA1G-H    ............................................................  1377

Consensus    RVLRLLRTLRPLRVISRAQGLKLVVETLMSSLKPIGNIVVICCAFFIIFGILGVQLFKGK  1437
CACNA1G-M    ............................................................  1438
CACNA1G-GP   ............................................................  1435
CACNA1G-R    ............................................................  1350
CACNA1G-H    ............................................................  1437

Consensus    FFVCQGEDTRNITNKSDCAEASYRWVRHKYNFDNLGQALMSLFVLASKDGWVDIMYDGLD  1497
CACNA1G-M    ............................................................  1498
CACNA1G-GP   ............................................................  1495
CACNA1G-R    ............................................................  1410
CACNA1G-H    ............................................................  1497

Consensus    AVGVDQQPIMNHNPWMLLYFISFLLIVAFFVLNMFVGVVVENFHKCRQHQEEEEARRREE  1557
CACNA1G-M    ............................................................  1558
CACNA1G-GP   ............................................................  1555
CACNA1G-R    ............................................................  1470
CACNA1G-H    ............................................................  1557

Consensus    KRLRRLEKKRRXXXXXXXBLMLDDVIASGSSASAASEAQCKPYYSDYSRFRLLVHHLCTS  1617
CACNA1G-M    ...K.......SKEKQMAD.........................................  1618
CACNA1G-GP   ...........SKEKQMAD.........................................  1615
CACNA1G-R    ...........-------N.........................................  1523
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CACNA1G-H      ...........-------N.........................................  1610

Consensus      HYLDLFITGVIGLNVVTMAMEHYQQPQILDEALKICNYIFTVIFVLESVFKLVAFGFRRF  1677
CACNA1G-M      ............................................................  1678
CACNA1G-GP     ............................................................  1675
CACNA1G-R      ............................................................  1583
CACNA1G-H      ............................................................  1670

Consensus      FQDRWNQLDLAIVLLSIMGITLEEIEVNASLPINPTIIRIMRVLRIARVLKLLKMAVGMR  1737
CACNA1G-M      ............................................................  1738
CACNA1G-GP     ............................................................  1735
CACNA1G-R      ............................................................  1643
CACNA1G-H      ............................................................  1730

Consensus      ALLDTVMQALPQVGNLGLLFMLLFFIFAALGVELFGDLECDETHPCEGLGRHATFRNFGM  1797
CACNA1G-M      ............................................................  1798
CACNA1G-GP     ....................V.......................................  1795
CACNA1G-R      ............................................................  1703
CACNA1G-H      ............................................................  1790

Consensus      AFLTLFRVSTGDNWNGIMKDTLRDCDQESTCYNTVISPIYFVSFVLTAQFVLVNVVIAVL  1857
CACNA1G-M      ............................................................  1858
CACNA1G-GP     ............................................................  1855
CACNA1G-R      ............................................................  1763
CACNA1G-H      ............................................................  1850

Consensus      MKHLEESNKEAKEEAELEAELELEMKTLSPQPHSPLGSPFLWPGVEGPDSPDSPKPGAPH  1917
CACNA1G-M      ...............................................VN...........  1918
CACNA1G-GP     .............................................Q.........SR..Y  1915
CACNA1G-R      ........................L.......R...........A........S.....Q  1823
CACNA1G-H      ..........................................................L.  1910

Consensus      PAAHXRAAS-XFSLEHPTDRQLFDTISLLIQGSLDGELKLMDELAGPGG-QPSAFPSAPS  1975
CACNA1G-M      TT..IG...SG.....--------------------------------------------  1934
CACNA1G-GP     K.--------AH.......G.............................S..A......G  1967
CACNA1G-R      ....T....-R..............................E.......-..........  1881
CACNA1G-H      ....A.S..-H.......................EW.............-..........  1968

Consensus      PGGSDPQIPLAEMEALSLTSEIVSEPSCSLALTDDSLPDDXHTLLLSALESNMEPHPEEX  2035
CACNA1G-M      --------------------------------------------------PT.V..T..G  1944
CACNA1G-GP     ........................................T...S......G....L..A  2027
CACNA1G-R      ....E...A......M......L.D..............EP.........R........V  1941
CACNA1G-H      L.......................................M............Q...T.L  2028

Consensus      PXALGPDLLTVRKSGVSRTHSLPNDSYMCRDGSTAEGSLGHRGWGLPKAQSGSXLSVHSQ  2095
CACNA1G-M      .VP...........................N.....R................I......  2004
CACNA1G-GP     .G...........T.................R........R.S..........I......  2087
CACNA1G-R      .A...........A..........................P............V......  2001
CACNA1G-H      .---..........................H......P...............V......  2085

Consensus      PADTSYILQLPKDAPHLLQPHSAPTWGTIPKLPPPGRSPLAQRPLRRQAAIRTDSLDVQG  2155
CACNA1G-M      .....C........HY.....G.....A................................  2064
CACNA1G-GP     .......P.....V..M.....I.....................................  2147
CACNA1G-R      ......N........N............................................  2061
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CACNA1G-H    ............................................................  2145

Consensus    LGSREDLLSEVSGPSPPLARSSSFWGXSSIQXQQHXRSQSKXSKHXTXPAPCPGPEPSWS  2215
CACNA1G-M    ...............C..T.......G....V..RSG....V...IRL......L....A  2124
CACNA1G-GP   ...Q........R.............H....V...F.NL..V...I.P....L....HQ.  2207
CACNA1G-R    ..........AR..............RP..RAR..F.....I...MALS.L.......R.  2121
CACNA1G-H    ........A...........AY....Q..T.A...S..H..I...M.P.........N.G  2205

Consensus    KGPPETRSSLELDTELSWXSGDLLXXGSQEEPPSPRDLKKCYSVEAQSCRRRPXSWLDEQ  2275
CACNA1G-M    .D.Q..............I.....P-S.....L....................G......  2183
CACNA1G-GP   E.................V...A.AI......T....................S......  2267
CACNA1G-R    .........F........V.....AL....A.................G....V......  2181
CACNA1G-H    ..................I.....PP.G.....................Q...T......  2265

Consensus    RRHSIAVSCLDSGSQPRLGPDPSSLGGQPLGGPGSRPKKKLSPPSISIDPPESQGPRPPP  2335
CACNA1G-M    ..................C.S......................................C  2243
CACNA1G-GP   .......................................................S....  2327
CACNA1G-R    ...........G..---------..A.............................A...A  2232
CACNA1G-H    ................H..T...N......................T..........T..  2325

Consensus    SPGXCLRRRAPSSDSKDPXASGPPDSMAASPSPKKDVLSLSGLSSDPADLDP          2387
CACNA1G-M    ...V.......A......S..S.L..T.........A..........T....          2295
CACNA1G-GP   ...V..............L.L...........L............EQ.....          2379
CACNA1G-R    ...I..........A...S....S............................          2284
CACNA1G-H    ...I..............L.................................          2377


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**CACNA1H**
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Consensus  MTEGAXAADEVRVPLGAPPSGPAAXVXASPXSPGAPGREAERGSXLSVSPPESPAAERGA    60
CACNA1H-H  .....R.............P....L.G...E.............E.G...S.........    60
CACNA1H-M  ....TL...........S..A...P.R...A...V....EQ...GS..LA....GT.C..    60
CACNA1H-GP ...D.P...............L..G--T.SS......SS.....R..A...........V    58

Consensus  XLGADEEQPVPYPALAATVFFCLGQTTRPRSWCLRLVCXPWFEHVSMLVIMLNCVTLGMF   120
CACNA1H-H  E.......R.............................N.....................   120
CACNA1H-M  D....................................SRR....I...............   120
CACNA1H-GP V...G.................................S.....................   118

Consensus  RPCEDVECRSERCSILEAFDDFIFAFFAVEMVIKMVALGLFGQKCYLGDTWNRLDFFIVM   180
CACNA1H-H  ........G....N......A......................................V   180
CACNA1H-M  ............................................................   180
CACNA1H-GP ......A.....................................................   178

Consensus  AGMMEYSLDGHNVSLSAIRTVRVLRPLRAINRVPSMRILVTLLLDTLPMLGNVLLLCFFV   240
CACNA1H-H  ............................................................   240
CACNA1H-M  ............................................................   240
CACNA1H-GP ............................................................   238

Consensus  FFIFGIVGVQLWAGLLRNRCFLDSAFVRNNNLTFLRPYYQTEEGEENPFICSSRRDNGMQ   300
CACNA1H-H  ............................................................   300
CACNA1H-M  ............................................................   300
CACNA1H-GP ........................T...............P...................   298
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Consensus   KCSHIPSRRELRMQCTLGWEAYGQPQAEXXGAGRNACINWNQYYNVCRSGDSNPHNGAIN   360
CACNA1H-H   ......G......P........T.....GV..A...........................   360
CACNA1H-M   ............V...............DG....................EF........   360
CACNA1H-GP  ........................SPT.AA.I...G.......................S   358

Consensus   FDNIGYAWIAIFQVITLEGWVDIMYYVMDAHSFYNFIYFILLIIVGSFFMINLCLVVIAT   420
CACNA1H-H   ............................................................   420
CACNA1H-M   ............................................................   420
CACNA1H-GP  ............................................................   418

Consensus   QFSETKQRENQLMREQRARYLSNDSTLASFSEPGSCYEELLKYVGHIFRKVKRRSLRLYA   480
CACNA1H-H   .........S.........H........................................   480
CACNA1H-M   ............................................................   480
CACNA1H-GP  ...........................................M..V.............   478

Consensus   RWQSRWRKKVDPSATLHGQGPGXRQRRAGRRTASVHHLVYHHHHHHHHHYHFSHGGPRRP   540
CACNA1H-H   ..............-VQ.....H.......H........................S....   539
CACNA1H-M   .............S.......RR.P...................................   540
CACNA1H-GP  ......H..A............Q...Q....AT...........................   538

Consensus   XPEPGAXDTRLVRAGXPPSPPSPGXGPPDSESVHSIYHADCHVEGPQERARVAHAAAT-A   599
CACNA1H-H   G.....C........A........R....A............I...............A.   599
CACNA1H-M   S.....G.......CV........H.............................TI..-.   599
CACNA1H-GP  N.D.--S.....P..M.SC.....Q...N............................--T   594

Consensus   ASLKLASGLGTMNYPTILPSGXGNSKGSTSSRPKGKRXAGXPGATGHSPLSLGSPDPYEK   659
CACNA1H-H   ...R..T..............V.SG.....PG....WAG.P..TG..G....N.......   659
CACNA1H-M   .....................AV............L.S..T....A.........S....   659
CACNA1H-GP  .........S...........M....S--........N..NA..................   652

Consensus   IQHVVGEHGLGRAPSHLSGLSVPCPLPSPPAGTLTCELKSCPYCAXALEDPEFEFSGSES   719
CACNA1H-H   .P.........Q..G.............................TR......G.L.....   719
CACNA1H-M   .......Q.....S...............Q...............S..............   719
CACNA1H-GP  ...A................N...S...........A........N..............   712

Consensus   GDSDXHGVYEFTQDVRHGDCRDPXQXPXAXDTPGXGX---XRRXQXXAAXGEPGGLGRLW   776
CACNA1H-H   ....GR.............RW..TRP.R.T....P.PGSPQ..A.QR..P....WM....   779
CACNA1H-M   ....A..................V.Q.HEGG...H.N---E.WRPPLRTASQ........   776
CACNA1H-GP  ....V...........RD....SM.L.S.A.M.SQ.S---V..S.GQ..S.......H..   769

Consensus   ASFSGKLRRIVDSKYFNRGIMXAILVNTLSMGVEYHEQPDELTNALEISNIVFTSMFALE   836
CACNA1H-H   VT..............S....M.................E....................   839
CACNA1H-M   ....S................A......................................   836
CACNA1H-GP  .....................V......................................   829

Consensus   MLLKLLACGPLGYIRNPYNIFDGIIVVISVWEIVGQADGGLSVLRTFRLLRVLKLVRFLP   896
CACNA1H-H   ............................................................   899
CACNA1H-M   ........................V.I.................................   896
CACNA1H-GP  ............................................................   889

Consensus   ALRRQLVVLMKTMDNVATFCMLLMLFIFIFSILGMHLFGCKFSLKTDTGDTVPDRKNFDS   956
CACNA1H-H   .........V..........T.......................................   959
CACNA1H-M   ..........R....................................S............   956
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CACNA1H-GP ............................................................   949

Consensus  LLWAIVTVFQILTQEDWNVVLYNGMASTSSWAALYFVALMTFGNYVLFNLLVAILVEGFQ  1016
CACNA1H-H  ............................................................  1019
CACNA1H-M  ............................................................  1016
CACNA1H-GP ............................................................  1009

Consensus  AEGDANRSDTDEDKTSTHFEEDFDKLRDLQATEMKMYSLAVTPNGHLEGRGSLPPPLIMH  1076
CACNA1H-H  ................V......H...E..T..L..C................S.....C  1079
CACNA1H-M  .....T............L.........V.............................T.  1076
CACNA1H-GP .................R..........................................  1069

Consensus  TAATPMPTPKSSPHLDAAHXLLDSRRSSSGSXDPQLGDQKSLASLRSSPCAPWGPNSAWS  1136
CACNA1H-H  .............F....PS.P....G..S.G..P.....PP.............SG...  1139
CACNA1H-M  ................M..T...........V..........................G.  1136
CACNA1H-GP .........RN........G...........M..................TH........  1129

Consensus  SRRSSWNSLGRAPSLKRRSQCGERESLLSGEGKGSTDDEAEDSRXX-------XPGPRAT  1189
CACNA1H-H  ......S...........G.......................G.A--------A......  1191
CACNA1H-M  ............................................PNSGTHPGAS......  1196
CACNA1H-GP ............................................LG----------MVTR  1179

Consensus  PLRRAESLDHXSTXDLXPPRPATLLPTKXRDCXGQXVALPSEFFLRIDSHREDAAEFDDD  1249
CACNA1H-H  .........P------R.L...A.P...C..RD..V.....D..............L...  1245
CACNA1H-M  ........G.R..M..C...........F...N..M..............K.........  1256
CACNA1H-GP ..........H..L..QS..L..V..A.LH..P..S....N...........E..D....  1239

Consensus  XEDSCCFRLHKVLEPYXPQWCRSRESWALYLFSPQNRLRVSCQKVIAHKMFDHVVLVFIF  1309
CACNA1H-H  S.....L.........K........A...........F........T.............  1305
CACNA1H-M  I...............A....S..........P...........................  1316
CACNA1H-GP V...............T.....N................AF...............L...  1299

Consensus  LNCITIALERPDIDPGSTERAFLSVSNYIFTAIFVAEMMVKVVALGLLWGEHAYLQSSWN  1369
CACNA1H-H  ...V................V...........................S...........  1365
CACNA1H-M  ...................................V........................  1376
CACNA1H-GP ...............N...................................R........  1359

Consensus  VLDGLLVLVSLVDIIVAMASAGGAKILGVLRVLRLLRTLRPLRVISRAPGLKLVVETLIS  1429
CACNA1H-H  L.............V.............................................  1425
CACNA1H-M  .................V..........................................  1436
CACNA1H-GP ............................I...............................  1419

Consensus  SLRPIGNIVLICCAFFIIFGILGVQLFKGKFYYCEGXDTRNISTKAECRAAHYRWVRRKY  1489
CACNA1H-H  ....................................P.........Q.............  1485
CACNA1H-M  ....................................T.....T.....H...........  1496
CACNA1H-GP ................................F...A.......................  1479

Consensus  NFDNLGQALMSLFVLSSKDGWVNIMYDGLDAVGIDQQPVQNHNPWMLLYFISFLLIVSFF  1549
CACNA1H-H  .................................V..........................  1545
CACNA1H-M  ............................................................  1556
CACNA1H-GP ............................................................  1539

Consensus  VLNMFVGVVVENFHKCRQHQEAEEARRREEKRLRRLERRRRSTFPXPEAQRRPYYADYSH  1609
CACNA1H-H  .............................................S.............P  1605
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CACNA1H-M   .............................................N..............  1616
CACNA1H-GP  ...................................M.KK..------K............  1593

Consensus   TRRSIHSLCTSHYLDLFITFIICLNVITMSMEHYNQPKSLDEALKYCNYVFTIVFVFEAA  1669
CACNA1H-H   .......................V....................................  1665
CACNA1H-M   ............................................................  1676
CACNA1H-GP  ......T...............G.....................................  1653

Consensus   LKLVAFGFRRFFKDRWNQLDLAIVLLSIMGIALEEIEMNAALPINPTIIRIMRVLRIARV  1729
CACNA1H-H   ...........................L...T......S.....................  1725
CACNA1H-M   ............................................................  1736
CACNA1H-GP  ............................................................  1713

Consensus   LKLLKMATGMRALLDTVVQALPQVGNLGLLFMLLFFIYAALGVELFGRLECSEDNPCEGL  1789
CACNA1H-H   ............................................................  1785
CACNA1H-M   ............................................................  1796
CACNA1H-GP  ............................................................  1773

Consensus   SRHATFSNFGMAFLTLFRVSTGDNWNGIMKDTLRECTREDKHCLSYLPALSPVYFVTFVL  1849
CACNA1H-H   ....................................S.......................  1845
CACNA1H-M   ......T.....................................................  1856
CACNA1H-GP  ....................................................I.......  1833

Consensus   VAQFVLVNVVVAVLMKHLEESNKEAREDAEMDAEIELEXAQGXXAXP------PPXAQES  1903
CACNA1H-H   ..............................L.......M...PGSARRVDADR..LP...  1905
CACNA1H-M   ......................................I...ST.Q.------.ST....  1910
CACNA1H-GP  ..................................V..QL..EAP.H.------L.R.PN.  1887

Consensus   PGXXPDTPNXLVXRKVSVSRMLSLPNDSYMFRPVAPAXAPHXHPLQEVEMETYXX-----  1958
CACNA1H-H   ..A-R.A-PN..A.....................V..S...PR..........GAGTPLG  1963
CACNA1H-M   Q.TE.....L..V........................A...S...........TG-----  1965
CACNA1H-GP  ..CG.....P-.I............S...........T..--...........SS-----  1939

Consensus   XVTSAHSPPLEPCASLQVPXAXSSPARXSDPLCALSPRGTPRSPSLSRLLCRQEAXHTES  2018
CACNA1H-H   S.A.V....A.S.....I.L.V.....SGE..H.......A..............V..D.  2023
CACNA1H-M   P.......S...RT.F...S.A.....V..........D....L....I......M.A..  2025
CACNA1H-GP  TA.................P.M....KG...Q..PP.Q.A......G........L....  1999

Consensus   LEGQIDXPXEXSXPDXTEPXEKTPVRQAXLGXSLXSPPRSPRPASVRTRKHTFGQRCISS  2078
CACNA1H-H   ...K..S.RDTLD--PA..G......PVTQ.G..Q......................V..  2081
CACNA1H-M   ......DAG.D.I..Y...A.NISMS..P..-T.R...C................H....  2084
CACNA1H-GP  ....V.N.-.N.G..S.G.V........S..A..K......W....H.............  2058

Consensus   RPXAXGGDEAEAADPADEEVSHITSSAHPWPA-TEPHSPEASPXASPAXXXVGSXRDLHR  2137
CACNA1H-H   ..A.P..E....S..............C..QPTA...G.....V.-------.GE...R.  2134
CACNA1H-M   ..PTL...D.......................-..........T....KGT...G..P..  2143
CACNA1H-GP  .LL.S...............R...........-..........M....ARG...R.....  2117

Consensus   LCSVDAQGFLDKPGRADXQRWPSVELXXGDGHLEPGEVKARXPELEPALGARRKKKMSPP  2197
CACNA1H-H   .Y...............E.WR..A..GS.----....A..WG..A...............  2190
CACNA1H-M   F......S.......P.A...S....DN......S...R..AS.................  2203
CACNA1H-GP  ...L.......M.....T........SG.......E...T.V..................  2177

Consensus   CISVEPPAEDEGSXRPPAAEGGXTTLRRRTPSCEAAPHRDCLEPTEGXGTGGDPAAKGER  2257
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CACNA1H-H  .............A..S.....S............T....S......S.A..........  2250
CACNA1H-M  ...ID..T.....S........N.............L....P.S...P......V.....  2263
CACNA1H-GP .............T...V...S-S..............K.....M.--..........D.  2234

Consensus  WGQASCRAEHLTVPSFAFEPLDMGGPSGDPFLDSSQSVTPEPRVSSSGAIVPLXPXETEL  2317
CACNA1H-H  ......................L.V........G.H.....S.A.........E.P.S.P  2310
CACNA1H-M  ..............N...........G..C....D...........L......I-L....  2322
CACNA1H-GP ...GP................N.....EI........I...........T...D.H....  2294

Consensus  SMPXGDPPEKXRGLYLTVPQTPLKKPGSPPATPAPGDXADEPV                    2360
CACNA1H-H  P..V......R.........C..E.....S......GG..D..                    2353
CACNA1H-M  ...S......EQ.......................D.SG....                    2365
CACNA1H-GP .VSTV....RG.....M....SM..L...........T.E..M                    2337


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**Casq2**
-------------------------------------------------------------------------------
Consensus MKQMKRTHLXVVGVYLLSSCRAEEGLNFPTYDGKDRVVSLSEKNFKQILKKYDLLCLYYH   60
CASQ2-M   ---...IY.LM.......LSG.......................L..M..R.........   57
CASQ2-GP  .........L.L.................I..............................   60
CASQ2-R   ---...A..F..................................................   57
CASQ2-H   ---......FI..I.F...............................V............   57

Consensus EPVSSDKVAQKQFQLKEIVLELVAQVLEHKXIGFVMVDAKKEAKLAKKLGFDEEGSLYIL  120
CASQ2-M   ........S.....................N.......SR.......R...S......V.  117
CASQ2-GP  ..............................D....................A........  120
CASQ2-R   A...A.........................E.............................  117
CASQ2-H   ........T.....................A.............................  117

