

NROB2 regulation during Primary Sclerosing Cholangitis defines a metabolic and pre-malignant reprogramming of Cholangiocyte

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SUMMARY:

Primary Sclerosing Cholangitis (PSC) is an idiopathic, cholestatic liver disease that is characterized by persistent, progressive, biliary inflammation leading to cirrhosis. These patients present higher risk for developing bile duct cancers.

Biomedical text-mining related to PSC symptoms like: biliary inflammation, biliary fibrosis, biliary cholestasis was initiated to collect gene associations with this pathophysiology. The text mining work was integrated in distinct omics data such as human transcriptome of PSC liver, Farnesoid X receptor (FXR) functional liver transcriptome and liver single cell transcriptome of the *Abcb4*^{-/-} model of PSC. A molecular network implicated in abnormal hepatobiliary system physiology was built and confirming a major implication of *Nr0b2* and its associated nuclear receptors like FXR in a metabolic cascade that could influence immune response. TNFRSF12A/TWEAK receptor, was found up regulated in PSC liver independently of FXR regulation and TWEAK signaling is known for its implication in pre-conditioning niche of cholangiocarcinoma. *NROB2* deregulation in PSC liver was found independent of gender, age and body mass index surrogates. At single cell level, *Nr0b2* up regulation was

found in cholangiocytes but not in hepatocytes. In affected cholangiocytes, the cell trajectory built on Nr0b2 expression, revealed implication of several metabolic pathways for detoxification like sulfur, glutathione derivative and monocarboxylic acid metabolisms. On this cell trajectory it was discovered some molecules potentially implicated in carcinogenesis like: GSTA3, ID2 and mainly TMEM45A a transmembrane molecule from golgi apparatus considered as oncogene in several cancers. All together, these observations found in humanPSC liver and in its murine models allowed to highlight an independent deregulation of NR0B2 with a metabolic and premalignant reprogramming of cholangiocytes.

KEYWORDS: cholangiocyte, primary sclerosing cholangitis, metabolism, Farnesoid X receptor, transcriptome, Small Heterodimer Partner, pre-malignancy, TMEM45A

INTRODUCTION

Primary sclerosing cholangitis is a progressive, cholestatic hepatic disease of unknown etiology. It is characterized by progressive inflammation, destruction, and fibrosis of the intrahepatic and extrahepatic bile ducts (Lazaridis & LaRusso, 2016). PSC is a rare disease with an incidence that ranges from 0 to 1.3 cases per 100,000 persons per year (Molodecky et al., 2011). Co-occurrence of inflammatory bowel disease (IBD), most commonly ulcerative colitis (UC), has been reported in up to 80% of patients with PSC (Mertz, Nguyen, Katsanos, & Kwok, 2019). The close association between PSC and IBD indicates the involvement of the gut-liver axis. Also, environmental factor like microbiota has emerged as one of the most important potential environmental players in chronic inflammatory diseases like PSC (Rühlemann et al., 2019). Enterohepatic circulation referred to the metabolite exchange between liver and intestine may play an important aspect of the PSC pathophysiology because metabolome of PSC portal blood and bile samples signed a peculiar molecular profile as compared to ones of disease and non-disease controls (Tietz-Bogert et al., 2018, p.).

PSC causes multifocal strictures of the biliary tree, biliary infections, and accumulation of toxic bile acids, which results in an increased expression of adhesion and antigen-presenting molecules and inflammatory mediators. These observations are a good field for emergence of carcinogenesis that could affect biliary tracts (Chalasanani et al., 2000; Rizvi, Eaton, & Gores, 2015). There is no effective treatment which can delay its progression or ameliorate the

transplant-free survival. More recently, novel pharmacological agents emerged aiming at: modulation of bile composition, immunomodulation, targeting the gut microbiome, targeting fibrosis (Floreani & De Martin, 2021).

Many aspects of the pathogenesis of PSC remain unclear. Biomedical literature is traditionally used as a way to inform scientists of the relevance of genes in relation to a research topic (Fleuren & Alkema, 2015). Previously, test of distinct biomedical text mining web tools to integrate gene relations with omics data highlighted ‘Génie’ algorithm (Fontaine, Priller, Barbosa-Silva, & Andrade-Navarro, 2011) as a robust and sensitive machine learning tool to rank best literature associated genes. By textmining (Génie) integration in single cell transcriptome it could be possible to highlighted podocytes markers implicated in Focal Segmental Glomerular Sclerosis (Desterke, Lorenzo, & Candelier, 2021). ‘Génie’ algorithm also contributed to understand lipidome deregulations during nonalcoholic fatty liver disease (Pirola & Sookoian, 2021). ‘Génie’ is a powerful and fast tool that prioritizes the whole gene sets of hundreds of species for any biomedical topic, taking advantage of annotations-linking gene and bibliography (Fontaine et al., 2011). In this work, biomedical text-mining related to PSC symptoms allowed to enrich a gene set of molecules that was used originally to analyze different omics data coming from human PSC liver biopsies and distinct animal models of PSC. Independent deregulation of NR0B2 in PSC allowed to highlight a metabolic and pre-malignant reprogramming of the affected cholangiocytes.