Consensus KGDRTIEFDGEFAADVLVEFLLDLIEDPVEIINSKLEVQAFERIEDQIKLJGFFKSEDSE  180
CASQ2-M   ...............................V.N.............T..L...N....  177
CASQ2-GP  ..................................................L.Y.......  180
CASQ2-R   ..............................................H...I.....A...  177
CASQ2-H   ................................S.............Y...I.........  177

Consensus YYKAFEEAAEHFQPYIKFFATFDKGVAKKLSLKMNEVDFYEPFMDEPTAIPNKPYTEEEL  240
CASQ2-M   .....Q..................A............G.........NV...........  237
CASQ2-GP  H............................F...I.....................S....  240
CASQ2-R   ................................................P...........  237
CASQ2-H   ...............................................I............  237

Consensus VEFVKEHQRPTLRRLRPEDMFETWEDDLNGIHIVAFAEKSDPDGYEFLEILKQVARDNTD  300
CASQ2-M   ............................................................  297
CASQ2-GP  .................Q....................R....................N  300
CASQ2-R   ..................................P.........................  297
CASQ2-H   ..................E.........................................  297

Consensus NPDLSIXWIDPDDFPLLVAYWEKTFKIDLFKPQIGVVNVTDADSVWMEIPDDDDLPTAEE  360
CASQ2-M   ......L.....................................I...............  357
CASQ2-GP  ......V..........................................S..........  360
CASQ2-R   ......V.....................................................  357
CASQ2-H   ......L.......................R.............................  357
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Consensus LEDWIEDVLSGKINTEDDDNEDEDDDDDBDDDDXX------SDEEDNXDSDDDDDEDE    412
CASQ2-M   ..........................G.DN...DDDDDDNDNSD...E.......D..    415
CASQ2-GP  ............................N...N---------.....E.T......--    408
CASQ2-R   ............................N....DDN---GN......D...E..E---    409
CASQ2-H   ...................ED.D..NSD---------------....D........--    399


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**FKBP1A**
------------------------------------------------------------------------------
Consensus MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKFDSSRDRNKPFKFMLGKQEVIRGW   60
FKBP1A-M  .................................................T..........   60
FKBP1A-GP ............................................................   60
FKBP1A-H  ............................................................   60
FKBP1A-R  ............................................................   60

Consensus EEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE            108
FKBP1A-M  ...............I..S.............................            108
FKBP1A-GP .........................K......................            108
FKBP1A-H  ................................................            108
FKBP1A-R  ................................................            108


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**HCN2**
------------------------------------------------------------------------------
Consensus  MYMDARGGGGRPGXSPGATPAPGPPPPPPPPXPPQPQPPPXPPPNPXXXX--XXP-----   53
HCN2-GP    ..H..WPRP.A--P..K.H.WA.LA......PG.H.H.--HLGG..AATH----------   46
HCN2-M     --...........D...T.............A........A.....------TT.-----   47
HCN2-H     --...........E................A-...Q....P...A.PPGPGPAP.QHPPR   57

Consensus  ---XXPEXADEXGPRXRLXSRDSXCXXX-------XAKGXXNGECGRGEPQCSPXXXEGP  103
HCN2-GP    -------------------------------------------Q.ETP---QL.LSVHR.   60
HCN2-M     ---SH..S...P...A..C....A.TPG-------A...GA.............---...   94
HCN2-H     AEALP..A...G...G..R....S.GRPGTPGAAST...SP.............AGP...  117

Consensus  ARGPKVSFSCRGAASGP----XXAEEAGSEEAGPAGEPRGSQASFXQRQFGALLQPGVNK  159
HCN2-GP    .H.D----------------------------------K..-------------------   67
HCN2-M     .................----SA......................L..............  150
HCN2-H     .................APGPGP......................M..............  177

Consensus  FSLRMFGSQKAVEREQERVKSAGAWIIHPYSDFRFYWDFTMLLFMVGNLIIIPVGITFFK  219
HCN2-GP    -RCGCSAARRQ.................................................  126
HCN2-M     ............................................................  210
HCN2-H     ............................................................  237

Consensus  DETTAPWIVFNVVSDTFFLMDLVLNFRTGIVIEDNTEIILDPEKIKKKYLRTWFVVDFVS  279
HCN2-GP    ...................................................S........  186
HCN2-M     ............................................................  270
HCN2-H     ............................................................  297

Consensus  SIPVDYIFLIVEKGIDSEVYKTARALRIVRFTKILSLLRLLRLSRLIRYIHQWEEIFHMT  339
HCN2-GP    ............................................................  246
HCN2-M     ............................................................  330
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HCN2-H      ............................................................  357

Consensus   YDLASAVMRICNLISMMLLLCHWDGCLQFLVPMLQDFPSNCWVSINNMVNHSWSELYSFA  399
HCN2-GP     ............................................................  306
HCN2-M      .......................................D....................  390
HCN2-H      ......................................R.......G.............  417

Consensus   LFKAMSHMLCIGYGRQAPESMTDIWLTMLSMIVGATCYAMFIGHATALIQSLDSSRRQYQ  459
HCN2-GP     ............................................................  366
HCN2-M      ............................................................  450
HCN2-H      ............................................................  477

Consensus   EKYKQVEQYMSFHKLPADFRQKIHDYYEHRYQGKMFDEDSILGELNGPLREEIVNFNCRK  519
HCN2-GP     ............................................................  426
HCN2-M      ............................................................  510
HCN2-H      ............................................................  537

Consensus   LVASMPLFANADPNFVTAMLTKLKFEVFQPGDYIIREGTIGKKMYFIQHGVVSVLTKGNK  579
HCN2-GP     .......................................V....................  486
HCN2-M      ............................................................  570
HCN2-H      ............................................................  597

Consensus   EMKLSDGSYFGEICLLTRGRRTASVRADTYCRLYSLSVDNFNEVLEEYPMMRRAFETVAI  639
HCN2-GP     ............................................................  546
HCN2-M      ............................................................  630
HCN2-H      ............................................................  657

Consensus   DRLDRIGKKNSILLHKVQHDLSSGVFNNQENAIIQEIVKYDREMVQQAELGQRVGLFPPP  699
HCN2-GP     ...........................................................Q  606
HCN2-M      ............................................................  690
HCN2-H      .....................N......................................  717

Consensus   P-PPQVTSAIATLQQAVAMSFCPQVARPLVGPLALGSPRLVRRXPPGPXPPAASPGPPXX  758
HCN2-GP     .-.........................................Q.R.RF..QPWAP.VGG  665
HCN2-M      .-.........................................A....L.........-A  748
HCN2-H      .P..............A..........................P....A.A.......PP  777

Consensus   ASPPAAP-----SSPRAPRTSPYGXPGXPAXX------XGP----------ALPARRLSR  797
HCN2-GP     -.A..P.RGAPA.HS.G.SP..SPS..P..SPGCEHSSR.GHCHSHVTRWSPI.TCP...  724
HCN2-M      .......-----............V..S..TR------V..----------.........  787
HCN2-H      ....G..-----A...........GLP-A.PL------A..----------.........  815

Consensus   ASRPLSASQPSLPHGXPXPXPAASARPASSSTPRLG---PX-PXARTAAPSPDRRDSASP  853
HCN2-GP     .NYQ-.SG.VRT.NAW.Q.HGSEV....DMAA..EQFLA.GS.R.P..SSP.A.PQF.H.  783
HCN2-M      ...............V.A.S................---.A-.T................  843
HCN2-H      ...............A.G--....T...........---.T-.A..A.............  869

Consensus   GAAXGLDPXDSARSRLSSNL                                          873
HCN2-GP     --------------------                                          783
HCN2-M      ...S....L...........                                          863
HCN2-H      ...G....Q...........                                          889


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**HCN4**
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Consensus    MDKLPPSMRKRLYSLPQQVGAKAWIMDEEEDAEEEGAGGRQDPXRRSIRLRPLPSPSPSA    60
HCN4-GP      .................................D..S......R................    60
HCN4-M       ...............................G...........S...............V    60
HCN4-R       ...........................................R...............P    60
HCN4-H       ...........................................S................    60

Consensus    AAG-----GXESRGAALGAAX-SEGPARSAGKS------STNGDCRRFRGSLASLGSRGG   108
HCN4-GP      ..X--------P...T..PSG-AG.T...VTI.SAGQIPTRTATAGA.............   111
HCN4-M       ...-----CS.........TE-....G......------.....................   108
HCN4-R       S.AAAAAG.A........G.ADG.....------GAAKS.....................   114
HCN4-H       ...-----.T...SS.....D-......G....------.....................   108

Consensus    GSG-GAGGGXSHGHLHDSAEERRLI-AEGDASPGEDRTPPGLAAEPERPGAXAQPAASPP   166
HCN4-GP      .---.....G...............-.........................T........   167
HCN4-M       ...-.....S.L.............A.................T.....ATA.......-   166
HCN4-R       .G.G.ST..G...............-.........................P.P......   173
HCN4-H       ...-.T.S.S...............-.........................S........   166

Consensus    PPQQXXQPASASCEQPSADTAIKVEGGAAAXDQILPEAEVRLGQAGFMQRQFGAMLQPGV   226
HCN4-GP      .A.H---SG...R...A.............S.............................   224
HCN4-M       ....PP........................S.............S...............   226
HCN4-R       ------.VP.SCG..RP..A.V........G........A....................   227
HCN4-H       ....PP...........V............G.............................   226

Consensus    NKFSLRMFGSQKAVEREQERVKSAGFWIIHPYSDFRFYWDLTMLLLMVGNLIIIPVGITF   286
HCN4-GP      ............................................................   284
HCN4-M       ............................................................   286
HCN4-R       ............................................................   287
HCN4-H       ............................................................   286

Consensus    FKDENTTPWIVFNVVSDTFFLIDLVLNFRTGIVVEDNTEIILDPQRIKMKYLKSWFVVDF   346
HCN4-GP      ............................................................   344
HCN4-M       ............................................................   346
HCN4-R       ......................................D.....R...............   347
HCN4-H       ........................................................M...   346

Consensus    ISSIPVDYIFLIVETRIDSEVYKTARALRIVRFTKILSLLRLLRLSRLIRYIHQWEEIFH   406
HCN4-GP      ............................................................   404
HCN4-M       ............................................................   406
HCN4-R       V...........................................................   407
HCN4-H       ............................................................   406

Consensus    MTYDLASAVVRIVNLIGMMLLLCHWDGCLQFLVPMLQDFPDDCWVSJNNMVNNSWGKQYS   466
HCN4-GP      ........................................S.....L.D...........   464
HCN4-M       ........................................H.....I.G...........   466
HCN4-R       ..............................................L.............   467
HCN4-H       ..............................................I.............   466

Consensus    YALFKAMSHMLCIGYGRQAPVGMSDVWLTMLSMIVGATCYAMFIGHATALIQSLDSSRRQ   526
HCN4-GP      ................K...........................................   524
HCN4-M       ............................................................   526
HCN4-R       ....................M.......................................   527
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HCN4-H        ............................................................   526

Consensus     YQEKYKQVEQYMSFHKLPPDTRQRIHDYYEHRYQGKMFDEESILGELSEPLREEIINFNC   586
HCN4-GP       ............................................................   584
HCN4-M        ............................................................   586
HCN4-R        ............................................................   587
HCN4-H        ............................................................   586

Consensus     RKLVASMPLFANADPNFVTSMLTKLRFEVFQPGDYIIREGTIGKKMYFIQHGVVSVLTKG   646
HCN4-GP       ............................................................   644
HCN4-M        ............................................................   646
HCN4-R        ............................................................   647
HCN4-H        ............................................................   646

Consensus     NKETKLADGSYFGEICLLTRGRRTASVRADTYCRLYSLSVDNFNEVLEEYPMMRRAFETV   706
HCN4-GP       ............................................................   704
HCN4-M        ............................................................   706
HCN4-R        ............................................................   707
HCN4-H        ............................................................   706

Consensus     ALDRLDRIGKKNSILLHKVQHDLNSGVFNYQENEIIQQIVQHDREMAHCAHRVQAAASAT   766
HCN4-GP       ........................................................-...   763
HCN4-M        ........................................R...................   766
HCN4-R        .......................S...S.....A.V.R............R.A..TT---   764
HCN4-H        ............................................................   766

Consensus     PTPTPVIWTPLIQAPLQAAAATTSVAIALTHHPRLPAAIFRPPPGPG-LGXLGAGQTPRH   825
HCN4-GP       ...............................................-..S.........   822
HCN4-M        ...............................................-..N.........   825
HCN4-R        -PVA.A........................................TT..S.........   823
HCN4-H        .............................................S.-..N.........   825

Consensus     LXRLQSLIPSALGSASPASSPSQVDTPSSSSFHIQQLAGFSAPAGLSPLLPSSSSSPPPG   885
HCN4-GP       .K.........................................................R   882
HCN4-M        PR.........................................P................   885
HCN4-R        .R.....A...PSP.........P.....A.L.V.P.P.C.T....GS...TAG.-----   878
HCN4-H        .K..........................................................   885

Consensus     ACGSPXAPTPSTX-AXAXTTAGFGHFHKALGGSLSSSDSPLLTPLQPGARSPQAAQPPPP   944
HCN4-GP       .....S.....SA-.A.T......................................L...   941
HCN4-M        .....P......ST.A.AS.T.......................................   945
HCN4-R        ----.P....P.----TAGA...S...R................M.SA.....Q---...   927
HCN4-H        .....S.....AGV.-.T.I.....................................S.A   944

Consensus     XPGARGGLGLLEHFLPPPPSSRSPSSSPGQLGQPPGELSLGLATGPPSTPETPPRQPERP  1004
HCN4-GP       L......................................Q................A.Q.  1001
HCN4-M        L..........................................A..S........-....  1004
HCN4-R        P...PA............A--...T..............P..GS...G...........L   985
HCN4-H        P.........P...................................L...........P.  1004

Consensus     SFVAGASGGASPVAFTPRGGLSPPGHSPGPPRTFPSAPPRASGSHGSLLLPPASSPPP--  1062
HCN4-GP       ...V....V................................................A--  1059
HCN4-M        ..M.......................................................--  1062
HCN4-R        P.A....A.......S....P........T............................PP  1045
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HCN4-H       .L...........G............................................--  1062

Consensus    -PQVPQRRGTPPLTPGRLTQDLKLISASQPALPQDGAQTLRRASPHS-SGESVAAFPLFP  1120
HCN4-GP      -..............................................-..........L.  1117
HCN4-M       -..............................................-........S.Y.  1120
HCN4-R       P.PA...A...A...S...............................S.......L.P..  1105
HCN4-H       -..............................................-....M.......  1120

Consensus    RAGGGSXXXGSSGGLGPPGRPXGAIPGQHV--TLPRKTSSGSLPPPLSLFGARAXSSGGP  1178
HCN4-GP      ..E...GGS............P........--......................T.....  1175
HCN4-M       ......---............Y........--......................A.....  1175
HCN4-R       ..---------------....P..G.....TL.....A.............P..APA...  1150
HCN4-H       ......GGS............Y........--......................T.....  1178

Consensus    PLT-AAPQREPGARSEPVRSKLPSNL                                    1203
HCN4-GP      ...-......................                                    1200
HCN4-M       ...T......................                                    1201
HCN4-R       R..-.........K............                                    1175
HCN4-H       ...-.G........P...........                                    1203


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**ITPKA**
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Consensus MFAEXXXTLXGGPTGMARPGG--------XX-----XARP------------CSPGLERX   35
ITPKA-H   ------M..P...........----------------...------------.......A   26
ITPKA-M   ------M..P.R.......R.----------------.G.------------.......A   26
ITPKA-R   ----MPT.TRP..GPSQE..A--------GLSRGWQGP.HLGHYWPPPSRDALAGSWN.R   48
ITPKA-GP  ....QDTSHRSA.HQGRVQ.SVLSRRDPLGLLCLYTG..ATKLVLEL-------TE.P.R   53

Consensus PRRSVGELRLXFEXRCAAVAAAAAXXEXXXXXXXXXXXXVPNGLXXX-XAPXIPQLTVTX   94
ITPKA-H   ..........L..A..........AG.PRARGAKRRGGQ.....PRAPP..V.......A   86
ITPKA-M   ..........L..A..........AG.PRARGAKRRGGQ.....PRAAP..V.......S   86
ITPKA-R   SSTGCRRGKQWLSP..HSA.S.HG--K------------LRYK.-----K.SDA.ARARR   89
ITPKA-GP  TGKA.SQWWSWW.PG-----------------------------------.SHSK-----   73

Consensus E-PDXXPCSPGPPXXEXPCLPXAGXSXXXXXXXLXXXSLSXTGSSSLLXXXEDDLLXDSE  153
ITPKA-H   .E..VP.T.....ER.RD...A..S.HLQQPRR.STS.V.S.......EDS.....S...  146
ITPKA-M   .-E.VT.A.....DQ.GNW..A..-.HLQQPRR.STS...S.......EDS.....S...  144
ITPKA-R   RR.SPSQ.RRATEQTQA..G.SRFRW--------------------------ARGGAGPG  123
ITPKA-GP  ----PRA.Y.-V.KAGV..SVSVCAD-------.---N..-P.PKGHV---AHEA.AA.S  114

Consensus SRXRX----GNVQLETGEDVXQKSHWQKIRTMVNLPVMSPFXKRYXWVQLAGHTGSFKAA  209
ITPKA-H   ..S.-----......A....G..N.............I...K...A..............  201
ITPKA-M   ..S.-----.......S...G....................R...S..............  199
ITPKA-R   .QG.GRVRRRHADPRSAPCRF....................K...A..............  183
ITPKA-GP  GFG.GAPASLTHY.H..THCF....................R...S..............  174

Consensus GTSGLILKRSSEPERYCLARLMADALRGCVPAFHGVVERDGESYLQLQDLLDGFDGPCVL  269
ITPKA-H   .........C..................................................  261
ITPKA-M   ..............H...V.....V..........I........................  259
ITPKA-R   ...............S............................................  243
ITPKA-GP  ..................G...G........T............................  234
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Consensus DCKMGVRTYLEEELTKARERPKLRKDMYKKMLAVDPEAPTEEEHAQRAVTKPRYMQWREG  329
ITPKA-H   ............................................................  321
ITPKA-M   ............................................................  319
ITPKA-R   ....................................A.......................  303
ITPKA-GP  ............................................................  294

Consensus ISSSTTLGFRIEGIKKADGSCSTDFKTTRSREQVTRVFEEFVQGDAEVLRRYLNRLQQIR  389
ITPKA-H   ..................................L..........E..............  381
ITPKA-M   .........................................M..................  379
ITPKA-R   ..................................I.........................  363
ITPKA-GP  .............................................M..............  354

Consensus DTLEVSEFFRRHEVIGSSLLFVHDHCHRAGVWLIDFGKTTPLPDGQILDHRRPWEEGNRE  449
ITPKA-H   ............................................................  441
ITPKA-M   ....I.D.....................................................  439
ITPKA-R   ...................................................L........  423
ITPKA-GP  ..........K.................................................  414

Consensus DGYLLGLDNLIGILASLAER                                          469
ITPKA-H   ....................                                          461
ITPKA-M   ....................                                          459
ITPKA-R   ...........S........                                          443
ITPKA-GP  ....................                                          434


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**KCNE1**
-------------------------------------------------------------------------------
Consensus   MILPNSTAVMPFLTTLWQETXQ-QGXNASGLARRSPLRDDGKLEALYILMVLGFFGFFTL   59
KCNE1-H     ...S.T...T....K.....V.-..G.M........RSS........V............   59
KCNE1-M     .S.....T.L...AR.....AE-..G.V.....K.Q....S...................   59
KCNE1-R     ..P..A..........GE..AHL..SS.TS....G..G...QM.................   60
KCNE1-GP    ...............V..G.V.-PSS..................................   59

Consensus   GIMLSYIRSKKLEHSHDPFNVYIESDAWQEKDKAYFQARVLESCRSCYVIENQLAVEQPN  119
KCNE1-H     ...............N...................V.......Y.....V..H..I....  119
KCNE1-M     ...............................G..V........F.A.......A.....A  119
KCNE1-R     .........Q..............AND.....R............G...L.......H.D  120
KCNE1-GP    ..........................T.......F.......N....C......T.....  119

Consensus   THLPELKPSX                                                    129
KCNE1-H     .....T...P                                                    129
KCNE1-M     ........LS                                                    129
KCNE1-R     .........L                                                    130
KCNE1-GP    .Y....----                                                    125


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**KCNH2**
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Consensus   MPVRRGHVAPQNTFLDTIIRKFEGQSRKFIIANARVENCAVIYCNDGFCELCGYSRAEVM    60
KCNH2-H     ............................................................    60
KCNH2-M     ............................................................    60
KCNH2-R     ............................................................    60
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KCNH2-GP    A.A..--------------GRLAAGG..................................    46

Consensus   QRPCTCDFLHGPRTQRRAAAQIAQALLGAEERKVEIAFYRKDGSCFLCLVDVVPVKNEDG   120
KCNH2-H     ............................................................   120
KCNH2-M     ............................................................   120
KCNH2-R     ............................................................   120
KCNH2-GP    ............................................................   106

Consensus   AVIMFILNFEVVMEKDMVGSPAXDTNHRGPPTSWLAPGRAKTFRLKLPALLALTARES-S   179
KCNH2-H     ......................H...................................-.   179
KCNH2-M     ......................H.......S.....S.....................-.   179
KCNH2-R     ......................R...................................-.   179
KCNH2-GP    ......................R............T..................T...S.   166

Consensus   VRPGGAGGAGAPGAVVVDVDLTPAAPSSESLALDEVSAMDNHVAGLGPAEERRALVGPGS   239
KCNH2-H     ..S.................................T.......................   239
KCNH2-M     ..T.SMHS....................................................   239
KCNH2-R     ....................................P....................SC.   239
KCNH2-GP    .....T..S.............................L.....--..........A...   224

Consensus   PPPPXSAPGPHPSPRAHSLNPDASGSSCSLARTRSRESCASVRRASSADDIEAMRAGALP   299
KCNH2-H     .--.R....QL..............................................V..   297
KCNH2-M     AS.VA.IR........Q...........................................   299
KCNH2-R     ....V........L..............................................   299
KCNH2-GP    ..SS-VPGP..T................................................   283

Consensus   PPPRHASTGAMHPLRSGLLNSTSDSDLVRYRTISKIPQITLNFVDLKGDPFLASPTSDRE   359
KCNH2-H     ............................................................   357
KCNH2-M     ............................................................   359
KCNH2-R     ............................................................   359
KCNH2-GP    ............................................................   343

Consensus   IIAPKIKERTHNVTEKVTQVLSLGADVLPEYKLQAPRIHRWTILHYSPFKAVWDWLILLL   419
KCNH2-H     ............................................................   417
KCNH2-M     ............................................................   419
KCNH2-R     ............................................................   419
KCNH2-GP    ............................................................   403

Consensus   VIYTAVFTPYSAAFLLKETEEGPXAPXCGYACQPLAVVDLIVDIMFIVDILINFRTTYVN   479
KCNH2-H     .......................P.TE.................................   477
KCNH2-M     ....................D.SQ..D.................................   479
KCNH2-R     .......................P..E.................................   479
KCNH2-GP    ..................P..DAQTAD.................................   463

Consensus   ANEEVVSHPGRIAVHYFKGWFLIDMVAAIPFDLLIFGSGSEELIGLLKTARLLRLVRVAR   539
KCNH2-H     ............................................................   537
KCNH2-M     ............................................................   539
KCNH2-R     ............................................................   539
KCNH2-GP    ............................................................   523

Consensus   KLDRYSEYGAAVLFLLMCTFALIAHWLACIWYAIGNMEQPHMDSRIGWLHNLGDQIGKPY   599
KCNH2-H     ............................................................   597
KCNH2-M     ............................................H...............   599
KCNH2-R     .............L.........................................M....   599
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KCNH2-GP     ........................................D.N.................   583

Consensus    NSSGLGGPSIKDKYVTALYFTFSSLTSVGFGNVSPNTNSEKIFSICVMLIGSLMYASIFG   659
KCNH2-H      ............................................................   657
KCNH2-M      ............................................................   659
KCNH2-R      ................G...........................................   659
KCNH2-GP     ............................................................   643

Consensus    NVSAIIQRLYSGTARYHTQMLRVREFIRFHQIPNPLRQRLEEYFQHAWSYTNGIDMNAVL   719
KCNH2-H      ............................................................   717
KCNH2-M      ............................................................   719
KCNH2-R      ............................................................   719
KCNH2-GP     ............................................................   703

Consensus    KGFPECLQADICLHLNRSLLQHCKPFRGATKGCLRALAMKFKTTHAPPGDTLVHAGDLLT   779
KCNH2-H      ............................................................   777
KCNH2-M      ............................................................   779
KCNH2-R      ...............................D............................   779
KCNH2-GP     ............................................................   763

Consensus    ALYFISRGSIEILRGDVVVAILGKNDIFGEPLNLYARPGKSNGDVRALTYCDLHKIHRDD   839
KCNH2-H      ............................................................   837
KCNH2-M      ............................................................   839
KCNH2-R      ............................................................   839
KCNH2-GP     ............................................................   823

Consensus    LLEVLDMYPEFSDHFWSSLEITFNLRDTNMIPGSPGSTELEGGFNRQRKRKLSFRRRTDK   899
KCNH2-H      ............................................S...............   897
KCNH2-M      .....................................A...S..................   899
KCNH2-R      .......................................W....................   899
KCNH2-GP     ................................................R...........   883

Consensus    DTEQPGEVSALGP-XXRXGAGPSSRGRPGGPWGESPSSGPSSPESSEDEGPGRSSSPLRL   958
KCNH2-H      .............--G.A..........................................   955
KCNH2-M      ............QGPA.V.P...C..Q.................................   959
KCNH2-R      .............--G.A..........................................   957
KCNH2-GP     .P......P...--PA.V......W....T...D................Q.........   941

Consensus    VPFSSPRPPGEPPGGEPLTEDXEKXSDTCNPLSGAFSGVSNIFSFWGDSRGRQYQELPRC  1018
KCNH2-H      ..................M..C..S...................................  1015
KCNH2-M      ..........D..........G..-...................................  1018
KCNH2-R      .....................C..S...................................  1017
KCNH2-GP     ............R.A.T....GD.-...................................  1000

Consensus    PAPAPSLLNIPLSSPGRRPRGDVESRLDALQRQLNRLETRLSADMATVLQLLQRQMTLVP  1078
KCNH2-H      ...T........................................................  1075
KCNH2-M      ..................S.........................................  1078
KCNH2-R      ...............S............................................  1077
KCNH2-GP     ............................................................  1060

Consensus    PAYSAVTTPGPGPTSTSPLLPVSPXPTLTLDSLSQVSQFXAXEELPPGAPELPQXGPTRR  1138
KCNH2-H      ........................L..............M.C............E.....  1135
KCNH2-M      ...............A......G.V..............V.F....A.......D.....  1138
KCNH2-R      ........................F..............M.C............E.....  1137
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KCNH2-GP    .............A.......I..I..............V.F............D.....  1120

Consensus   LSLPGQLGALTSQPLHRHGSDPGS                                      1162
KCNH2-H     ........................                                      1159
KCNH2-M     ........................                                      1162
KCNH2-R     ........................                                      1161
KCNH2-GP    ........................                                      1144


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**KCNMA1**
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Consensus MANGGGGGGGSSGGGGGGGGGGSGLRMSSNIHANHLSLDASSSSSSSSSS-SSSSSSSSS    59
KCNH2-GP  ------------------------------------------------------------
KCNH2-M   ..............-...................N...............-.........    58
KCNH2-R   .................................S................-.........    59
KCNH2-H   ...............--......S..........................S.........    58

Consensus SSVHEPKMDALIIPVTMEVPCDSRGQRMWWAFLASSMVTFFGGLFIILLWRTLKYLWTVC   119
KCNH2-GP  -------------------------------------------------------FELLI     5
KCNH2-M   ............................................................   118
KCNH2-R   ............................................................   119
KCNH2-H   ............................................................   118

Consensus CHCGGKTKEAQKI----------------NNGSSQADGTLKPVDEKEEAVAAEVGWMTSV   163
KCNH2-GP  ER...HLQGVFLSFPVISALSGIGLSSQSDKS.AFTNTHME.SQ---RGLVLGL-LFMNE    61
KCNH2-M   .............----------------...................V...........   162
KCNH2-R   ......A......----------------...............................   163
KCNH2-H   .............----------------...............................   162

Consensus KDWAGVMISAQTLTGRVLVVLVFALSIGALVIYFIDSSNPIESCQNFYKDFTLQIDMAFN   223
KCNH2-GP  EA.P.CSG---HTPSPFA..........................................   118
KCNH2-M   ............................................................   222
KCNH2-R   ............................................................   223
KCNH2-H   ............................................................   222

Consensus VFFLLYFGLRFIAANDKLWFWLEVNSVVDFFTVPPVFVSVYLNRSWLGLRFLRALRLIQF   283
KCNH2-GP  ............................................................   178
KCNH2-M   ............................................................   282
KCNH2-R   ............................................................   283
KCNH2-H   ............................................................   282

Consensus SEILQFLNILKTSNSIKLVNLLSIFISTWLTAAGFIHLVENSGDPWENFQNNQALTYWEC   343
KCNH2-GP  ............................................................   238
KCNH2-M   ............................................................   342
KCNH2-R   ............................................................   343
KCNH2-H   ............................................................   342

Consensus VYLLMVTMSTVGYGDVYAKTTLGRLFMVFFILGGLAMFASYVPEIIELIGNRKKYGGSYS   403
KCNH2-GP  ............................................................   298
KCNH2-M   ............................................................   402
KCNH2-R   ............................................................   403
KCNH2-H   ............................................................   402
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Consensus AVSGRKHIVVCGHITLESVSNFLKDFLHKDRDDVNVEIVFLHNISPNLELEALFKRHFTQ   463
KCNH2-GP  ............................................................   358
KCNH2-M   ............................................................   462
KCNH2-R   ............................................................   463
KCNH2-H   ............................................................   462

Consensus VEFYQGSVLNPHDLARVKIESADACLILANKYCADPDAEDASNIMRVISIKNYHPKIRII   523
KCNH2-GP  ............................................................   418
KCNH2-M   ............................................................   522
KCNH2-R   ............................................................   523
KCNH2-H   ............................................................   522

Consensus TQMLQYHNKAHLLNIPSWNWKEGDDAICLAELKLGFIAQSCLAQGLSTMLANLFSMRSFI   583
KCNH2-GP  ............................................................   478
KCNH2-M   ............................................................   582
KCNH2-R   ............................................................   583
KCNH2-H   ............................................................   582

Consensus KIEEDTWQKYYLEGVSNEMYTEYLSSAFVGLSFPTVCELCFVKLKLLMIAIEYKSANRES   643
KCNH2-GP  ............................................................   538
KCNH2-M   ............................................................   642
KCNH2-R   ............................................................   643
KCNH2-H   ............................................................   642

Consensus X---RILINPGNHLKIQEGTLGFFIASDAKEVKRAFFYCKACHDDITDPKRIKKCGCKRX   700
KCNH2-GP  R---S..............................Y.......................P   595
KCNH2-M   RSRK.........................................V...........R.-   701
KCNH2-R   ----.......................................................-   698
KCNH2-H   ----.......................................................P   698

Consensus XXXXXXXXXXXXXXXXXXXXXXXXXXXXX-XXXXXXXXXXXXXXXXXXXXXXXXX-XXED   758
KCNH2-GP  KMSIYKRMRRACCFDCGRSERDCSCMSGRMRGNVDTLERAFPLSSVSVNDCSTSFPAF..   655
KCNH2-M   ---------------------------------------------------------L..   704
KCNH2-R   ---------------------------------------------------------L..   701
KCNH2-H   KMSIYKRMRRACCFDCGRSERDCSCMSGRVRGNVDTLERAFPLSSVSVNDCSTSFRAF..   758

Consensus EQPSTLSPKKKQRNGGMRNSPNXSPKLMRHDPLLIPGNDQIDNMDSNVKKYDSTGMFHWC   818
KCNH2-GP  ......................S.....................................   715
KCNH2-M   ...P..................T.....................................   764
KCNH2-R   ......................S.....................................   761
KCNH2-H   ......................T.....................................   818

Consensus APKEIEKVILTRSEAAMTVLSGHVVVCIFGDVSSALIGLRNLVMPLRASNFHYHELKHIV   878
KCNH2-GP  ............................................................   775
KCNH2-M   ............................................................   824
KCNH2-R   ............................................................   821
KCNH2-H   ............................................................   878

Consensus FVGSIEYLKREWETLHNFPKVSILPGTPLSRADLRAVNINLCDMCVILSANQNNIDDTSL   938
KCNH2-GP  ............................................................   835
KCNH2-M   ............................................................   884
KCNH2-R   ............................................................   881
KCNH2-H   ............................................................   938
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Consensus QDKECILASLNIKSMQFDDSIGVLQANSQGFTPPGMDRSSPDNSPVHGMLRQPSITTGVN   998
KCNH2-GP  ............................................................   895
KCNH2-M   ............................................................   944
KCNH2-R   ............................................................   941
KCNH2-H   ............................................................   998

Consensus IPIIT---------------------------ELVNDTNVQFLDQDDDDDPDTELYLTQP  1031
KCNH2-GP  .....---------------------------............................   928
KCNH2-M   .....ELAKPGKLPLVSVNQEKNSGTHILMIT............................  1004
KCNH2-R   .....---------------------------............................   974
KCNH2-H   .....---------------------------............................  1031

Consensus FACGTAFAVSVLDSLMSATYFNDNILTLIRTLVTGGATPELEALIAEENALRGGYSTPQT  1091
KCNH2-GP  ............................................................   988
KCNH2-M   ............................................................  1064
KCNH2-R   ............................................................  1034
KCNH2-H   ............................................................  1091

Consensus LANRDRCRVAQLALLDGPFADLGDGGCYGDLFCKALKTYNMLCFGIYRLRDAHLSTPSQC  1151
KCNH2-GP  ............................................................  1048
KCNH2-M   ............................................................  1124
KCNH2-R   ............................................................  1094
KCNH2-H   ............................................................  1151

Consensus TKRYVITNPPYEFELVPTDLIFCLMQFDHNAGQSRASLSHSSHSSQSSSKKSSSVHSIPS  1211
KCNH2-GP  ............................................................  1108
KCNH2-M   ............................................................  1184
KCNH2-R   ............................................................  1154
KCNH2-H   ............................................................  1211

Consensus TANRQNRPKSRESRDKQKYVQEERL                                     1236
KCNH2-GP  .........................                                     1133
KCNH2-M   ....P............NRKEMVYR                                     1209
KCNH2-R   .........................                                     1179
KCNH2-H   .........................                                     1236


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**KCNN1**
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Consensus   SPQVSLESLPPCHARPWTPRHLPSHRAQVAMXSHSXNGSVGXPLGSGPGXLGRDPXDPEA   60
KCNN1-M     ------------------------------.S...H.....Q.......F..WE.V....   30
KCNN1-H     ------------------------------.N...Y.....R.......A.....P....   30
KCNN1-GP    ...............................IG..R...A.W.......M.....L....   60

Consensus   GRPXQPXHGPGLQVVXAKSEPARLSPGSPRGQPQDQXEEEDEDEEDEAXRXRASGKPPTV  120
KCNN1-M     ...L..TQ.....M.-..GQ.V.....GS..H..E.E...E.E..---EDKTG.......   86
KCNN1-H     .H.P..P.S......V.......P............DDD..-......G.Q......SN.   89
KCNN1-GP    ...E..L.......LL....................S...........D.P..RAR....  120

Consensus   GHRLGHRRALFEKRKRLSDYALIFGMFGIVVMVTETELSWGVYTKESLYSFALKCLISLS  180
KCNN1-M     S...............................................C...........  146
KCNN1-H     ............................................................  149
KCNN1-GP    ........................................S....A..............  180
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Consensus   TVILLGLVVLYHAREIQLFMVDNGADDWRIAMTXERVXLISLELAVCAIHPVPGHYRFTW  240
KCNN1-M     ........I..........L.............W...S......V...............  206
KCNN1-H     .A...............................C...F......................  209
KCNN1-GP    ....................A............R..IL......................  240

Consensus   TARLAFTYAPSVAEADVDVLLSIPMFLRLYLLGRVMLLHSKIFTDASSRSIGALNKITFN  300
KCNN1-M     ......SLV..A....L...............A.......R..............RV...  266
KCNN1-H     ............................................................  269
KCNN1-GP    ...................................L........................  300

Consensus   TRFVMKTLMTICPGTVLLVFSISSWIIAAWTVRVCERYHDKQEVTSNFLGAMWLISITFL  360
KCNN1-M     ....T................V....V.................................  326
KCNN1-H     ............................................................  329
KCNN1-GP    .........................V..................................  360

Consensus   SIGYGDMVPHTYCGKGVCLLTGIMGAGCTALVVAVVARKLELTKAEKHVHNFMMDTQLTK  420
KCNN1-M     ............................................................  386
KCNN1-H     ............................................................  389
KCNN1-GP    ............................................................  420

Consensus   RVKNAAANVLRETWLIYKHTRLVKKPDQARVRKHQRKFLQAIHQAQKLRSVKIEQGKLND  480
KCNN1-M     ............................G............................V..  446
KCNN1-H     ............................................................  449
KCNN1-GP    ............................................---.........R...  477

Consensus   QANTLADLAKTQXIMYELVSELHAQHEELEARLAXLESRLDXLGASLQALPGLIAQAIXP  540
KCNN1-M     ......E...A.S.A..V....Q..Q........A......V................C.  506
KCNN1-H     .....T......TV..D.................T......A................R.  509
KCNN1-GP    ...S........G.....L....G..........M..A...S..........PCRP----  533

Consensus   XPPXXXPRPGPGPXXXAXXSXPSXWXPXXXSDCG                            574
KCNN1-M     L..---.W....HLAT.TH.PQ.H.L.TMG....                            537
KCNN1-H     P..PLP.......QDQ.AR.S.CR.T.VAP....                            543
KCNN1-GP    SHAATVT......GPA.LS-H..LL-.-------                            558


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**KCNN2**
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Consensus   MPIVLXRPXNRTRRLDSTGAGMGPSSHQQXESPLPTITHCAGCTTAWSPCSFNXSDMETP   60
KCNN2-R     ------------------------------------------------------------
KCNN2-M     .....V..T....................Q.......................S......   60
KCNN2-H     ------------------------------------------------------------
KCNN2-GP    .....A..A....................P.......................G......   60

Consensus   LQFQRGFFPEQPPXPPRSSHLHCQQQQQSQDKPCXPFAPLPHXXPHHHPHLAHQXPGSGG  120
KCNN2-R     ------------------------------------------------------------
KCNN2-M     .............P....................A.......--..........Q.....  118
KCNN2-H     ------------------------------------------------------------
KCNN2-GP    .............-....................P.......PH..........P.....  119

Consensus   SSPCLRCNSCASSGAXAAGXXAGAGDNLSLLLRTSSPGGAFRTRTSSPLSGSSCCCCCSS  180
KCNN2-R     ------------------------------------------------------------
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KCNN2-M      ...............P...--.......................................   176
KCNN2-H      ------------------------------------------------------------
KCNN2-GP     ...............L...AG.......................................   179

Consensus    RRGSQLNVSELTPSSHASALRQQXAQQPASASQYHQCHSLQPAXSPTGSLGSLXSGPPLS   240
KCNN2-R      ------------------------------------------------------------
KCNN2-M      .......................Y...................T.........G......   236
KCNN2-H      ------------------------------------------------------------
KCNN2-GP     .......................P...................A.........C......   239

Consensus    HXHHHXXHPAHHQXXQPQARRESNPFTEIAMSSCRYNGGVMRPLSNLSASRRNLHEMDSE   300
KCNN2-R      ------------------------------..............................    30
KCNN2-M      .-...HP......HH.................................S.....Q.....   295
KCNN2-H      ------------------------------..............................    30
KCNN2-GP     .H...AA......PL.............................................   299

Consensus    AQPLQPPASVGGG-GGASSPSAAX---AAASSSAPEIVVSKPEHNNSNNLALYGXGGGGS   356
KCNN2-R      ........PGA---......C..----.....P.....................A....-    82
KCNN2-M      ..........V..G.........----...........................T.....   351
KCNN2-H      .............-.........AAAA..V........................T.....    89
KCNN2-GP     ........A....-.........A----..........................A.....   354

Consensus    TGGGG--GGSGHGSSSGTKSSKKKNQNIGYKLGHRRALFEKRKRLSDYALIFGMFGIVVM   414
KCNN2-R      ----------------.P.P........................................   126
KCNN2-M      .....--.....................................................   409
KCNN2-H      .....GG.....................................................   149
KCNN2-GP     .....--..........A..........................................   412

Consensus    VIETELSWGAYDKASLYSLALKCLISLSTIILLGLIIVYHAREIQLFMVDNGADDWRIAM   474
KCNN2-R      .............................V..............................   186
KCNN2-M      ............................................................   469
KCNN2-H      ............................................................   209
KCNN2-GP     ............................................................   472

Consensus    TYERIFFICLEILVCAIHPIPGNYTFTWTARLAFSYAPSTTTADVDIILSIPMFLRLYLI   534
KCNN2-R      ............................................................   246
KCNN2-M      ............................................................   529
KCNN2-H      ............................................................   269
KCNN2-GP     ....................................T.......................   532

Consensus    ARVMLLHSKLFTDASSRSIGALNKINFNTRFVMKTLMTICPGTVLLVFSISLWIIAAWTV   594
KCNN2-R      ............................................................   306
KCNN2-M      ............................................................   589
KCNN2-H      ............................................................   329
KCNN2-GP     ............................................................   592

Consensus    RACERYHDQQDVTSNFLGAMWLISITFLSIGYGDMVPNTYCGKGVCLLTGIMGAGCTALV   654
KCNN2-R      ............................................................   366
KCNN2-M      ............................................................   649
KCNN2-H      ............................................................   389
KCNN2-GP     ............................................................   652

Consensus    VAVVARKLELTKAEKHVHNFMMDTQLTKRVKNAAANVLRETWLIYKNTKLVKKIDHAKVR   714
KCNN2-R      ............................................................   426
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KCNN2-M     ............................................................  709
KCNN2-H     ............................................................  449
KCNN2-GP    ............................................................  712

Consensus   KHQRKFLQAIHQLRSVKMEQRKLNDQANTLVDLAKTQNIMYDMISDLNERSEDFEKRIVT  774
KCNN2-R     ............................................................  486
KCNN2-M     ............................................................  769
KCNN2-H     ............................................................  509
KCNN2-GP    ............................................................  772

Consensus   LETKLETLIGSIHALPGLISQTIRQQQRDFIEAQMENYDKHVTYNAERSRSSSRRRRSSS  834
KCNN2-R     ............Q.....L...L.......L...L.AR...GP.E.A.............  546
KCNN2-M     ................................T.........S.................  829
KCNN2-H     ....................................S.......................  569
KCNN2-GP    ............................................................  832

Consensus   TAPPTSSESS                                                    844
KCNN2-R     ..........                                                    556
KCNN2-M     ..........                                                    839
KCNN2-H     ..........                                                    579
KCNN2-GP    ..........                                                    842


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**KCNN3**
-------------------------------------------------------------------------------
Consensus   MDTSGHFHDSGVGDLDEDPKCPCPSSGDEQQQQQX-XQQQPPPPPAPPAAPQQPPGPSLQ   59
KCNN3-R     ..................................Q--...L....V..............   58
KCNN3-M     ................................-----............V.......L..   55
KCNN3-H     ..................................QQQ...Q.............L.....   60
KCNN3-GP    .................................P--Q....................P..   58

Consensus   PQPPQLQQQQXXX------XXQQXXQPPHPLSQLAQLQSQXVHPGLLHSSPTAFRAPXSA  113
KCNN3-R     ......P...P----------PPPPP.S......T.....P................T.G  108
KCNN3-M     .....P....SQQQQQQQSQQ..QQA.L...P........L................T..  115
KCNN3-H     ..........QQQ------QQ..QQ...............P................P.S  114
KCNN3-GP    .......----------------PP...............L................P..  103

Consensus   NSTAILHPSSRQGSQLNLNDHLLGHSPSSTATSGPGGGSRHRQASPLVHRRDSNPFTEIA  173
KCNN3-R     ....T.......................................................  168
KCNN3-M     ............................................................  175
KCNN3-H     ............................................................  174
KCNN3-GP    ............................................................  163

Consensus   MSSCKYSGGVMKPLSRLSASRRNLIEAEPEGQPLQLFSPSNPPEIVISSREDNHAHQTLL  233
KCNN3-R     .......................................................Q....  228
KCNN3-M     .............................................I..............  235
KCNN3-H     ............................T...............................  234
KCNN3-GP    ........................................................L...  223

Consensus   HHPNATHNHQHAGTTASSTTFPKANKRKNQNIGYKLGHRRALFEKRKRLSDYALIFGMFG  293
KCNN3-R     .............PP.............................................  288
KCNN3-M     ................G...........................................  295
KCNN3-H     ............................................................  294
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KCNN3-GP    ............................................................  283

Consensus   IVVMVIETELSWGLYSKDSMFSLALKCLISLSTIILLGLIIAYHTREVQLFVIDNGADDW  353
KCNN3-R     ............................................................  348
KCNN3-M     .................................V..........................  355
KCNN3-H     ............................................................  354
KCNN3-GP    ............................................................  343

Consensus   RIAMTYERILYISLEMLVCAIHPIPGEYKFFWTARLAFSYTPSRAEADVDIILSIPMFLR  413
KCNN3-R     ............................................................  408
KCNN3-M     ............................................................  415
KCNN3-H     ............................................................  414
KCNN3-GP    ........................................A...................  403

Consensus   LYLIARVMLLHSKLFTDASSRSIGALNKINFNTRFVMKTLMTICPGTVLLVFSISLWIIA  473
KCNN3-R     ............................................................  468
KCNN3-M     ............................................................  475
KCNN3-H     ............................................................  474
KCNN3-GP    ............................................................  463

Consensus   AWTVRVCE---------------RYHDQQDVTSNFLGAMWLISITFLSIGYGDMVPHTYC  518
KCNN3-R     ........SPESPGRLSRSSLPAW....................................  528
KCNN3-M     ........---------------.....................................  520
KCNN3-H     ........---------------.....................................  519
KCNN3-GP    ........---------------.....................................  508

Consensus   GKGVCLLTGIMGAGCTALVVAVVARKLELTKAEKHVHNFMMDTQLTKRIKNAAANVLRET  578
KCNN3-R     ............................................................  588
KCNN3-M     ............................................................  580
KCNN3-H     ............................................................  579
KCNN3-GP    ............................................................  568

Consensus   WLIYKHTKLLKKIDHAKVRKHQRKFLQAIHQLRSVKMEQRKLSDQANTLVDLSKMQNVMY  638
KCNN3-R     ............................................................  648
KCNN3-M     .................................G..........................  640
KCNN3-H     ............................................................  639
KCNN3-GP    ............................................................  628

Consensus   DLITELNDRSEDLEKQIGSLESKLEHLTASFNSLPLLIADTLRQQQQQLLXAILEARGVS  698
KCNN3-R     ......S........................H........A.........S.V.......  708
KCNN3-M     ..................................................T.FV....I.  700
KCNN3-H     ..................................................S..I......  699
KCNN3-GP    ..................................................T.........  688

Consensus   VAVGTTHAPISDSPIGVSSTSFPTPYTSSSSC                              730
KCNN3-R     .........L.E....................                              740
KCNN3-M     .....S...P......I...............                              732
KCNN3-H     .......T........................                              731
KCNN3-GP    ................................                              720


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**KCNQ1**
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Consensus   MAAASSPPRAERKRXGWXRLXGARRGSAGLAKKCPFSLELAEGGPAGXXLYAPXAPPGAP   60
KCNQ1-H     ..............W..G..P..........................GA....I..-...   59
KCNQ1-M     .DT.....S.....A..S..L.......-VV..............E.STV...I..T...   59
KCNQ1-R     .....T.........S.S..P..Q.E................S..PSSA....VS..S..   60
KCNQ1-GP    .........T....G..G..L.S.....S..................GT....V.....L   60

Consensus   GPAPPASPASPAXPPAAADLGPRPPVSLDPRVSIYSARRPLLARTHIQGRVYNFLERPTG  120
KCNQ1-H     .........A..A..V.S..................T...V.....V.............  119
KCNQ1-M     .L...M.TPVS-PA..P.......R...................................  118
KCNQ1-R     E...........P.--...Q..Q.............V.......................  118
KCNQ1-GP    S.GS..P.....A...GLE.........................................  120

Consensus   WKCFVYHFXVFLIVLVCLIFSVLSTIEQYAALATGTLFWMEIVLVVFFGTEYVVRLWSAG  180
KCNQ1-H     ........A...................................................  179
KCNQ1-M     ........T...................................................  178
KCNQ1-R     ....A...T.....................T.............................  178
KCNQ1-GP    ........A......A............................................  180

Consensus   CRSKYVGJWGRLRFARKPISIIDLIVVVASMVVLCVGSKGQVFATSAIRGIRFLQILRML  240
KCNQ1-H     .......L....................................................  239
KCNQ1-M     .......I....................................................  238
KCNQ1-R     .......L....................................................  238
KCNQ1-GP    .......I....................................................  240

Consensus   HVDRQGGTWRLLGSVVFIHRQELITTLYIGFLGLIFSSYFVYLAEKDAVNESGRVEFGSY  300
KCNQ1-H     ............................................................  299
KCNQ1-M     ......................................................I.....  298
KCNQ1-R     ............................................................  298
KCNQ1-GP    ............................................................  300

Consensus   ADALWWGVVTVTTIGYGDKVPQTWVGKTIASCFSVFAISFFALPAGILGSGFALKVQQKQ  360
KCNQ1-H     ............................................................  359
KCNQ1-M     ............................................................  358
KCNQ1-R     ............................................................  358
KCNQ1-GP    ............................................................  360

Consensus   RQKHFNRQIPAAASLIQTAWRCYAAENPDSXTWKIYXRKPARSHTLLSPSPKPKKSXMVK  420
KCNQ1-H     ..............................S.....I..AP...............VV..  419
KCNQ1-M     ..............................A.....V...................V...  418
KCNQ1-R     ..............................A.....I...T.G.A...........A...  418
KCNQ1-GP    ..............................S.....V...................A..R  420

Consensus   KKKFKLDKDNGVSPGEKMLTVPHITCDPPEERRPDHFSVDGYDSSVRKSPTLLEVSTPHF  480
KCNQ1-H     ............T....................L......................M...  479
KCNQ1-M     ...........M......FN.....Y....D.......I.....................  478
KCNQ1-R     .................T.P..Q...E..........P..SH.G......A.......Q.  478
KCNQ1-GP    .....P..................................................PT..  480

Consensus   XRTNSFAEDLDLEGETLLTPITHVSQLREHHRATIKVIRRMQYFVAKKKFQQARKPYDVR  540
KCNQ1-H     M......................I....................................  539
KCNQ1-M     L...........................D...............................  538
KCNQ1-R     L.................A...............V.........................  538
KCNQ1-GP    M...........................................................  540
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Consensus   DVIEQYSQGHLNLMVRIKELQRRLDQSIGKPSLFIPISEKSKDRGSNTIGARLNRVEDKV  600
KCNQ1-H     ...................................SV.......................  599
KCNQ1-M     ............................................................  598
KCNQ1-R     ..................................V............S............  598
KCNQ1-GP    ............................................................  600

Consensus   TQLDQRLVLITDMLHQLLSLHQGX--X--GPXXXGG-XXVQPCXEGGSIDPELFLPSNSL  655
KCNQ1-H     .......A.............G.STPGSG..PRE..AHIT...GS...V.........T.  659
KCNQ1-M     ........I..........MQ..G------.TCNSR-SQ.VASN.....N..........  651
KCNQ1-R     ..........A...Q...A....RCHGGAH.AQ---------ARD.DPA......-----  644
KCNQ1-GP    ........V..............------..HSG..PQM....S.D...H..........  654

Consensus   PTYEQLTVPXRGPDEGS                                             672
KCNQ1-H     .........R.......                                             676
KCNQ1-M     .........QT......                                             668
KCNQ1-R     .........R.D.E...                                             661
KCNQ1-GP    .........Q.....A.                                             671


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**Orai1**
-------------------------------------------------------------------------------
Consensus   MHPEPAPPPSSS--SPELPLSGGSTTSGSRRSRRRSGDGEPPGXPP-PAPPPAVSYPDWI   57
Orai1-H     ..........R.--.....P.......................A..-.-..S..T.....   56
Orai1-M     ..........H.--N....V....S................S.A..L.P...........   58
Orai1-R     ...........H--...................-.........S..-.............   56
Orai1-GP       .R..........RG.Q....G..---........H........S..--.......C...V   55

Consensus   GQSYSEVMSLNEHSMQALSWRKLYLSRAKLKASSRTSALLSGFAMVAMVEVQLDAXHDYP  117
Orai1-H     .......................................................D....  116
Orai1-M     ......................................................TD....  118
Orai1-R     .....K.................................................E....  116
Orai1-GP       .......................................................E....  115

Consensus   PGLLIAFSACTTVLVAVHLFALMISTCILPNIEAVSNVHNLNSVKESPHERMHRHIELAW  177
Orai1-H     ............................................................  176
Orai1-M     .....V......................................................  178
Orai1-R     ............................................................  176
Orai1-GP       ...............................V............................  175

Consensus   AFSTVIGTLLFLAEVVLLCWVKFLPLKKQP--GQPRPTSKPPAXGAAANXSSSSGITPGQ  235
Orai1-H     ..............................--...........S.....-V.T.......  233
Orai1-M     ...........................R.A--...S..KP.AESVIV..H.D.......E  236
Orai1-R     ..............................--...........G...S.N..E.......  234
Orai1-GP       ..............................EP......GRL.PG.ELP-TNG........  234

Consensus   AAAIASTTIMVPFGLXFIVFAVHFYRSLVSHKTDRQFQELNELAEFARLQDQLDHRGDHP  295
Orai1-H     ...............I............................................  293
Orai1-M     .......A....C..V...........................................S  296
Orai1-R     ...............V........................S...........M.......  294
Orai1-GP       ...............I............................................  294

Consensus   LTPGSHYA                                                      303
Orai1-H     ........                                                      301
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Orai1-M     ....T...                                                      304
Orai1-R     ........                                                      302
Orai1-GP       ........                                                      302


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**Orai2**
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Consensus   MLGPAPTMSAELNVPXDPSXPACPEPGHKGMDYRDWVRRSYLELVTSNHHSVQALSWRKL   60
ORAI2-H     -------........I...A........................................   53
ORAI2-M     -------........M...A........................................   53
ORAI2-GP    ............S..A...T-.R.....................................   59
ORAI2-R     -------........V...T...S....................................   53

Consensus   YLSRAKLKASSRTSALLSGFAMVAMVEVQLETQYQYPRPLLIAFSACTTVLVAVHLFALL  120
ORAI2-H     ............................................................  113
ORAI2-M     ................................K....Q......................  113
ORAI2-GP    ............................................................  119
ORAI2-R     ............................................................  113

Consensus   ISTCILPNVEAVSNIHNLNSISESPHERMHPYIELAWGFSTVLGILLFLAEVVLLCWIKF  180
ORAI2-H     ............................................................  173
ORAI2-M     ............................................................  173
ORAI2-GP    ............................................................  179
ORAI2-R     ............................................................  173

Consensus   LPVDARRQPGPXXXSGSHTGWQAALVSTIIMVPVGLIFVVFTIHFYRSLVRHKTERHNRE  240
ORAI2-H     ...........PPGP.............................................  233
ORAI2-M     .....KD...----.H............................................  229
ORAI2-GP    ......H...HE--.ST...........................................  237
ORAI2-R     ....S......LPGA.G...........................................  233

Consensus   IEELHKLKVQLDGHERSLQVV                                         261
ORAI2-H     ....................L                                         254
ORAI2-M     .....................                                         250
ORAI2-GP    .............Q.......                                         258
ORAI2-R     ................G....                                         254


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**Orai3**
-------------------------------------------------------------------------------
Consensus   MWPRRLRLRPSSCFGLGCPASAPGATRRRLQFPGAGCPRSHSRRAGGWGVPPASAAPSGA   60
ORAI3-H     ------------------------------------------------------------
ORAI3-M     ------------------------------------------------------------
ORAI3-GP    ------------------------------------------------------------
ORAI3-R     ............................................................   60

Consensus   PKAPRPRRDRRLPGAAPRMKGGEGDAGEQAPLNPEVESPAGSATYREFVHRGYLDLMGAS  120
ORAI3-H     ------------------.................G........................   42
ORAI3-M     ------------------.......T..........D.......................   42
ORAI3-GP    ------------------.R......A..........C......................   42
ORAI3-R     ..................................Q......T..................  120
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Consensus   QHSLRALSWRRLYLSRAKLKASSRTSALLSGFAMVAMVEVQLEXDHEYPPGLLVAFSACT  180
ORAI3-H     ...........................................S................  102
ORAI3-M     ...........................................N................  102
ORAI3-GP    ...........................................N................  102
ORAI3-R     ...........................................SN...............  180

Consensus   TVLVAVHLFALMVSTCLLPHIEAVSNIHNLNSVHQSPHQRLHRYVELAWGFSTALGTFLF  240
ORAI3-H     ............................................................  162
ORAI3-M     ............................................................  162
ORAI3-GP    ..........................................H.................  162
ORAI3-R     ............................................................  240

Consensus   LAEVVLV-GWVKFVPIGAPLXTPAPVVPXSQVPGXLXPVATSLSPASNLPXSSASA-XXX  298
ORAI3-H     .......-............D..T.M..T.R...T.A.............R.....-APS  220
ORAI3-M     .......-...........MGK......M....P----.TV...L....TP....ITTSQ  217
ORAI3-GP    ..GEP.WDL.C-------------------------------------------------  222
ORAI3-R     .......-............N.......AT...N.P.A......P....A.....----  295

Consensus   QXXXACPPRQAC-DGGGAHGPGWQAAMASTAIMVPVGLVFVAFALHFYRSLVAHKTDRHK  357
ORAI3-H     .AEP........-G............................................Y.  279
ORAI3-M     .PSK......V.-.--S.......................M...................  274
ORAI3-GP    ------------------------------------------------------------  282
ORAI3-R     -----A......A....S..........................................  350

Consensus   QELEELSRLQGELQAV                                              373
ORAI3-H     ......N.........                                              295
ORAI3-M     ................                                              290
ORAI3-GP    ----------------                                              173
ORAI3-R     ................                                              366

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**PDE4A**
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Consensus             MEPPAAPSERSLSLSLPGPREGQATLKPPPQHLWRQPRTPIRIQQRGYSDSAERSEPERX   60
PDE4A-M               ...........................................................S   60
PDE4A-GP              ......T....................................................P   60
PDE4A-H               ....TV................................................A.R..Q   60

Consensus             PHRPIERADAVDTSDRPGLRTTRMSWPSSFHGTGTXSGXAGGGSSRRFEAENGPTPSPGR  120
PDE4A-M               .............G.....................-----.......L............  115
PDE4A-GP              .................................S.S..S.....G...............  120
PDE4A-H               ..........M........................G..G.....................  120

Consensus             SPLDSQASPGLVLHAGAATSQRRESFLYRSDSDYDMSPKTMSRNSSVTSEAHAEDLIVTP  180
PDE4A-M               ...........M...................................A....G.......  175
PDE4A-GP              .A..........................................................  180
PDE4A-H               ............................................................  180

Consensus             FAQVLASLRSVRSNFSLLTNVPIPSNKRSPLGGPTPVCKATLSEETCQQLARETLEELDW  240
PDE4A-M               .........N........................PS........................  235
PDE4A-GP              .........................H..................................  240
PDE4A-H               ......................V.....................................  240
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Consensus              CLEQLETMQTYRSVSEMASHKFKRMLNRELTHLSEMSRSGNQVSEYISTTFLDKQNEVEI  300
PDE4A-M                ................................................N......H....  295
PDE4A-GP               ............................................................  300
PDE4A-H                ............................................................  300

Consensus              PSPTMKXREXQXAPRXRPXQ-PPPPPVPHLQPMSQITGLKKLXHXXSLNNXNIPRFGVKT  359
PDE4A-M                ....PRQ---------..F.Q...AA.QQA............V.TG..-.I.V.......  345
PDE4A-GP               ......D..P.E...Q..C.-QL...............V.R.S.NSG...AS........  359
PDE4A-H                ......E..K.Q...P..S.-.....................M.SN....S.........  359

Consensus              DQEELLAQELENLSKWGLNIFCVSDYAGGRSLSCIMYTIFQERDLLKKFHIPVDTMVTYM  419
PDE4A-M                ...D....................E...............................M...  405
PDE4A-GP               ...........................................................V  419
PDE4A-H                .............N..................T....M...........R..........  419

Consensus              LTLEDHYHADVAYHNSLHAADVLQSTHVLLATPALDAVFTDLEILAALFAAAIHDVDHPG  479
PDE4A-M                ............................................................  465
PDE4A-GP               ........S...................................................  479
PDE4A-H                ............................................................  479

Consensus              VSNQFLINTNSELALMYNDESVLENHHLAVGFKLLQEENCDIFQNLSKRQRQSLRKMVID  539
PDE4A-M                ............................................................  525
PDE4A-GP               ............................................................  539
PDE4A-H                .....................................D......................  539

Consensus              MVLATDMSKHMTLLADLKTMVETKKVTSSGVLLLDNYSDRIQVLRNMVHCADLSNPTKPL  599
PDE4A-M                ............................................................  585
PDE4A-GP               ............................................................  599
PDE4A-H                ............................................................  599

Consensus              ELYRQWTDRIMAEFFQQGDRERERGMEISPMCDKHTASVEKSQVGFIDYIVHPLWETWAD  659
PDE4A-M                ............................................................  645
PDE4A-GP               ............................................................  659
PDE4A-H                ............................................................  659

Consensus              LVHPDAQDILDTLEDNRDWYYSAIRQSPSPPPEEEPXGLXHPALPDKFQFELTLEEEEEE  719
PDE4A-M                ....................H.........TL....GV.SD................D..  705
PDE4A-GP               ..............E.....................S..R.C.P.E..............  719
PDE4A-H                .......E...........................SR.PG..P.................  719

Consensus              EX-XXAQXPCTXXXXLXXXGXXXVEEX---------------XXVMXQEAXXGXLPAXLE  763
PDE4A-M                DSLEVPGL...EETL.APHDTR--------------------AQA.E.SKVK.QS..VV.  745
PDE4A-GP               .A-CL..DS------MKTL.SFR...L---------------GK..G...ET.H..RG.A  757
PDE4A-H                .I-SM..I...AQEA.TAQ.LSG...ALDATIAWEASPAQESLE..A...S---.E.E..  775

Consensus              XVXXXXQ--XTXSAPXAP------EE---XSXXAXXXXLSLESPLLPALRTLSXSEEAPG  812
PDE4A-M                VAESLK.--E.A..HG..------.----E.AE.VGHSF...TSI..D.....P....Q.  793
PDE4A-GP               S.CVV--------P.M.Q------..----.VD.GSCD.......R.....Q.TP..S..  799
PDE4A-H                A.YLTQ.AQS.G...V..DEFSSR..FVVAVSHSSPSA.A.Q......W....V..H...  835

Consensus              LPGLPSMAAEVEAQRDHQAAXRACSACXGTSGEDXAXLPAPGGWGSGGDPX           863
PDE4A-M                .L...........P...L..M......S....DNS.VIS...R.......A           844
PDE4A-GP               P..........G........T...CT.T...W..P.I..V.S..E.....P           850
PDE4A-H                ......T........E....K......A..F...TSA......G......T           886
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**PLN**
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Consensus            MEKVQYLTRSAIRRASTIEMPQQARQNLQNLFINFCLILICLLLICIIVMLL  52
PLN-H                ..........................K.........................  52
PLN-M                ....................................................  52
PLN-R                ....................................................  52
PLN-GP               .....H..............................................  52


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**Ryr2**
-------------------------------------------------------------------------------
Consensus            MADGGEGEDEIQFLRTDDEVVLQCTATIHKEQQKLCLAAEGFGNRLCFLESTSNSKNVPP    60
RYR2-H               ............................................................    60
RYR2-M               ...A........................................................    60
RYR2-R               ............................................................    60
RYR2-GP              ---------------------------------------------MIQ.YNHDLAQ....    15

Consensus            DLSICTFVLEQSLSVRALQEMLANTVEKSEGQVDVEKWKFMMKTAQGGGHRTLLYGHAIL   120
RYR2-H               ............................................................   120
RYR2-M               ............................................................   120
RYR2-R               ............................................................   120
RYR2-GP              ............................................................    75

Consensus            LRHSYSGMYLCCLSTSRSSTDKLAFDVGLQEDTTGEACWWTIHPASKQRSEGEKVRVGDD   180
RYR2-H               ............................................................   180
RYR2-M               ............................................................   180
RYR2-R               ............................................................   180
RYR2-GP              ............................................................   135

Consensus            LILVSVSSERYLHLSYGNGSLHVDAAFQQTLWSVAPISSGSEAAQGYLIGGDVLRLLHGH   240
RYR2-H               ............................................................   240
RYR2-M               ..................S.W.......................................   240
RYR2-R               ............................................................   240
RYR2-GP              .................T..........................................   195

Consensus            MDECLTVPSGEHGEEQRRTVHYEGGAVSVHARSLWRLETLRVAWSGSHIRWGQPFRLRHV   300
RYR2-H               ............................................................   300
RYR2-M               ............................................................   300
RYR2-R               ............................................................   300
RYR2-GP              ............................................................   255

Consensus            TTGKYLSLMEDKNLLLMDKEKADVKSTAFTFRSSKEKLDVGVRKEVDGMGTSEIKYGDSX   360
RYR2-H               ...........................................................V   360
RYR2-M               .............................A.............................I   360
RYR2-R               .......................................G...................I   360
RYR2-GP              ........L...............................S..................V   315

Consensus            CYIQHVDTGLWLTYQSVDVKSVRMGSIQRKAIMHHEGHMDDGLNLSRSQHEESRTARVIR   420
RYR2-H               ..........................................IS................   420
RYR2-M               ...............A.....A......................................   420
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RYR2-R                  ............................................................   420
RYR2-GP                 ............................................................   375

Consensus               STVFLFNRFIRGLDALSKKXKAXTVDLPIESVSLSLQDLIGYFHPPDEHLEHEDKQNRLR   480
RYR2-H                  ...................A..S.....................................   480
RYR2-M                  ...................V.LP.I...................................   480
RYR2-R                  ...................A..SS....................................   480
RYR2-GP                 ...................V.VPA....................................   435

Consensus               ALKNRQNLFQEEGMINLVLECIDRLHVYSSAAHFADVAGREAGESWKSILNSLYELLAAL   540
RYR2-H                  ............................................................   540
RYR2-M                  ............................................................   540
RYR2-R                  ............................................................   540
RYR2-GP                 ............................................A...............   495

Consensus               IRGNRKNCAQFSGSLDWLISRLERLEASSGILEVLHCVLVESPEALNIIKEGHIKSIISL   600
RYR2-H                  ............................................................   600
RYR2-M                  ............................................................   600
RYR2-R                  ............................................................   600
RYR2-GP                 ............................................................   555

Consensus               LDKHGRNHKVLDVLCSLCVCHGVAVRSNQHLICDNLLPGRDLLLQTRLVNHVSSMRPNIF   660
RYR2-H                  ............................................................   660
RYR2-M                  ............................................................   660
RYR2-R                  ............................................................   660
RYR2-GP                 ............................................................   615

Consensus               LGVSEGSAQYKKWYYELMVDHTEPFVTAEATHLRVGWASTEGYSPYPGGGEEWGGNGVGD   720
RYR2-H                  ............................................................   720
RYR2-M                  ............................................................   720
RYR2-R                  ............................................................   720
RYR2-GP                 ..I.........................................................   675

Consensus               DLFSYGFDGLHLWSGCIARTVSSPNQHLLRTDDVISCCLDLSAPSISFRINGQPVQGMFE   780
RYR2-H                  ............................................................   780
RYR2-M                  ............................................................   780
RYR2-R                  ............................................................   780
RYR2-GP                 .............................K..............................   735

Consensus               NFNIDGLFFPVVSFSAGIKVRFLLGGRHGEFKFLPPPGYAPCYEAVLPKEKLKVEHSREY   840
RYR2-H                  ............................................................   840
RYR2-M                  ........................................A...................   840
RYR2-R                  ............................................................   840
RYR2-GP                 ............................................................   795

Consensus               KQERTYTRDLLGPTVSLTQAAFTPIPVDTSQIVLPPHLERIREKLAENIHELWVMNKIEL   900
RYR2-H                  ............................................................   900
RYR2-M                  ........................V..................R................   900
RYR2-R                  ............................................................   900
RYR2-GP                 .............................T..............................   855

Consensus               GWQYGPVRDDNKRQHPCLVEFSKLPEQERNYNLQMSLETLKTLLALGCHVGISDEHAEEK   960
RYR2-H                  ..........................................................D.   960
RYR2-M                  .....................C..............................A.......   960
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RYR2-R                    ............................................................  960
RYR2-GP                   ...................................................L........  915

Consensus                 VKKMKLPKNYQLTSGYKPAPMDLSFIKLTPSQEAMVDKLAENAHNVWARDRIRQGWTYGI 1020
RYR2-H                    ............................................................ 1020
RYR2-M                    ............................................................ 1020
RYR2-R                    ............................................................ 1020
RYR2-GP                   ..............................A......R......................  975

Consensus                 QQDVKNRRNPRLVPYTLLDDRTKKSNKDSLREAVRTLLGYGYNLEAPDQDHAARAEVCSG 1080
RYR2-H                    ............................................................ 1080
RYR2-M                    ..........................................H.........S....... 1080
RYR2-R                    ............................................................ 1080
RYR2-GP                   ............................................................ 1035

Consensus                 TGERFRIFRAEKTYAVKAGRWYFEFEAVTAGDMRVGWSRPGCQPDQELGSDERAFAFDGF 1140
RYR2-H                    ..........................T................................. 1140
RYR2-M                    .............................................L.....D........ 1140
RYR2-R                    .............................S.............................. 1140
RYR2-GP                   ............................................................ 1095

Consensus                 KAQRWHQGNEHYGRSWQAGDVVGCMVDMNEHTMMFTLNGEILLDDSGSELAFKDFDVGDG 1200
RYR2-H                    ............................................................ 1200
RYR2-M                    ............................................................ 1200
RYR2-R                    ............................................................ 1200
RYR2-GP                   ............................................................ 1155

Consensus                 FIPVCSLGVAQVGRMNFGKDVSTLKYFTICGLQEGYEPFAVNTNRDITMWLSKRLPQFLQ 1260
RYR2-H                    ............................................................ 1260
RYR2-M                    ............................................................ 1260
RYR2-R                    ............................................................ 1260
RYR2-GP                   ...A........................................................ 1215

Consensus                 VPSNHEHIEVTRIDGTIDSSPCLKVTQKSFGSQNSNTDIMFYRLSMPIECAEVFSKTVAG 1320
RYR2-H                    ............................................................ 1320
RYR2-M                    ..................................N.....................S... 1320
RYR2-R                    ..........................................................P. 1320
RYR2-GP                   ...................................S..L..................M.. 1275

Consensus                 GLPGAGLFGPKNDLEDYDADSDFEVLMKTAHGHLVPDRVDKDKEXTKPEFNNHKDYAQEK 1380
RYR2-H                    ............................................A............... 1380
RYR2-M                    ......FY........F.V...................I.....TP.............. 1380
RYR2-R                    ............................................T..A............ 1380
RYR2-GP                   ............................................AS.............. 1335

Consensus                 PSRLKQRFLLRRTKPDYSTSHSARLTEDVLADDRDDYDXLMQTSTYYYSVRIFPGQEPAN 1440
RYR2-H                    ......................................F..................... 1440
RYR2-M                    ...................G.................EY..................... 1440
RYR2-R                    ......................................F..................... 1440
RYR2-GP                   ......................................Y..................... 1395

Consensus                 VWVGWITSDFHQYDTGFDLDRVRTVTVTLGDEKGKVHESIKRSNCYMVCAGESMSPGQGR 1500
RYR2-H                    ............................................................ 1500
RYR2-M                    ............................................................ 1500
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RYR2-R                   ............................................................  1500
RYR2-GP                  ............................................................  1455

Consensus                NN-NGLEIGCVVDAASGLLTFIANGKELSTYYQVEPSTKLFPAVFAQATSPNVFQFELGR  1559
RYR2-H                   ..-.........................................................  1559
RYR2-M                   ..S.........................................................  1560
RYR2-R                   ..-.........................................................  1559
RYR2-GP                  ..-.........................................................  1514

Consensus                IKNVMPLSAGLFKSEHKNPVPQCPPRLHVQFLSHVLWSRMPNQFLKVDVSRISERQGWLV  1619
RYR2-H                   ............................................................  1619
RYR2-M                   ............................................................  1620
RYR2-R                   ............................................................  1619
RYR2-GP                  ............................................................  1574

Consensus                QCLDPLQFMSLHIPEENRSVDILELTEQEELLKFHYHTLRLYSAVCALGNHRVAHALCSH  1679
RYR2-H                   ............................................................  1679
RYR2-M                   ................................Q...........................  1680
RYR2-R                   ............................................................  1679
RYR2-GP                  ............................................................  1634

Consensus                VDEPQLLYAIENKYMPGLLRAGYYDLLIDIHLSSYATARLMMNNEFIVPMTEETKSITLF  1739
RYR2-H                   .............................................Y..............  1739
RYR2-M                   ............................................................  1740
RYR2-R                   ....................T.......................................  1739
RYR2-GP                  ....................S.......................................  1694

Consensus                PDENKKHGLPGIGLSTSLRPRMQFSSPSFVSISNECYQYSPEFPLDILKAKTIQMLTEAV  1799
RYR2-H                   .................................................S..........  1799
RYR2-M                   ......................R...........D.........................  1800
RYR2-R                   ................................N...........................  1799
RYR2-GP                  ....................................................M.......  1754

Consensus                KEGSLHARDPVGGTTEFLFVPLIKLFYTLLIMGIFHNEDLKHILQLIEPSVFKEAATPEE  1859
RYR2-H                   ............................................................  1859
RYR2-M                   ........................................................V...  1860
RYR2-R                   ........................................R............D......  1859
RYR2-GP                  .................................................R......CV..  1814

Consensus                EGDTLEKELSVEDAKLEGAGEEEAKGGKRPKEGLLQMKLPEPVKLQMCLLLQYLCDCQVR  1919
RYR2-H                   .S.........D....Q...........................................  1919
RYR2-M                   ..G.P...I.I.......--........................................  1918
RYR2-R                   ......E.P....T...........M..................................  1919
RYR2-GP                  ...V......T..S........DV.V..A...............................  1874

Consensus                HRIEAIVAFSDDFVAKLQDNQRFRYNEVMQALNMSAALTARKTKEFRSPPQEQINMLLNF  1979
RYR2-H                   ............................................................  1979
RYR2-M                   ...........................................R................  1978
RYR2-R                   ............................................................  1979
RYR2-GP                  ............................................................  1934

Consensus                KDDKSECPCPEEIRDQLLDFHEDLMTHCGIELDEDGSLDGNSDLTIRGRLLSLVEKVTYL  2039
RYR2-H                   ............................................................  2039
RYR2-M                   ........................................SN..................  2038
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RYR2-R        ............................................................  2039
RYR2-GP       ............................................................  1994

Consensus     KKKQAEKPVXSDSXKSSXLQQLISETMVRWAQESVIEDPELVRAMFVLLHRQYDGIGGLV  2099
RYR2-H        .........E...K...T..........................................  2099
RYR2-M        .........A...R.C.S..........................................  2098
RYR2-R        ....T....E...R...T..........................................  2099
RYR2-GP       ....S....A..AK...S................I.........................  2054

Consensus     RALPKTYTINGVSVEDTINLLASLGQIRSLLSVRMGKEEEKLMIRGLGDIMNNKVFYQHP  2159
RYR2-H        ............................................................  2159
RYR2-M        ............................................................  2158
RYR2-R        ............................................................  2159
RYR2-GP       ............................................................  2114

Consensus     NLMRALGMHETVMEVMVNVLGGGESKEITFPKMVANCCRFLCYFCRISRQNQKAMFDHLS  2219
RYR2-H        ............................................................  2219
RYR2-M        ............................................................  2218
RYR2-R        ............................................................  2219
RYR2-GP       ..........................V---------------------------------  2141

Consensus     YLLENSSVGLASPAMRGSTPLDVAAASVMDNNELALALREPDLEKVVRYLAGCGLQSCQM  2279
RYR2-H        ............................................................  2279
RYR2-M        ............................................................  2278
RYR2-R        ............................................................  2279
RYR2-GP       --------KET.................................................  2193

Consensus     LVSKGYPDIGWNPVEGERYLDFLRFAVFCNGESVEENANVVVRLLIRRPECFGPALRGEG  2339
RYR2-H        ............................................................  2339
RYR2-M        ............................................................  2338
RYR2-R        ............................................................  2339
RYR2-GP       ............................................................  2253

Consensus     GNGLLAAMEEAIKIAEDPSRDGPSPTSGSSKTLDTEEEEDDTIHMGNAIMTFYAALIDLL  2399
RYR2-H        .........................N...........................S......  2399
RYR2-M        ..................................I.........................  2398
RYR2-R        ............................................................  2399
RYR2-GP       ............................................................  2313

Consensus     GRCAPEMHLIHAGKGEAIRIRSILRSLIPLGDLVGVISIAFQMPTIAKDGNVVEPDMSAG  2459
RYR2-H        ............................................................  2459
RYR2-M        ..................................................K.........  2458
RYR2-R        ............................................................  2459
RYR2-GP       ............................................................  2373

Consensus     FCPDHKAAMVLFLDRVYGIEVQDFLLHLLEVGFLPDLRAAASLDTAALSATDMALALNRY  2519
RYR2-H        ............................................................  2519
RYR2-M        ............................................................  2518
RYR2-R        ............................................................  2519
RYR2-GP       ............................................................  2433

Consensus     LCTAVLPLLTRCAPLFAGTEHHASLIDSLLHTVYRLSKGCSLTKAQRDSIEVCLLSICGQ  2579
RYR2-H        ............................................................  2579
RYR2-M        ............................................................  2578
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RYR2-R                ............................................................  2579
RYR2-GP               ............................................................  2493

Consensus             LRPSMMQHLLRRLVFDVPLLNEHAKMPLKLLTNHYERCWKYYCLPGGWGNFGAASEEELH  2639
RYR2-H                ............................................................  2639
RYR2-M                ............................................................  2638
RYR2-R                ............................................................  2639
RYR2-GP               ............................................................  2553

Consensus             LSRKLFWGIFDALSQKKYEQELFKLALPCLSAVAGALPPDYMESNYVSMMEKQSSMDSEG  2699
RYR2-H                ............................................................  2699
RYR2-M                ............................................................  2698
RYR2-R                ............................................................  2699
RYR2-GP               ............................................................  2613

Consensus             NFNPQPVDTSNITIPEKLEYFINKYAEHSHDKWSMDKLANGWIYGEIYSDSSKIQPLMKP  2759
RYR2-H                .....................................................V......  2759
RYR2-M                ............................................................  2758
RYR2-R                ............I...............................................  2759
RYR2-GP               ............................................................  2673

Consensus             YKLLSEKEKEIYRWPIKESLKTMLAWGWRIERTREGDSMALYNRTRRISQTSQVSVDAAH  2819
RYR2-H                ............................................................  2819
RYR2-M                .......................................................I....  2818
RYR2-R                ............................................................  2819
RYR2-GP               ............................................................  2733

Consensus             GYSPRAIDMSNVTLSRDLHAMAEMMAENYHNIWAKKKKLELESKGGGNHPLLVPYDTLTA  2879
RYR2-H                ......................................M.....................  2879
RYR2-M                ............................................................  2878
RYR2-R                ............................................................  2879
RYR2-GP               ............................................................  2793

Consensus             KEKAKDREKAQDILKFLQINGYAVSRGFKDLELDTPSIEKRFAYSFLQQLIRYVDEAHQY  2939
RYR2-H                ............................................................  2939
RYR2-M                .............F.....S..V........D............................  2938
RYR2-R                ............................................................  2939
RYR2-GP               ............................................................  2853

Consensus             ILEFDGGSRSKGEHFPYEQEIKFFAKVVLPLIDQYFKNHRLYFLSAASRPLCSGGHASNK  2999
RYR2-H                .........G..................................................  2999
RYR2-M                ....................................................T.......  2998
RYR2-R                ............................................................  2999
RYR2-GP               ............................................................  2913

Consensus             EKEMVTSLFCKLGVLVRHRISLFGNDATSIVNCLHILGQTLDARTVMKTGLESVKSALRA  3059
RYR2-H                ............................................................  3059
RYR2-M                ...................................................D........  3058
RYR2-R                ............................................................  3059
RYR2-GP               ............................................................  2973

Consensus             FLDNAAEDLEKTMENLKQGQFTHTRNQPKGVTQIINYTTVALLPMLSSLFEHIGQHQFGE  3119
RYR2-H                ............................................................  3119
RYR2-M                .........................S..................................  3118
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RYR2-R      ............................R...............................  3119
RYR2-GP     ..........N.................................................  3033

Consensus   DLILEDVQVSCYRILTSLYALGTSKSIYVERQRSALGECLAAFAGAFPVAFLETHLDKHN  3179
RYR2-H      ............................................................  3179
RYR2-M      ................................................I...........  3178
RYR2-R      ........................................................N...  3179
RYR2-GP     ............................................................  3093

Consensus   XYSIYNTKSSRERAALSLPANVEDVCPNIPSLEKLMEEIVELAESGIRYTQMPHVMEVXL  3239
RYR2-H      I..................T......................................I.  3239
RYR2-M      V......R............................T..I.............YM...V.  3238
RYR2-R      I.........................................................I.  3239
RYR2-GP     VH..............N..P......................................V.  3153

Consensus   PMLCSYMSRWWEHGPENNPERAEMCCTALNSEHMNTLLGNILKIIYNNLGIDEGAWMKRL  3299
RYR2-H      ............................................................  3299
RYR2-M      .................H..........................................  3298
RYR2-R      ................S..G........................................  3299
RYR2-GP     .....................S......................................  3213

Consensus   AVFSQPIINKVKPQLLKTHFLPLMEKLKKKAAMVVSEEDHLKAEARGDMSEAELLILDEF  3359
RYR2-H      ................................T...........................  3359
RYR2-M      ............................................................  3358
RYR2-R      ............................................................  3359
RYR2-GP     ...................................A........................  3273

Consensus   TTLARDLYAFYPLLIRFVDYNRAKWLKEPNPEAEELFRMVAEVFIYWSKSHNFKREEQNF  3419
RYR2-H      ............................................................  3419
RYR2-M      ............................................................  3418
RYR2-R      .............................T..............................  3419
RYR2-GP     ............................................................  3333

Consensus   VVQNEINNMSFLITDTKSKMSKAAVSDQERKKMKRKGDRYSMQTSLIVAALKRLLPIGLN  3479
RYR2-H      ............................................................  3479
RYR2-M      ........................I...................................  3478
RYR2-R      ............................................................  3479
RYR2-GP     ............................................................  3393

Consensus   ICAPGDQELIALAKNRFSLKDTEDEVRDIIRSNIHLQGKLEDPAIRWQMALYKDLPNRTE  3539
RYR2-H      ...........................................................D  3539
RYR2-M      .......................E....................................  3538
RYR2-R      ...............................N............................  3539
RYR2-GP     ............................................................  3453

Consensus   DTSDPEXTVERVLDIANVLFHLEQKSKXXGRRYYXLVEHPQRSKKAVWHKLLSKQRKRAV  3599
RYR2-H      ......K....................RV...H.C.........................  3599
RYR2-M      .P....R......G.............YT..G.FS.........................  3598
RYR2-R      E.....K....................FI.....N.........................  3599
RYR2-GP     ......R.................------------........................  3501

Consensus   VACFRMAPLYNLPRHRAVNLFLQGYEKSWIETEEHYFEDKLIEDLAKPGAEPPEEDEATK  3659
RYR2-H      .........................................................G..  3659
RYR2-M      ...................................................L......M.  3658
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RYR2-R         .........................................................V..  3659
RYR2-GP        ..................................................K.......A.  3561

Consensus      RVDPLHQLILLFSRTALTEKCKLEEDFLYMAYADIMAKSCHDEEDDDGEEEVKSFE----  3715
RYR2-H         ........................................................----  3715
RYR2-M         ........................................................----  3714
RYR2-R         ........................................................----  3715
RYR2-GP        ........................................................VTGS  3621

Consensus      ----EKEMEKQKLLYQQARLHDRGAAEMVLQTISASKGETGPMVAATLKLGIAILNGGNS  3771
RYR2-H         ----........................................................  3771
RYR2-M         ----........................................................  3770
RYR2-R         ----........................................................  3771
RYR2-GP        QRSK........................................................  3681

Consensus      TVQQKMLDYLKEKKDVGFFQSLAGLMQSCSVLDLNAFERQNKAEGLGMVTEEGSGEKVLQ  3831
RYR2-H         ............................................................  3831
RYR2-M         ............................................................  3830
RYR2-R         ............................................................  3831
RYR2-GP        ............................................................  3741

Consensus      DDEFTCDLFRFLQLLCEGHNSDFQNYLRTQTGNNTTVNIIISTVDYLLRVQESISDFYWY  3891
RYR2-H         ............................................................  3891
RYR2-M         ............................................................  3890
RYR2-R         ............................................................  3891
RYR2-GP        ............................................................  3801

Consensus      YSGKDVIDEQGQRNFSKAIQVAKQVFNTLTEYIQGPCTGNQQSLAHSRLWDAVVGFLHVF  3951
RYR2-H         ............................................................  3951
RYR2-M         .....I......................................................  3950
RYR2-R         ............................................................  3951
RYR2-GP        ............................................................  3861

Consensus      AHMQMKLSQDSSQIELLKELMDLQKDMVVMLLSMLEGNVVNGTIGKQMVDMLVESSNNVE  4011
RYR2-H         ............................................................  4011
RYR2-M         ............................................................  4010
RYR2-R         ............................................................  4011
RYR2-GP        ............................................................  3921

Consensus      MILKFFDMFLKLKDLTSSDTFKEYDPDGKGVISKRDFHKAMESHKHYTQSETEFLLSCAE  4071
RYR2-H         ............................................................  4071
RYR2-M         ............................................................  4070
RYR2-R         ..............................I.............................  4071
RYR2-GP        ............................................................  3981

Consensus      TDENETLDYEEFVKRFHEPAKDIGFNVAVLLTNLSEHMPNDTRLQTFLELAESVLNYFQP  4131
RYR2-H         ............................................................  4131
RYR2-M         ............................................................  4130
RYR2-R         ........................................E...................  4131
RYR2-GP        ............................................................  4041

Consensus      FLGRIEIMGSAKRIERVYFEISESSRTQWEKPQVKESKRQFIFDVVNEGGEKEKMELFVN  4191
RYR2-H         ............................................................  4191
RYR2-M         ............................................................  4190
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RYR2-R               ............................................................  4191
RYR2-GP              ............................................................  4101

Consensus            FCEDTIFEMQLAAQISESDLNERSANKEESEKERPEEQGPRMGFFSILTVRSALFALRYN  4251
RYR2-H               ..........................................A.................  4251
RYR2-M               .......................L..............A.......L..IQ.........  4250
RYR2-R               ........................................K.....V.............  4251
RYR2-GP              ........................T.........L...................L.....  4161

Consensus            ILTLMRMLSLKSLKKQMKKMKKMTVKDMVTAFFSSYWSXFXTLLHFVASVXRGFFRIVCS  4311
RYR2-H               ...................V..................I.M.........F......I..  4311
RYR2-M               V...V.............R..........L........V.V.........C.......S.  4310
RYR2-R               ......................................I.M.........F.........  4311
RYR2-GP              ........................M.............V.V.........C.........  4221

Consensus            LLLGGSLVEGAKKIKVAELLANMPDPTQDEVRGDGEEGERKPXETALPSEDLTDLKELTE  4371
RYR2-H               ..........................................L.A...............  4371
RYR2-M               ..................................E.......L.S...............  4370
RYR2-R               ..........................................M..T..............  4371
RYR2-GP              ..........................................M..P............A.  4281

Consensus            ESDLLSDIFGLDLKREGGQYKLIPHNPNAGLSDLMSNPVPIPEVQEKFQEQKXKEEEKEE  4431
RYR2-H               ........................................M...........A.......  4431
RYR2-M               ...................................T....V...........A..-....  4429
RYR2-R               .......................................L...E........T.......  4431
RYR2-GP              ...............................G....................T.......  4341

Consensus            KEETKSEPEKAEGEDGEKEEKAKEDKGKQKLRQLHTHRYGEPEVPESAFWKKIIAYQQKL  4491
RYR2-H               ............................................................  4491
RYR2-M               .......................DE.S.................................  4489
RYR2-R               .....................V......................................  4491
RYR2-GP              ............................................................  4401

Consensus            LNYFARNFYNMRMLALFVAFAINFILLFYKVSTSSVVEGKELPTRSSSENAKVTTSLDSS  4551
RYR2-H               .....................................................-......  4550
RYR2-M               .............................................T..DT....N.....  4549
RYR2-R               ...........................................S..T.............  4551
RYR2-GP              .................................A..A.........P..S..........  4461

Consensus            SHRIIAVHYVLEESSGYMEPTLRILAILHTVISFFCIIGYYCLKVPLVIFKREKEVARKL  4611
RYR2-H               ............................................................  4610
RYR2-M               P.............................I.............................  4609
RYR2-R               ............................................................  4611
RYR2-GP              ............................................................  4521

Consensus            EFDGLYITEQPSEDDIKGQWDRLVINTQSFPNNYWDKFVKRKVMDKYGEFYGRDRISELL  4671
RYR2-H               ............................................................  4670
RYR2-M               ............................................................  4669
RYR2-R               ............................................................  4671
RYR2-GP              ............................................................  4581

Consensus            GMDKAALDFSDAREKKKPKKDSSLSAVLNSIDVKYQMWKLGVVFTDNSFLYLAWYMTMSV  4731
RYR2-H               ............................................................  4730
RYR2-M               ............................................................  4729
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RYR2-R                ...........................................................I  4731
RYR2-GP               ............................................................  4641

Consensus             LGHYNNFFFAAHLLDIAMGFKTLRTILSSVTHNGKQLVLTVGLLAVVVYLYTVVAFNFFR  4791
RYR2-H                ............................................................  4790
RYR2-M                ............................................................  4789
RYR2-R                ............................................................  4791
RYR2-GP               ............................................................  4701

Consensus             KFYNKSEDGDTPDMKCDDMLTCYMFHMYVGVRAGGGIGDEIEDPAGDEYEIYRIIFDITF  4851
RYR2-H                ............................................................  4850
RYR2-M                ............................................................  4849
RYR2-R                ............................................................  4851
RYR2-GP               ............................................................  4761

Consensus             FFFVIVILLAIIQGLIIDAFGELRDQQEQVKEDMETKCFICGIGNDYFDTVPHGFETHTL  4911
RYR2-H                ............................................................  4910
RYR2-M                ............................................................  4909
RYR2-R                ............................................................  4911
RYR2-GP               ............................................................  4821

Consensus             QEHNLANYLFFLMYLINKDETEHTGQESYVWKMYQERCWEFFPAGDCFRKQYEDQLN     4968
RYR2-H                .........................................................     4967
RYR2-M                .........................................................     4966
RYR2-R                .........................................................     4968
RYR2-GP               .........................................................     4878


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**SCN1A**
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Consensus   MEQTVLVPPGPDSFNFFTRESLAAIERRIAEEKAKNPKPDKKDDDENGPKPNSDLEAGKN    60
SCN1A-H     ............................................................    60
SCN1A-M     ............................................................    60
SCN1A-GP    ............................................................    60
SCN1A-R     ............................................................    60

Consensus   LPFIYGDIPPEMVSEPLEDLDPYYINKKTFIVLNKGKAIFRFSATSALYILTPFNPLRKI   120
SCN1A-H     ............................................................   120
SCN1A-M     ............................................................   120
SCN1A-GP    ............................................................   120
SCN1A-R     ............................................................   120

Consensus   AIKILVHSL----------------FSMLIMCTILTNCVFMTMSNPPDWTKNVEYTFTGI   164
SCN1A-H     .........----------------...................................   164
SCN1A-M     .........----------------...................................   164
SCN1A-GP    ........YPFQVININYFYIIDNPLP.................................   180
SCN1A-R     .........----------------...................................   164

Consensus   YTFESLIKIIARGFCLEDFTFLRDPWNWLDFTVITFAYVTEFVDLGNVSALRTFRVLRAL   224
SCN1A-H     ............................................................   224
SCN1A-M     ............................................................   224
SCN1A-GP    ............................................................   240
SCN1A-R     ............................................................   224
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Consensus   KTISVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCXQWPPTN   284
SCN1A-H     .....................................................I......   284
SCN1A-M     .....................................................V......   284
SCN1A-GP    .....................................................V......   300
SCN1A-R     .....................................................I......   284

Consensus   ASLEEHSIEKNITVDYNGTLVNETVFEFDWKSYIQDSRYHYFLEGXLDALLCGNSSDAGQ   344
SCN1A-H     ..............N.....I........................F..............   344
SCN1A-M     .............M...............................V..............   344
SCN1A-GP    .........................Y...................F..............   360
SCN1A-R     ...............N...I................T........V..............   344

Consensus   CPEGYMCVKAGRNPNYGYTSFDTFSWAFLSLFRLMTQDFWENLYQLTLRAAGKTYMIFFV   404
SCN1A-H     ............................................................   404
SCN1A-M     ............................................................   404
SCN1A-GP    ............................................................   420
SCN1A-R     ............................................................   404

Consensus   LVIFLGSFYLINLILAVVAMAYEEQNQATLEEAEQKEAEFQQMLEQLKKQQEAAQQAAAX   464
SCN1A-H     ...........................................I..............TA   464
SCN1A-M     ...........................................................T   464
SCN1A-GP    ...........................................................A   480
SCN1A-R     ...........................................................T   464

Consensus   TASEHSREPSAAGRLSDSSSEASKLSSKSAKERRNRRKKRKQKEQSGGEEKDEDEFXKSE   524
SCN1A-H     ........................................................Q...   524
SCN1A-M     ....................................................D...H...   524
SCN1A-GP    .V......................................................H...   540
SCN1A-R     ........................................................Q...   524

Consensus   SEDSIRRKGFRFSIEGNRLTYEKRYSSPHQSLLSIRGSLFSPRRNSRTSLFSFRGRAKDV   584
SCN1A-H     ............................................................   584
SCN1A-M     ............................................................   584
SCN1A-GP    ............................................................   600
SCN1A-R     ............................................................   584

Consensus   GSENDFADDEHSTFEDNESRRDSLFVPRRHGERRNSNLSQTSRSSRMLAVFPANGKMHST   644
SCN1A-H     ............................................................   644
SCN1A-M     ............................................................   644
SCN1A-GP    ............................................................   660
SCN1A-R     ...........................................................S   644

Consensus   VDCNGVVSLVGGPSVPTSPVGQLLPEVIIDKPATDDNGTTTETEMRKRRSSSFHVSMDFL   704
SCN1A-H     ............................................................   704
SCN1A-M     ............................................................   704
SCN1A-GP    ............................................................   720
SCN1A-R     ............................................................   704

Consensus   EDPSQRQRAMSIASILTNTVEELEESRQKCPPCWYKFSNIFLIWDCSPYWLKVKHIVNLV   764
SCN1A-H     .......................................................V....   764
SCN1A-M     ............................................................   764
SCN1A-GP    .......................................................F....   780
SCN1A-R     ............................................................   764
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Consensus    VMDPFVDLAITICIVLNTLFMAMEHYPMTEHFNNVLTVGNLVFTGIFTAEMFLKIIAMDP   824
SCN1A-H      .............................D..............................   824
SCN1A-M      .................................H..........................   824
SCN1A-GP     ............................................................   840
SCN1A-R      ....................................A.......................   824

Consensus    YYYFQEGWNIFDGFIVTLSLVELGLANVEGLSVLRSFRLLRVFKLAKSWPTLNMLIKIIG   884
SCN1A-H      ............................................................   884
SCN1A-M      ............................................................   884
SCN1A-GP     ..........................D.................................   900
SCN1A-R      ............................................................   884

Consensus    NSVGALGNLTLVLAIIVFIFAVVGMQLFGKSYKDCVCKIASDCKLPRWHMNDFFHSFLIV   944
SCN1A-H      ...........................................Q................   944
SCN1A-M      ........................................T...................   944
SCN1A-GP     ............................................................   960
SCN1A-R      ............................................................   944

Consensus    FRVLCGEWIETMWDCMEVAGQAMCLTVFMMVMVIGNLVVLNLFLALLLSSFSADNLAATD  1004
SCN1A-H      ............................................................  1004
SCN1A-M      ............................................................  1004
SCN1A-GP     ............................................................  1020
SCN1A-R      ............................................................  1004

Consensus    DDNEMNNLQIAVDRMHKGIAYVKRKIYEFIQQSFVRKQKILDEIKPLDDLNNKKDSCMSN  1064
SCN1A-H      ..................V...............I.........................  1064
SCN1A-M      ...................................K................R..N.I..  1064
SCN1A-GP     ..............I.................A....K......................  1080
SCN1A-R      ............................................................  1064

Consensus    HTAEIGKDLDYLKDVNGTTSGIGTGSSVEKYIIDESDYMSFINNPSLTVTVPIAVGESDF  1124
SCN1A-H      ............................................................  1124
SCN1A-M      ..T.......C.................................................  1124
SCN1A-GP     ..G.....I...R...............................................  1140
SCN1A-R      ............................................................  1124

Consensus    ENLNTEDFSSESDLEESKEKLNESSSSSEGSTVDIGAPAEEQPVVEPEETLEPEACFTEG  1184
SCN1A-H      ......................................V.....................  1184
SCN1A-M      ............................................I...............  1184
SCN1A-GP     ............................................................  1200
SCN1A-R      ............................................................  1184

Consensus    CVQRFKCCQISVEEGRGKQWWNLRRTCFRIVEHNWFETFIVFMILLSSGALAFEDIYIDQ  1244
SCN1A-H      ..........N.................................................  1244
SCN1A-M      ............................................................  1244
SCN1A-GP     .........V..................................................  1260
SCN1A-R      ............................................................  1244

Consensus    RKTIKTMLEYADKVFTYIFILEMLLKWVAYGYQTYFTNAWCWLDFLIVDVSLVSLTANAL  1304
SCN1A-H      ............................................................  1304
SCN1A-M      ............................................................  1304
SCN1A-GP     ..................................................E..LVEKIE-  1319
SCN1A-R      ............................................................  1304
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Consensus   GYSELGAIKSLRTLRALRPLRALSRFEGMRVVVNALLGAIPSIMNVLLVCLIFWLIFSIM  1364
SCN1A-H     ............................................................  1364
SCN1A-M     ............................................................  1364
SCN1A-GP    --------------------------KLKT..............................  1353
SCN1A-R     ............................................................  1364

Consensus   GVNLFAGKFYHCXNTTTGDMFEISEVNNHSDCLKLIERNETARWKNVKVNFDNVGFGYLS  1424
SCN1A-H     ............I......R.D.ED....T..............................  1424
SCN1A-M     ............V......I........................................  1424
SCN1A-GP    ............V...............................................  1413
SCN1A-R     ............I..........T....................................  1424

Consensus   LLQVATFKGWMDIMYAAVDSRNVELQPKYEESLYMYLYFVIFIIFGSFFTLNLFIGVIID  1484
SCN1A-H     ............................................................  1484
SCN1A-M     ............................................................  1484
SCN1A-GP    ............................................................  1473
SCN1A-R     ............................................................  1484

Consensus   NFNQQKKKFGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRPGNKFQGMVFDFVTRQVFD  1544
SCN1A-H     ............................................................  1544
SCN1A-M     ............................................................  1544
SCN1A-GP    ........I-S.................................................  1532
SCN1A-R     ............................................................  1544

Consensus   ISIMILICLNMVTMMVETDDQSXYVTNILSRINLVFIVLFTGECVLKLISLRHYYFTIGW  1604
SCN1A-H     ......................E...T.................................  1604
SCN1A-M     ......................D...S.................................  1604
SCN1A-GP    ......................E.M......................M............  1592
SCN1A-R     ......................D.....................................  1604

Consensus   NIFDFVVVILSIVGMFLAELIEKYFVSPTLFRVIRLARIGRILRLIKGAKGIRTLLFALM  1664
SCN1A-H     ............................................................  1664
SCN1A-M     ............................................................  1664
SCN1A-GP    ............................................................  1652
SCN1A-R     ............................................................  1664

Consensus   MSLPALFNIGLLLFLVMFIYAIFGMSNFAYVKREVGIDDMFNFETFGNSMICLFQITTSA  1724
SCN1A-H     ............................................................  1724
SCN1A-M     ............................................................  1724
SCN1A-GP    ............................................................  1712
SCN1A-R     ............................................................  1724

Consensus   GWDGLLAPILNSKPPDCDPNKVNPGSSVKGDCGNPSVGIFFFVSYIIISFLVVVNMYIAV  1784
SCN1A-H     ............................................................  1784
SCN1A-M     ............................................................  1784
SCN1A-GP    ............G...............................................  1772
SCN1A-R     ............................................................  1784

Consensus   ILENFSVATEESAEPLSEDDFEMFYEVWEKFDPDATQFMEFEKLSQFAAALEPPLNLPQP  1844
SCN1A-H     ............................................................  1844
SCN1A-M     ............................................................  1844
SCN1A-GP    ............................................................  1832
SCN1A-R     ............................................................  1844
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Consensus   NKLQLIAMDLPMVSGDRIHCLDILFAFTKRVLGESGEMDALRIQMEERFMASNPSKVSYQ  1904
SCN1A-H     ............................................................  1904
SCN1A-M     ............................................................  1904
SCN1A-GP    ............................................................  1892
SCN1A-R     ............................................................  1904

Consensus   PITTTLKRKQEEVSAVIIQRAYRRHLLKRTVKQASFTYNKNKJKGGANLLVKEDMIIDRI  1964
SCN1A-H     ..........................................I.......I.........  1964
SCN1A-M     ..........................................L............L....  1964
SCN1A-GP    ..........................................L.................  1952
SCN1A-R     ..........................................I.S...............  1964

Consensus   NENSITEKTDLTMSTAACPPSYDRVTKPIVEKHEQEGKDEKAKGK                 2009
SCN1A-H     .............................................                 2009
SCN1A-M     .............................................                 2009
SCN1A-GP    ................V............................                 1997
SCN1A-R     .............................................                 2009


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**SCN3A**
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Consensus   MAQALLVPPGPESFRLFTRESLAAIEKRAAEEKAKKPKKEQDNDDENKPKPNSDLEAGKN    60
SCN3A-GP    ..........................................-.................    59
SCN3A-M     ..........................................I.................    60
SCN3A-R     ...T........................................................    60
SCN3A-H     ............................................................    60

Consensus   LPFIYGDIPPEMVSEPLEDLDPYYINKKTFIVLNKGKAIFRFSATSALYILTPLNPVRKI   120
SCN3A-GP    ...............................................F------------   107
SCN3A-M     ........................VS....V.............................   120
SCN3A-R     .....................S......................................   120
SCN3A-H     ................................M...........................   120

Consensus   AIKILVHSLFSMLIMCTILTNCVFMTLSNPPDWTKNVEYTFTGIYTFESLIKILARGFCL   180
SCN3A-GP    -----------.................................................   156
SCN3A-M     ............................................................   180
SCN3A-R     ............................................................   180
SCN3A-H     ............................................................   180

Consensus   EDFTFLRDPWNWLDFSVIVMAYVTEFVXLGNVSALRTFRVLRALKTISVIPGLKTIVGAL   240
SCN3A-GP    ...........................S................................   216
SCN3A-M     ...........................D................................   240
SCN3A-R     ...........................D................................   240
SCN3A-H     ...........................S................................   240

Consensus   IQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCLQWPPSDSAFETNTTSYFNGTMD   300
SCN3A-GP    ...........................................N........T.......   276
SCN3A-M     ................................................I...........   300
SCN3A-R     ........................................................S...   300
SCN3A-H     ............................................................   300

Consensus   SNGTFVNVTMSTFNWKDYIGDDSHFYVLDGQKDPLLCGNGSDAGQCPEGYICVKAGRNPN   360
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SCN3A-GP    .....I......................................H...............   336
SCN3A-M     ...................A........................................   360
SCN3A-R     .........TN..D.................N............................   360
SCN3A-H     ............................................................   360

Consensus   YGYTSFDTFSWAFLSLFRLMTQDYWENLYQLTLRAAGKTYMIFFVLVIFLGSFYLVNLIL   420
SCN3A-GP    ............................................................   396
SCN3A-M     ............................................................   420
SCN3A-R     ............................................................   420
SCN3A-H     ............................................................   420

Consensus   AVVAMAYEEQNQATLEEAEQKEAEFQQMLEQLKKQQEEAQAVAAASAASRDFSGIGGLGE   480
SCN3A-GP    ............................................................   456
SCN3A-M     ............................................................   480
SCN3A-R     ............................................................   480
SCN3A-H     ............................................................   480

Consensus   LLESSSEASKLSSKSAKEWRNRRKKRRQREHLEGNNXGEXDRFPKSESEDSVKRRSFLFS   540
SCN3A-GP    .............................D.S..H.R..A....................   516
SCN3A-M     ...................................HRP.G....................   540
SCN3A-R     ...............................F...SK..E....................   540
SCN3A-H     ....................................K..R.S............S.....   540

Consensus   MDGNRLXXDKKFCSPHQSLLSIRGSLFSPRRNSKTSIFSFRGRAKDVGSENDFADDEHST   600
SCN3A-GP    ......SS............................V......T................   576
SCN3A-M     L...P.SG...L................................................   600
SCN3A-R     ......TG....................................................   600
SCN3A-H     ......TS....................................................   600

Consensus   FEDSESRRDSLFVPHRHGERRNSNVSQASMSSRMVPGLPANGKMHSTVDCNGVVSLVGGP   660
SCN3A-GP    ..............P.........................D...................   636
SCN3A-M     ................P.......------------------------------------   624
SCN3A-R     ............................................................   660
SCN3A-H     ............................................................   660

Consensus   SALTSPTGQLQPEGTTTETEVRKRRLSSYQISMEMLEDSSGRQRAMSIASILTNTMEELE   720
SCN3A-GP    .V......PF..................................................   696
SCN3A-M     -------------...............................................   671
SCN3A-R     ...................D........................................   720
SCN3A-H     ..........P..................................V..............   720

Consensus   ESRQKCPPCWYRFANVFLIWDCCXAWLKVKHLVNLIVMDPFVDLAITICIVLNTLFMAME   780
SCN3A-GP    .......................E....................................   756
SCN3A-M     .......................DS...................................   731
SCN3A-R     .......................E......R.............................   780
SCN3A-H     .......................D....................................   780

Consensus   HYPMTXQFSSVLTVGNLVFTGIFTAEMVLKIIAMDPYYYFQEGWNIFDGIIVSLSLMELG   840
SCN3A-GP    .....D......................................................   816
SCN3A-M     .....E......................................................   791
SCN3A-R     .....D......A...............................................   840
SCN3A-H     .....E......................................................   840

Consensus   LANVEGLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVG   900
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SCN3A-GP     ............................................................   876
SCN3A-M      ............................................................   851
SCN3A-R      ............................................................   900
SCN3A-H      .S..........................................................   900

Consensus    MQLFGKSYKECVCKINEDCXLPRWHMNDFFHSFLIVFRVLCGEWIETMWDCMEVAGQTMC   960
SCN3A-GP     ...................T........................................   936
SCN3A-M      ...................K........................................   911
SCN3A-R      ...............SS..K........................................   960
SCN3A-H      ................D..T........................................   960

Consensus    LIVFMLVMVIGNLVVLNLFLALLLSSFSSDNLAATDDDNEMNNLQIAVGRMQKGIDYVKN  1020
SCN3A-GP     ...............................................I........F...   996
SCN3A-M      ............................................................   971
SCN3A-R      ...........................................................D  1020
SCN3A-H      ............................................................  1020

Consensus    KIRECFXKAFFRKPKVIEIHEGNKIDSCMSNNTGI-EISKELNYLKDGNGTTSGVGTGSS  1079
SCN3A-GP     ......Q..........................A.-........................  1055
SCN3A-M      ......R...........................VV........................  1031
SCN3A-R      ..Q...R......S..L........E..I......-........................  1079
SCN3A-H      .M....Q............................-.........R..............  1079

Consensus    VEKYVIDENDYMSFINNPSLTVTVPIAVGESDFENLNTEEFSSESELEESKEKLNATSSS  1139
SCN3A-GP     ............................................................  1115
SCN3A-M      ............................................................  1091
SCN3A-R      ............................................................  1139
SCN3A-H      ............................................................  1139

Consensus    EGSTVDVAPPREGEQAEXEPEEDLKPEACFTEGCIKKFPFCQVSTEEGKGKIWWNLRKTC  1199
SCN3A-GP     .................T..........................................  1175
SCN3A-M      .................I..........................................  1151
SCN3A-R      .................I..........................................  1199
SCN3A-H      .......VL........T..........................................  1199

Consensus    YSIVEHNWFETFIVFMILLSSGALAFEDIYIEQRKTIKTMLEYADKVFTYIFILEMLLKW  1259
SCN3A-GP     ............................................................  1235
SCN3A-M      ............................................................  1211
SCN3A-R      ............................................................  1259
SCN3A-H      ............................................................  1259

Consensus    VAYGFQTYFTNAWCWLDFLIVDVSLVSLVANALGYSELGAIKSLRTLRALRPLRALSRFE  1319
SCN3A-GP     ............................................................  1295
SCN3A-M      ............................................................  1271
SCN3A-R      .........................................R..................  1319
SCN3A-H      ............................................................  1319

Consensus    GMRVVVNALVGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFYHCVNMTTGNMFDVSEVN  1379
SCN3A-GP     ......................................................E.....  1355
SCN3A-M      ...................................................S...M....  1331
SCN3A-R      ....................................................R...K...  1379
SCN3A-H      .......................................................I.D..  1379

Consensus    NFSDCQALGKQARWKNVKVNFDNVGAGYLALLQVATFKGWMDIMYAAVDSRDVKLQPVYE  1439
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SCN3A-GP    ............................................................  1415
SCN3A-M     ............................................................  1391
SCN3A-R     .W.......N..................................................  1439
SCN3A-H     .L..........................................................  1439

Consensus   ENLYMYLYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKKFGGQDIFMTEEQKKYYNAMKKL  1499
SCN3A-GP    K.....................................I-S...................  1474
SCN3A-M     ............................................................  1451
SCN3A-R     ............................................................  1499
SCN3A-H     ............................................................  1499

Consensus   GSKKPQKPIPRPANKFQGMVFDFVTRQVFDISIMILICLNMVTMMVETDDQSKYMTLVLS  1559
SCN3A-GP    ............S...............................................  1534
SCN3A-M     ............................................................  1511
SCN3A-R     ...............L............................................  1559
SCN3A-H     ...................................................G........  1559

Consensus   RINLVFIVLFTGEFVLKLXSLRYYYFTIGWNIFDFVVVILSIVGMFLAEXIEKYFVSPTL  1619
SCN3A-GP    ..................I..............................M..........  1594
SCN3A-M     ..............L...I..............................L..........  1571
SCN3A-R     ..................V..............................L..........  1619
SCN3A-H     ..................V...H..........................M..........  1619

Consensus   FRVIRLARIGRILRLIKGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYAIFGMSNFAY  1679
SCN3A-GP    ............................................................  1654
SCN3A-M     ............................................................  1631
SCN3A-R     ............................................................  1679
SCN3A-H     ............................................................  1679

Consensus   VKKEAGIDDMFNFETFGNSMICLFQITTSAGWDGLLAPILNSAPPDCDPDXIHPGSSVKG  1739
SCN3A-GP    ..................................................A.........  1714
SCN3A-M     ..................................................A.........  1691
SCN3A-R     ..................................................T.........  1739
SCN3A-H     ..................................................T.........  1739

Consensus   DCGNPSVGIFFFVSYIIISFLVVVNMYIAVILENFSVATEESAEPLSEDDFEMFYEVWEK  1799
SCN3A-GP    ............................................................  1774
SCN3A-M     ............................................................  1751
SCN3A-R     ............................................................  1799
SCN3A-H     ............................................................  1799

Consensus   FDPDATQFIEFXKLSDFAAALDPPLLIAKPNKVQLIAMDLPMVSGDRIHCLDILFAFTKR  1859
SCN3A-GP    ...........C................................................  1834
SCN3A-M     ...........C................................................  1811
SCN3A-R     ...........S................................................  1859
SCN3A-H     ...........S................................................  1859

Consensus   VLGESGEMDALRIQMEDRFMASNPSKVSYEPITTTLKRKQEEVSAAIIQRNXRCYLLKQR  1919
SCN3A-GP    ...................................................F........  1894
SCN3A-M     ...................................................Y........  1871
SCN3A-R     ...................................................Y........  1919
SCN3A-H     ...................................................F........  1919

Consensus   LKNISSKYDKEXIKGRIDLPIKXDMXIDKLNGNSTPEKTDGSSSTTSPPSYDSVTKPDKE  1979
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SCN3A-GP    ...........T..........D..V..................................  1954
SCN3A-M     .....NT....T.....V....G..V..................................  1931
SCN3A-R     ..K........A..........E..I..................................  1979
SCN3A-H     ......N.N..A..........Q..I..................................  1979

Consensus   KFEKDKPEKESKGKEVRENQK                                         2000
SCN3A-GP    .....................                                         1975
SCN3A-M     ................-----                                         1947
SCN3A-R     ......T..............                                         2000
SCN3A-H     .....................                                         2000


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**SCN4A**
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Consensus MASSSLPTLVPLGPECLRPFTRESLAAIEQRAVEEEARLQRNKQMEIEEPERKPRSDLEA    60
SCN4A-M   ...........P..H......P..........M...........................    60
SCN4A-R   ........V....................R........Q.......V.............    60
SCN4A-H   ..RP..C.....................................................    60
SCN4A-GP  -MA..AVPNL....P.............................................    59

Consensus GKNLPLIYGDPPPEVIGIPLEDLDPYYSDKKTFIVLNKGKAIFRFSATPALYMLSPFSXV   120
SCN4A-M   .................V........................................I.   120
SCN4A-R   .............T...........................................NI.   120
SCN4A-H   .....M......................N.......................L.....V.   120
SCN4A-GP  ......................I...................................V.   119

Consensus RRGAIKVLIHXLFSMFIMITILTNCVFMTMSBPPPWSKNVEYTFTGIYTFESLIKMLARG   180
SCN4A-M   ..V.......A....................N..S...D.....................   180
SCN4A-R   ..C.......S....................N..A.........................   180
SCN4A-H   ..........A....................D.......................I....   180
SCN4A-GP  ..........S....................D............................   179

Consensus FCIDDFTFLRDPWNWLDFSVITMAYXTEFVDLGNISALRTFRVLRALKTITVIPGLKTIV   240
SCN4A-M   .........................V..................................   240
SCN4A-R   .........................L..................................   240
SCN4A-H   ..V..................M...L..................................   240
SCN4A-GP  .....................L...V..................................   239

Consensus GALIQSVKKLSDVMILTVFCLSVFALVGLQLFMGNLRQKCVRWPPPFNDTNTTWYGNDTW   300
SCN4A-M   ..............................................M.............   300
SCN4A-R   ............................................................   300
SCN4A-H   .......................................................S....   300
SCN4A-GP  ...................................................A..S.....   299

Consensus YGNDTWYGX------DTWYXNDTWNSHESWASNYTFDWDAYINDEGNFYFLEGXNDALLC   354
SCN4A-M   ........N------....G......Q...V..S....E..............S......   354
SCN4A-R   ......DD-----------------GR..........................A......   343
SCN4A-H   ........NEMWYGN.S..A.......A...T.D........S..........S......   360
SCN4A-GP  ..T------------....S.Y..G......................Y.....A......   347

Consensus GNSSDAGHCPEGYECXKAGRNPNYGYTSYDTFSWAFLALFRLMTQDYWENLFQLTLRAAG   414
SCN4A-M   ...............M............................................   414
SCN4A-R   ...............I............................................   403
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SCN4A-H   ...............I.T..........................................   420
SCN4A-GP  ...............M............................................   407

Consensus KTYMIFFVVIIFLGSFYLINLILAVVAMAYAEQNEATLAEDQEKEEEFQQMLEKFKKXQE   474
SCN4A-M   .........................................................H..   474
SCN4A-R   .........................................................Q..   463
SCN4A-H   .........................................K...............H..   480
SCN4A-GP  .........................................................Q..   467

Consensus EXEKAKAAQALEGGE-ADGDPXHXKDCNGSLDTS-GEKGXPRXSCSAESAISDAMEELEE   532
SCN4A-M   .L.............E.....T.S..........-....P..P.................   533
SCN4A-R   .Q.............-.A...T.S.........AP....A..Q.................   522
SCN4A-H   .L.............-.....A.G..........Q....A..Q.S.GD.G..........   539
SCN4A-GP  .Q...........VG-....LA.G..........-....P..P.................   525

Consensus AHQKCPPWWYKCAHKVLIWNCCAPWVKFKXIIHLIVMDPFVDLGITICIVLNTLFMAMEH   592
SCN4A-M   .............................H..L...........................   593
SCN4A-R   ......................T......N.V............................   582
SCN4A-H   .........................L...N..............................   599
SCN4A-GP  ..............T.......V......H..Y...........................   585

Consensus YPMTEHFDNVLSVGNLVFTGIFTAEMVLKLIAMDPYEYFQQGWNIFDSIIVTLSLVELGL   652
SCN4A-M   ................................................F...........   653
SCN4A-R   ............................................................   642
SCN4A-H   ...........T................................................   659
SCN4A-GP  .....Q..........................L...........................   645

Consensus ANVQGLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGM   712
SCN4A-M   ............................................................   713
SCN4A-R   ............................................................   702
SCN4A-H   ............................................................   719
SCN4A-GP  ............................................................   705

Consensus QLFGKSYKECVCKIASDCXLPRWHMHDFFHSFLIVFRILCGEWIETMWDCMEVAGQAMCL   772
SCN4A-M   ..................S.........................................   773
SCN4A-R   ...............A..S......Y..................................   762
SCN4A-H   ...............L..N.........................................   779
SCN4A-GP  ..................N.........................................   765

Consensus TVFLMVMVIGNLVVLNLFLALLLSSFSADSLAASDEDGEMNNLQIAIGRIKWGIGFAKAF   832
SCN4A-M   ......................................................A...T.   833
SCN4A-R   ...............................................A............   822
SCN4A-H   ...................................................L........   839
SCN4A-GP  ..................................................R.........   825

Consensus LLGLLHGKILSPKDIMLSLGEPGGAGEAGEAGESAPEDEKKEPPPE-EEXXDLKKDNHIL   891
SCN4A-M   ...........L...............---N...P...........DGN--KEL......   888
SCN4A-R   I.........................G.........G.........E..DK.......F.   882
SCN4A-H   .....................AD..........T..........E.-----.........   894
SCN4A-GP  .W..........NE..........T.....................-..DK.........   884

Consensus NHVGLADGPPSSIELDHLNFINNPYLTIQVPIASEESDLEMPTEEETDTFSEPEDSKKPL   951
SCN4A-M   .....T...R....M.............H..........................I....   948
SCN4A-R   ..........PG................................................   942
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SCN4A-H    ..M.........L..............................................P   954
SCN4A-GP   ......N.S..T...........................................G....   944

Consensus  QPLYDGNSSVCSTADYKPPEEDPEEQAEENPEGEQPEECFTEACVQRCPCLYVDISQGRG  1011
SCN4A-M    ..................................L..........K..............  1008
SCN4A-R    ..P-...........................D.................F..........  1001
SCN4A-H    ...............................................W............  1014
SCN4A-GP   ...............................................F............  1004

Consensus  KMWWTLRRACFKIVEHNWFETFIVFMILLSSGALAFEDIYIEQRRVIRTILEYADKVFTY  1071
SCN4A-M    ...............................................Q............  1068
SCN4A-R    .Q.....................................H....................  1061
SCN4A-H    .K..........................................................  1074
SCN4A-GP   ............................................................  1064

Consensus  IFIMEMLLKWVAYGFKVYFTNAWCWLDFLIVDVSIISLVANWLGYSELGPIKSLRTLRAL  1131
SCN4A-M    ...L........................................................  1128
SCN4A-R    ...V........................................................  1121
SCN4A-H    ............................................................  1134
SCN4A-GP   ............................................................  1124

Consensus  RPLRALSRFEGMRVVVNALLGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFYYCINTTT  1191
SCN4A-M    ............................................................  1188
SCN4A-R    ............................................................  1181
SCN4A-H    ............................................................  1194
SCN4A-GP   .......................................................M....  1184

Consensus  SERFDISEVNNKSECESLMHTGQVRWLNVKVNYDNVGLGYLSLLQVATFKGWMDIMYAAV  1251
SCN4A-M    .......V...........Y......M.................................  1248
SCN4A-R    .....V......................................................  1241
SCN4A-H    ............................................................  1254
SCN4A-GP   ............................................................  1244

Consensus  DSREKEEQPQYEVNLYMYLYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKKFGGKDIFMTE  1311
SCN4A-M    .........D..................................................  1308
SCN4A-R    .........A..................................................  1301
SCN4A-H    ..................................................L.........  1314
SCN4A-GP   ....Q.......................................................  1304

Consensus  EQKKYYNAMKKLGSKKPQKPIPRPQNKIQGMVYDXVTKQVFDITIMILICLNMVTMMVET  1371
SCN4A-M    ..................................F........S................  1368
SCN4A-R    .............A....................L..Q.M...I................  1361
SCN4A-H    ..................................L....A....................  1374
SCN4A-GP   ..............................-...F.........................  1363

Consensus  DDQSQLKVDILYNINMXFIXIFTGECVLKMXALRQYYFTXGWNIFDFVVVILSIVGLALS  1431
SCN4A-M    ................V..IV.........F...H....I....................  1428
SCN4A-R    ....E...........V..V..........L........V....................  1421
SCN4A-H    .N..............I..I..........L........V....................  1434
SCN4A-GP   ................I..V..........F........I....................  1423

Consensus  DLIQKYFVSPTLFRVIRLARIGRVLRLIRGAKGIRTLLFALMMSLPALFNIGLLLFLVMF  1491
SCN4A-M    ............................................................  1488
SCN4A-R    ............................................................  1481
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SCN4A-H   ............................................................  1494
SCN4A-GP  ............................................................  1483

Consensus IYSIFGMSNFAYVKKESGIDDMFNFETFGNSIICLFEITTSAGWDGLLNPILNSGPPDCD  1551
SCN4A-M   ............................................................  1548
SCN4A-R   ............................................................  1541
SCN4A-H   ............................................................  1554
SCN4A-GP  ............................................................  1543

Consensus PTLENPGTSVKGDCGNPSIGICFFCSYIIISFLIVVNMYIAIILENFNVATEESSEPLGE  1611
SCN4A-M   ........NI................................................C.  1608
SCN4A-R   ..........R.................................................  1601
SCN4A-H   .N..........................................................  1614
SCN4A-GP  ............................................................  1603

Consensus DDFEMFYETWEKFDPDATQFIDYSRLSDFVDTLQEPLRIAKPNKIKLITLDLPMVPGDKI  1671
SCN4A-M   .....................................K......................  1668
SCN4A-R   .......................C....................................  1661
SCN4A-H   .....................A......................................  1674
SCN4A-GP  ............................................................  1663

Consensus HCLDILFALTKEVLGDSGEMDALKQTMEEKFMAANPSKVSYEPITTTLKRKHEEVCAIKI  1731
SCN4A-M   ...................................................Q........  1728
SCN4A-R   ........................E...................................  1721
SCN4A-H   ............................................................  1734
SCN4A-GP  ............................................................  1723

Consensus QRAYRRHLLQRSVKQASYMYRHSQDGNGDXX-GAPEKEGLJANTMSKMYGPENGDSSVQS  1790
SCN4A-M   ........................E....---........L....N....S.KE.NG...  1785
SCN4A-R   .....................RG.N.G..GD-E.......I.DS.........R...AH.  1780
SCN4A-H   ............M..........H..S..---D.......L.........H...N..SP.  1791
SCN4A-GP  ............L................GDG........I..A..Q.......KT....  1783

Consensus QGEE-KGSTXDAGPXMGLXPISPSD---------TXLPPXPPPGQTVRPGVKESLV      1836
SCN4A-M   ...KE.D..E....TTEVTAP.S..TALTPPPPSPPP.SS..Q.............      1841
SCN4A-R   .EL.-...PE....AV..Q.G..P.---------.E.LAA.ALR............      1826
SCN4A-H   -P..-..EAG....T...M......---------.AW..A................      1836
SCN4A-GP  ..Q.-E...G.T.LA...V..N...---------.T...S................      1829


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**SCN5A**
--------------------------------------------------------------------------------
Consensus MANFLLPRGTSSFRRFTRESLAAIEKRMAEKQARGSATSQESREGLPEEEAPRPQLDLQA    60
SCN5A-R   ...L......G..........................A.....A................    60
SCN5A-GP  ............................................................    60
SCN5A-H   ....................................T.L.....................    60
SCN5A-M   ............................................................    60

Consensus SKKLPDLYGNPPRELIGEPLEDLDPFYSTQKTFIVLNKGKTIFRFSATNALYVLSPFHPX   120
SCN5A-R   ....................................................L......I   120
SCN5A-GP  ....................................................I......V   120
SCN5A-H   ............Q..............................................I   120
SCN5A-M   ...........................................................V   120
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Consensus RRAAVKILVHSLFSMLIMCTILTNCVFMAQHDPPPWTKYVEYTFTAIYTFESLVKILARG   180
SCN5A-R   ..............L...........................A.................   180
SCN5A-GP  ............................................................   180
SCN5A-H   .............N..............................................   180
SCN5A-M   ............................................................   180

Consensus FCLHAFTFLRDPWNWLDFSVIXMAYTTEFVDLGNVSALRTFRVLRALKTISVISGLKTIV   240
SCN5A-R   .....................V...............................A......   240
SCN5A-GP  .....................I...VS.NIK...L..................P......   240
SCN5A-H   .....................I......................................   240
SCN5A-M   .....................V......................................   240

Consensus GALIQSVKKLADVMVLTVFCLSVFALIGLQLFMGNLRHKCVRNFTALNXTNGSVEADGLV   300
SCN5A-R   ................................................D...........   300
SCN5A-GP  ................................................D.......E...   300
SCN5A-H   ................................................G...........   300
SCN5A-M   .............................................E..G.........I.   300

Consensus WNSLDLYLNDPXNYLLKNGTSDVLLCGNSSDAGTCPEGYRCLKAGENPDHGYTSFDSFAW   360
SCN5A-R   .....D.....G................................................   360
SCN5A-GP  .K......R..V.................................D..............   360
SCN5A-H   .E......S..E................................................   360
SCN5A-M   .....V.....A........T.......................................   360

Consensus AFLALFRLMTQDCWERLYQQTLRSAGKIYMIFFMLVIFLGSFYLVNLILAVVAMAYEEQN   420
SCN5A-R   ............................................................   420
SCN5A-GP  ............................................................   420
SCN5A-H   ............................................................   420
SCN5A-M   ............................................................   420

Consensus QATIAETEEKEKRFQEAMEMLKKEHEALTIRGVDTVSRSSLEMSPLAPVTNHERRSKRRK   480
SCN5A-R   ......S..............R......A.Q.........R........A..........   480
SCN5A-GP  ............................................................   480
SCN5A-H   .................................................NS.........   480
SCN5A-M   ............................................................   480

Consensus RXSSGTEECGDDRLPKSDSEDGPRAXNHLSLTRGLSRTSMXPRSSRGSIFTFRRRDLGSE   540
SCN5A-R   VL...........V.....D.....L...G.P..P..S.GR.......L...........   540
SCN5A-GP  .M.........E.F...........M..R.----.....VK...................   536
SCN5A-H   .M........E..............M..............K...................   540
SCN5A-M   .L.....DG................L.Q....H.......R...............Q...   540

Consensus ADFADDENSTAGESESHRTSLLVPWPLRRPSXQGQPXPGTSAPGHXLNGKRNSTVDCNGV   600
SCN5A-R   ...............................T...LG-----...A..............   595
SCN5A-GP  T...........D..............H...A....S.VA...S.VF.S...........   596
SCN5A-H   .................H...........T.A....S........A.H..K.........   600
SCN5A-M   ...............................T....GF.......V..............   600

Consensus VSLLGAGDAEATSPGSHLLRPXXLERPPDTTTPSEEPGGPQMLTPQAPCXDGFEEPGARQ   660
SCN5A-R   .....T............R..GVP...A.............V.S....GV..........   655
SCN5A-GP  ........T..M....R....MM..........................A..........   656
SCN5A-H   ........P............VM..H..................S....V..........   660
SCN5A-M   .....................IV.D........................A..........   660
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Consensus RALSAVSVLTSALEELEESXRKCPPCWNRFAQRYLIWECCPLWMSIKQKVKFVVMDPFAD   720
SCN5A-R   ...................R........H....C.........LAV..------------   703
SCN5A-GP  ...........V.......H.......I...K...........I................   716
SCN5A-H   ...................RH........L..................G..L......T.   720
SCN5A-M   ...................H............H...........................   720

Consensus LTITMCIVLNTLFMALEHYNMTXEFEEMLQVGNLVFTGIFTAEMTFKIIALDPYYYFQQG   780
SCN5A-R   ----------------------------------..........................   729
SCN5A-GP  ......................T.....................................   776
SCN5A-H   ......................S.....................................   780
SCN5A-M   ......................A.....................................   780

Consensus WNIFDSIIVILSLMELGLSRMGNLSVLRSFRLLRVFKLAKSWPTLNTLIKIIGNSVGALG   840
SCN5A-R   ............................................................   789
SCN5A-GP  ............................................................   836
SCN5A-H   .....................S......................................   840
SCN5A-M   ............................................................   840

Consensus NLTLVLAIIVFIFAVVGMQLFGKNYSELRHRISDSGLLPRWHMMDFFHAFLIIFRILCGE   900
SCN5A-R   ...........................Q......A.........................   849
SCN5A-GP  ...................................D........................   896
SCN5A-H   .............................D--............................   898
SCN5A-M   ............................................................   900

Consensus WIETMWDCMEVSGQSLCLLVFLLVMVIGNLVVLNLFLALLLSSFSADNLTAPDEDGEMNN   960
SCN5A-R   ............................................................   909
SCN5A-GP  ............................................................   956
SCN5A-H   .......................................................R....   958
SCN5A-M   ............................................................   960

Consensus LQLALARIQRGLRFVKRTTWDFCCGLLRQRPKKPAALAXHXQLPSCIAAPRSPPPPEVEK  1020
SCN5A-R   ...............R..AR.C.R....-..P..T...TCGP..P.V...S......A..   968
SCN5A-GP  ............H.L............Q........PTA.S.....MTS......A....  1016
SCN5A-H   ...............................Q......AQG.......T.Y......T..  1018
SCN5A-M   ............................R.........T.S...................  1020

Consensus APPARKETRFEEGKRPGQGTPGDPEPVCVPIAVAESDTDDQEEDEENSLGTEEESSXXQE  1080
SCN5A-R   P...H........R...E.A......M...........E.P..G.DD...S..D.-SKP.  1027
SCN5A-GP  ............S.H.......E....................ED...........KQ..  1076
SCN5A-H   V..T.........EQ.........................................KQ..  1078
SCN5A-M   ............D..........T..............................E.SK..  1080

Consensus SQPVSGGPEXPXEPRAWSQVSETXSSEAEASASQADWRQQRKAEPQAPGCGETXEDSYSE  1140
SCN5A-R   ......D..G.P......R....A.........R..GW.R.P..AG.A..P..H......  1087
SCN5A-GP  .....D...H.Q....R..G...TT....TGV...N.............SS..H......  1136
SCN5A-H   .........A.PDS.T.....A.A................W............P...C..  1138
SCN5A-M   ..V....H.P.Q...........T.......T.....Q.E.E...R.......P......  1140

Consensus GSTADMTNTADLLEQIPDLGEDVKDPEDCFTEGCVRRCPCCAVDTTQAPGKVWWRLRKTC  1200
SCN5A-R   ............M..........R....................V..G............  1147
SCN5A-GP  ...................................Q........................  1196
SCN5A-H   ..........E.........Q.......................................  1198
SCN5A-M   .........................................M..................  1200
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Consensus  YRIVEHSWFETFIIFMILLSSGALAFEDIYLEERKTIKVLLEYADKMFTYVFVLEMLLKW  1260
SCN5A-R    ..........S........................A..A.................V...  1207
SCN5A-GP   ............................................................  1256
SCN5A-H    .H..........................................................  1258
SCN5A-M    ............................................................  1260

Consensus  VAYGFKKYFTNAWCWLDFLIVDVSLVSLVANTLGFAEMGPIKSLRTLRALRPLRALSRFE  1320
SCN5A-R    ..........S..........A.............S........................  1267
SCN5A-GP   ............................................................  1316
SCN5A-H    ............................................................  1318
SCN5A-M    ............................................................  1320

Consensus  GMRVVVNALVGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFGRCINQTEGDLPLNYTIV  1380
SCN5A-R    ....................................................V...H.V.  1327
SCN5A-GP   ............................................................  1376
SCN5A-H    ............................................................  1378
SCN5A-M    ............................................................  1380

Consensus  NNKSECESFNVTGELYWTKVKVNFDNVGAGYLALLQVATFKGWMDIMYAAVDSRGYEEQP  1440
SCN5A-R    ............................................................  1387
SCN5A-GP   ......K...M.................................................  1436
SCN5A-H    ....Q...L.L.................................................  1438
SCN5A-M    ............................................................  1440

Consensus  QWEYNLYMYIYFVXFIIFGSFFTLNLFIGVIIDNFNQQKKKLGGQDIFMTEEQKKYYNAM  1500
SCN5A-R    ...N.........I...........................-------------------  1428
SCN5A-GP   .............V..............................................  1496
SCN5A-H    .............I..............................................  1498
SCN5A-M    ...D.........V..............................................  1500

Consensus  KKLGSKKPQKPIPRPLNKYQGFIFDIVTKQAFDVTIMFLICLNMVTMMVETDDQSPEKVN  1560
SCN5A-R    ------------------------------------------------------------  1428
SCN5A-GP   ...............V......L.....................................  1556
SCN5A-H    ..........................................................I.  1558
SCN5A-M    ............................................................  1560

Consensus  ILAKINLLFVAIFTGECIVKMAALRHYYFTNSWNIFDFVVVILSIVGTVLSDIIQKYFFS  1620
SCN5A-R    ---------------------------------------A....................  1449
SCN5A-GP   .....................T......................................  1616
SCN5A-H    ....................L.......................................  1618
SCN5A-M    ............................................................  1620

Consensus  PTLFRVIRLARIGRILRLIRGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYSIFGMAN  1680
SCN5A-R    ..............V......................................A......  1509
SCN5A-GP   ............................................................  1676
SCN5A-H    ............................................................  1678
SCN5A-M    ............................................................  1680

Consensus  FAYVKWEAGIDDMFNFQTFANSMLCLFQITTSAGWDGLLSPILNTGPPYCDPNLPNSNGS  1740
SCN5A-R    ....................................................S..TGS..  1569
SCN5A-GP   ........................................................N...  1736
SCN5A-H    ....................................................T.......  1738
SCN5A-M    ............................................................  1740
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Consensus RGNCGSPAVGILFFTTYIIISFLIVVNMYIAIILENFSVATEESTEPLSEDDFDMFYEIW  1800
SCN5A-R   ............................................................  1629
SCN5A-GP  ............................................................  1796
SCN5A-H   ..D.........................................................  1798
SCN5A-M   ............................................................  1800

Consensus EKFDPEATQFIEYSALSDFADALSEPLRIAKPNQISLINMDLPMVSGDRIHCMDILFAFT  1860
SCN5A-R   ................PA................L...S.....................  1689
SCN5A-GP  ............................................................  1856
SCN5A-H   ..............V.............................................  1858
SCN5A-M   .............L..............................................  1860

Consensus KRVLGESGEMDALKIQMEEKFMAANPSKISYEPITTTLRRKHEEVSATVIQRAFRRHLLQ  1920
SCN5A-R   ............................................................  1749
SCN5A-GP  ............................................................  1916
SCN5A-H   ...............................................M............  1918
SCN5A-M   ............................................................  1920

Consensus RSLKHASFLFRQQAGSXGLSEEDAPEREGLIAYMMXENFSRXXGPPSSSSISSTSFPPSY  1980
SCN5A-R   ...R........R...G.............L.RT.S.H.A.SP...C...V.....S...  1809
SCN5A-GP  ..M.............G..................N.....HDR.A..............  1976
SCN5A-H   ...............-S................V.S.....PL.................  1977
SCN5A-M   ..V.............S...D..............N.....RS..L..............  1980

Consensus DSVTRATSDNLXVRXSDYSXSEDLADFPPSPDRDRESIV                       2019
SCN5A-R   ...........P.A-..C.R..E....LLVS......V.                       1847
SCN5A-GP  ...........Q..V....H........A..E.......                       2015
SCN5A-H   ...........Q..G....H...................                       2016
SCN5A-M   ...........P..A....R...................                       2019


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**Slc8a1**
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Consensus            MYNMLRLSLSPTFSMGFHLLAXVALLFSHVDHXTAETEMEGEGNETGECTGSYYCKKGVI   60
SLC8A1-M             ---......P.NV....R.V.L..........I..D..A.TG....T.............   57
SLC8A1-H             ....R...............VT.S........VI..........................   60
SLC8A1-GP            ---.........Y.L......MMT..I.....I......VE...................   57
SLC8A1-R             ---.P.F....P.........I...F.FR...VS..........................   57

Consensus            LPIWEPQDPSFGDKIARATVYFVAMVYMFLGVSIIADRFMSSIEVITSQEKEITIKKPNG  120
SLC8A1-M             ............................................................  117
SLC8A1-H             ............................................................  120
SLC8A1-GP            ............................................................  117
SLC8A1-R             ............................................................  117

Consensus            ETTKTTVRIWNETVSNLTLMALGSSAPEILLSVIEVCGHNFTAGDLGPSTIVGSAAFNMF  180
SLC8A1-M             ............................................................  177
SLC8A1-H             ............................................................  180
SLC8A1-GP            ............................................................  177
SLC8A1-R             ............................................................  177

Consensus            IIIALCVYVVPDGETRKIKHLRVFFVTAAWSIFAYTWLYIILSVISPGVVEVWEGLLTFF  240
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SLC8A1-M      ............................................S............... 237
SLC8A1-H      ............................................................ 240
SLC8A1-GP     ............................................................ 237
SLC8A1-R      ................................................I........... 237

Consensus     FFPICVVFAWVADRRLLFYKYVYKRYRAGKQRGMIIEHEGDRPSSKTEIEMDGKVVNSHV 300
SLC8A1-M      ...........................................A................ 297
SLC8A1-H      ............................................................ 300
SLC8A1-GP     ............................................................ 297
SLC8A1-R      ............................................................ 297

Consensus     XNFLDGALVLEVDERDQDDEEARREMARILKELKQKHPEKEIEQLIELANYQVLSQQQKS 360
SLC8A1-M      D........................................................... 357
SLC8A1-H      E.....................................D..................... 360
SLC8A1-GP     E........................................................... 357
SLC8A1-R      D.........D................................................. 357

Consensus     RAFYRIQATRLMTGAGNILKRHAADQARKAVSMHEVNTEXAENDPVSKIFFEQGTYQCLE 420
SLC8A1-M      .....................................M.M.................... 417
SLC8A1-H      .......................................VT................... 420
SLC8A1-GP     .......................................V.................... 417
SLC8A1-R      .......................................M.................... 417

Consensus     NCGTVALTIIRRGGDLTNTVFVDFRTEDGTANAGSDYEFTEGTVVFKPGETQKEIRVGII 480
SLC8A1-M      .........M......ST..........................I............... 477
SLC8A1-H      .................................................D.......... 480
SLC8A1-GP     ............................................................ 477
SLC8A1-R      ............................................................ 477

Consensus     DDDIFEEDENFLVHLSNVKVSSEASEDGILEANHISTLACLGSPSTATVTIFDDDHAGIF 540
SLC8A1-M      ..................R...DV.......S..A.SI..........I........... 537
SLC8A1-H      ..................................V......................... 540
SLC8A1-GP     ............................................................ 537
SLC8A1-R      .......................T....................C............... 537

Consensus     TFEEPVTHVSESIGIMEVKVLRTSGARGNVIVPYKTIEGTARGGGEDFEDTCGELEFQND 600
SLC8A1-M      ...............................I............................ 597
SLC8A1-H      ............................................................ 600
SLC8A1-GP     ............................................................ 597
SLC8A1-R      ....S....................................................... 597

Consensus     EIVKTISVKVIDDEEYEKNKTFFLEIGEPRLVEMSEKKALLLNELGGFTITGKXLYGQPV 660
SLC8A1-M      .......................I.........................L...EM....I 657
SLC8A1-H      .....................................................Y.F.... 660
SLC8A1-GP     .....................................................H...... 657
SLC8A1-R      ....I.TIRIF.R.....ECSLS.VLE..KWIRRG-M.............---------- 646

Consensus     FRKVHARDHPIPSTVITIAXEYDDKQPLTSKEEEERRIAEMGRPILGEHTKLEVIIEESY 720
SLC8A1-M      ..................SE........................................ 717
SLC8A1-H      .......E...L.......D........................................ 720
SLC8A1-GP     L..................D....................L................... 717
SLC8A1-R      ------------------TE........................................ 688

Consensus     EFKSTVDKLIKKTNLALVVGTNSWREQFIEAITVSAGEDDDDDECGEEKLPSCFDYVMHF 780
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SLC8A1-M             ............................................................  777
SLC8A1-H             ............................................................  780
SLC8A1-GP            ............................................................  777
SLC8A1-R             ............................................................  748

Consensus            LTVFWKVLFAFVPPTEYWNGWACFIVSILMIGLLTAFIGDLASHFGCTIGLKDSVTAVVF  840
SLC8A1-M             ............................................................  837
SLC8A1-H             ............................................................  840
SLC8A1-GP            ............................................................  837
SLC8A1-R             ............................................................  808

Consensus            VALGTSVPDTFASKVAATQDQYADASIGNVTGSNAVNVFLGIGVAWSIAAIYHAANGEQF  900
SLC8A1-M             ............................................................  897
SLC8A1-H             ............................................................  900
SLC8A1-GP            ............................................................  897
SLC8A1-R             ..........................................................H.  868

Consensus            KVSPGTLAFSVTLFTIFAFINVGVLLYRRRPEIGGELGGPRTAKLLTSCLFVLLWLLYIF  960
SLC8A1-M             ................................................S...........  957
SLC8A1-H             ............................................................  960
SLC8A1-GP            ............................................................  957
SLC8A1-R             ............................................................  928

Consensus            FSSLEAYCHIKGF                                                 973
SLC8A1-M             .............                                                 970
SLC8A1-H             .............                                                 973
SLC8A1-GP            .............                                                 970
SLC8A1-R             .............                                                 941

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**Stim1**
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Consensus   MDVCARLALWLLWGLLLHQGQSLSHSHSEKATGAXSGATSEESTAAEFCRIDKPLCHSED   60
STIM1-H     ....V............................TS...N.....................   60
STIM1-M     ..............................N...S.........E...............   60
STIM1-R     ..............F.V..............A..G.....................D...   60
STIM1-GP    .N............................V...G.........................   60

Consensus   EKLSFEAVRNIHKLMDDDANGDVDVEESDEFLREDLNYHDPTVKHSTFHGEDKLISVEDL  120
STIM1-H     ............................................................  120
STIM1-M     ............................................................  120
STIM1-R     ............................................................  120
STIM1-GP    .Q..........................................................  120

Consensus   WKAWKSSEVYNWTVDEVVQWLITYVELPQYEETFRKLQLSGHAMPRLAVTNTTMTGTVLK  180
STIM1-H     ............................................................  180
STIM1-M     .................I.....................T....................  180
STIM1-R     ............................................................  180
STIM1-GP    ............................................................  180

Consensus   MTDRSHRQKLQLKALDTVLFGPPLLTRHNHLKDFMLVVSIVIGVGGCWFAYIQNRYSKEH  240
STIM1-H     ............................................................  240
STIM1-M     ............................................................  240
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STIM1-R     ............................................................  240
STIM1-GP    ............................................................  240

Consensus   MKKMMKDLEGLHRAEQSLHDLQERLHKAQEEHRTVEVEKVHLEKKLRDEINLAKQEAQRL  300
STIM1-H     ............................................................  300
STIM1-M     ............................................................  300
STIM1-R     ............................................................  300
STIM1-GP    ............................................................  300

Consensus   KELREGTENERSRQKYAEEELEQVREALRKAEKELESHSSWYAPEALQKWLQLTHEVEVQ  360
STIM1-H     ............................................................  360
STIM1-M     ............................................................  360
STIM1-R     ............................................................  360
STIM1-GP    ............................................................  360

Consensus   YYNIKKQNAEKQLLVAKEGAEKIKKKRNTLFGTFHVAHSSSLDDVDHKILTAKQALSEVT  420
STIM1-H     ............................................................  420
STIM1-M     ..........R.................................................  420
STIM1-R     ............................................................  420
STIM1-GP    ............................................................  420

Consensus   AALRERLHRWQQIEILCGFQIVNNPGIHSLVAALNIDPSWMGSTRPNPAHFIMTDDVDDM  480
STIM1-H     ............................................................  480
STIM1-M     ............................................................  480
STIM1-R     ............................................................  480
STIM1-GP    ...............................T............................  480

Consensus   DEEIVSPLSMQSPSLQSSVRQRLTEPQHGLGSQRDLTHSDSESSLHMSDRQRVAPKPPQM  540
STIM1-H     ............................................................  540
STIM1-M     ...........................L................................  540
STIM1-R     .........................S..........................M.......  540
STIM1-GP    ..............................................T......V......  540

Consensus   GRAADEALNAMPSNGSHRLIEGVHPGSLVEKLPDSPALAKKXLLALNHGLDKAHSLMELS  600
STIM1-H     S..........T.............................A..................  600
STIM1-M     .........................................TFM...............N  600
STIM1-R     V.T...V....I..S...........P...........T..TV.................  600
STIM1-GP    ........S......................Q.........A..................  600

Consensus   PSAPPGGSPXLDSSRSHSPSSPDPDTPSPVGDSRAXQXSRNTRIPHLAGKKAVAEEDNGS  660
STIM1-H     .........H.........................L.A......................  660
STIM1-M     ..V......L....H.L...............N..L.G..............M.......  660
STIM1-R     A.XXXXXXX.XXXXXXXXXXXXXXXXXXXX------X.XXXXQTR..SWG----QAEPAG  650
STIM1-GP    .....S...V..........P..............---.............V........  657

Consensus   IGEETDSSPGRKKFPLKIFKKPLKK                                     685
STIM1-H     .........................                                     685
STIM1-M     .........................                                     685
STIM1-R     QPQH.H....WQEGCG---------                                     666
STIM1-GP    .........................                                     682


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**Stim2**
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Consensus   MNVAGTRAPEAAGAEGTRLAPGRSPRRGRPEESPAAAPHGAGEWPAVGAAAPLPRPHPAA   60
STIM2-H     ------------------------------------------------------------
STIM2-M     ------------------------------------------------------------
STIM2-R     ............................................................   60
STIM2-GP    ------------------------------------------------------------

Consensus   TPGSASGWLRRRRRWAXMLLLGLLVAG-AADGC---ELVPRHLRGRRASGSAGAAASSSA  116
STIM2-H     -----------------..V.......-.....---............T...AT....P.   39
STIM2-M     -----------------...F......-V....---D....................P..   39
STIM2-R     ................AL.........-.....---..G...............G....S  116
STIM2-GP    ----------------MIK..EIVN..GLKTA.FRCHCLALF.H---------WTILRRQ   35

Consensus   AAAGESPALMTDPCMSLSPPCFTEEDRFSLEALQTIHKQMDDDKDGGIEVDESDEFIRED  176
STIM2-H     ....D.............................................E.........   99
STIM2-M     .....RQ..L..................................................   99
STIM2-R     ............................................................  176
STIM2-GP    .SL.LPLI.YY............D....................................   95

Consensus   MKYKDATNKHSHLHREDKHITVEDLWKQWKTSEVHNWTLEDTLQWLIEFVELPQYEKNFR  236
STIM2-H     .....................I.....R................................  159
STIM2-M     ............................................................  159
STIM2-R     ............................................................  236
STIM2-GP    ......................................V...I.................  155

Consensus   DNNVKGTTLPRIAVHEXSFMISQLKISDRSHRQKLQLKALDVVLFGPLTRPPHNWMKDFI  296
STIM2-H     ................P...........................................  219
STIM2-M     ................T...........................................  219
STIM2-R     ................P...........................................  296
STIM2-GP    .S..R..........DT.....H........................P............  215

Consensus   LTVSIVIGVGGCWFAYTQNKTSKEHVAKMMKDLESLQTAEQSLMDLQERLEKAQEENRNV  356
STIM2-H     ............................................................  279
STIM2-M     ..I......................................................T.  279
STIM2-R     ............................................................  356
STIM2-GP    ............................................................  275

Consensus   AVEKQNLERKMMDEINYAKEEACRLRELREGAECELSRRQYAEQELEQVRMALKKAEKEF  416
STIM2-H     ............................................................  339
STIM2-M     ............................................................  339
STIM2-R     ............................................................  416
STIM2-GP    ............................................................  335

Consensus   ELRSSWSVPDALQKWLQLTHEVEVQYYNIKRQNAEMQLAIAKDEAEKIKKKRSTVFGTLH  476
STIM2-H     ............................................................  399
STIM2-M     ............................................................  399
STIM2-R     ............................................................  476
STIM2-GP    ............................................................  395

Consensus   VAHSSSLDEVDHKILEAKKALSELTTCLRERLFRWQQIEKICGFQIAHNSGLPSLTSSLY  536
STIM2-H     ............................................................  459
STIM2-M     ............................................................  459
STIM2-R     ............................................................  536
STIM2-GP    ............................................................  455
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Consensus   SDHSWVVMPRVSIPPYPIAGGVDDLDEDTPPIVSQFPGTMAKPAGSLARSSSLCRSRRSI  596
STIM2-H     ...........................................P................  519
STIM2-M     .................................P.....V....................  519
STIM2-R     ............................................................  596
STIM2-GP    ............................................................  515

Consensus   VPSSPQSQRAQLPPHAPLPSHPRHPHHPQHXQHSLPSPDPDILSVSSCPALYRNEEEEEA  656
STIM2-H     ......P.....A....H............TP............................  579
STIM2-M     .............A....AA..........P.............................  579
STIM2-R     ...........P....A..P.A....L...T.............................  656
STIM2-GP    .................PT...........P.............................  575

Consensus   IYFXAEKQWEVPDTASECDSLNSSIGRKQSPPSSLEIYQTLSXRKISRDELSLEDSSRGE  716
STIM2-H     ...S............................L.........P.......V........D  639
STIM2-M     ...T....................S...P.......M.....S.................  639
STIM2-R     ...S.................................H....S..V..E...........  716
STIM2-GP    ...T.......L..............................P................G  635

Consensus   SPVTADXSRGSPDCVGLTETKSMIFSPASKVYNGILEKSCSMNQLSSGIPVPKPRHTSCS  776
STIM2-H     ....V.V.W...................................................  699
STIM2-M     ......V.....E................R............H.........H.......  699
STIM2-R     ......L.......A.............................................  776
STIM2-GP    ....T.L..........................................VM.........  695

Consensus   SAGNDSKPVQEAPSVARISSIPHDLCHNGEKSKKPSKIKSLFKKKSK               823
STIM2-H     ...............................................               746
STIM2-M     ............SN.S.V.............................               746
STIM2-R     .......AA....T....G............................               823
STIM2-GP    ........I......T...............................               742


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