MATERIAL AND METHODS

Biomedical Pubmed textmining

‘Génie’ Data mining tools performed gene prioritization (Fontaine et al., 2011) by linking scientific litterature from MEDLINE database with gene information from NCBI Gene database and orthologue gene information from different species with HomoloGene database (E. Sayers, 2010; E. W. Sayers et al., 2009). Génie algorithm works by connecting gene identifier and gene orthologue NCBI databases with genes related to input keywords obtained by building a textmining classifier with article abstracts from PUBMED literature ressource. Primary Sclerosing Cholangitis related symptom Medical Subject Headings (MeSH) terms were individually submitted to ‘Génie’ algorithm on 2021-july-2nd. All abstract of PUBMED

were taking as background for the analysis of genes corresponding to Homo sapiens coding proteins. All orthologue information were collected during the process, p-value cutoff for abstract selection was fixed to $p < 0.01$ and False Discovery Rate cutoff for gene selection was fixed to $p < 0.01$. This last step of FDR adjustment allowed to correct false positive discovery rate and so to minimize the influence of one peculiar article in the globality of the analysis of gene enrichment.

Public datasets

Transcriptome studies

1/ Human liver biopsies (n=134), GSE61256 (Horvath et al., 2014): transcriptome experiments performed on human biopsies were downloaded and annotated with the corresponding annotation platform: GPL11532 used for technology version DNAChipAffymetrix Human Gene 1.1 ST Array (alias HuGene-1_1-st) available at the following address: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL11532> (accessed on 2021, July 2nd).

2/ Mus musculus liver FXR functional study GSE54557 (Zhan et al., 2014): C57BL/6J Mus musculus liver samples of 10-16 weeks. Transcriptome of liver samples in presence or not of liver FXR knock-out and with or without treatment with GW4064 FXR agonist experience in triplicate. Transcriptome matrix was downloaded and annotated with the annotated platform GPL8321 corresponding to the DNAChip technology: Affymetrix Mouse Genome 430A 2.0 Array (alias Mouse430A_2) available at the following address: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL8321> (accessed on 2021, July 2nd).

Single cell transcriptome study

Mus musculus Abcb4^{-/-} single cell transcriptome liver samples GSE168758 (Reich et al., 2021): Single cell transcriptome libraries of liver cells were prepared with Chromium Single Cell 3' NextGEM Reagent Kit v3.1 (10X Genomics) to performed sequencing on NextSeq 550 (Illumina) and demultiplexing pipeline with CellRanger v5.0.0 (10x Genomics). MTX matrix file format were downloaded at the following address: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSM5165876> (accessed on 2021, July 2nd).

Bioinformatics analyses

Bioinformatics analysis were performed in R software environment version 4.1.0 under Ubuntu version 20.04 LTS. Graphical representation were performed with ggplot2 graph definition implemented in ggplot2 R-package version 3.3.5 (Wickham, 2009, p. 2).

Transcriptome Analyses

Unsupervised analysis performed by principal component analysis used FactoMineR R-package version 2.4 (Lê, Josse, & Husson, 2008). Gene Functional enrichment analyses were performed with Toppgene web application (J. Chen, Bardes, Aronow, & Jegga, 2009). Differential expressed genes were identified with Linear Model from Microarray (LIMMA) algorithm implemented in R Bioconductor package version 3.44.3 (Ritchie et al., 2015). FXR regulation dependency analysis with Pavlidis Template Matching algorithm with retaining significant genes on absolute value of correlation coefficient and with a cutoff p-value less than 0.05 (Pavlidis & Noble, 2001). Expression heatmap were drawn with pheatmap R-package version 1.012.

Single cell transcriptome analysis

Single transcriptome analyses at whole liver level were performed with Seurat4 R-package version 4.0.3 (Butler, Hoffman, Smibert, Papalexi, & Satija, 2018). Briefly, after canonical correlation, filtration (cells expressing minimally 300 genes) and scaling between replicated samples (n=4) of wildtype and *Abcb4*^{-/-} groups a normalized single cell object comprising 46.087 transcriptomes was built. Dimension reduction was carried out by principal component analysis on most variable features (50 components) and secondly: t-distributed stochastic neighbor embedding (t-SNE) and Uniform Manifold Approximation and Projection (UMAP) dimensionality reduction was performed on the 30 best components of the PCA. Cell cluster communities were detected graph-based clustering approaches (Xu & Su, 2015). *Abcb*^{-/-} cholangiocytes identified in clusters 0-5-11 were select were randomly down sampled to 1/10e of their initial amount to build a matrix finally containing 1316 cells. Single cell trajectory performed on *Abcb4*^{-/-} cholangiocyte with monocle2 R Bioconductor package version 2.20.0 (Trapnell et al., 2014). Cell hierarchy was construct on alternative expression of *Sox9* and *Nr0b2* in *Abcb4*^{-/-} cholangiocytes. Pseudotime transformation on cell trajectory

was performed with DDRtree algorithm and pseudotime cluster identification was done by pseudotime expression heatmap drawn with best genes found significant

Network analyses

Gene and function relations identified were collected with functional enrichment and network were built with Cytoscape standalone software version 3.6.0 (Cline et al., 2007) for their visualization. Protein-protein interaction (PPI) network were performed with NetworkAnalyst (Xia, Gill, & Hancock, 2015) webtools based on interaction network databases: STRING (Szklarczyk et al., 2017) or liver specific DifferentialNet. Functional inference was done on PPI networks with Gene Ontology Biological Process (GO-BP) database (The Gene Ontology Consortium, 2017).

RESULTS

Biomedical text mining for discovery of gene relations with symptoms of primary sclerosing cholangitis

Classically, the literature dealing with genes, as stored in the MEDLINE database (E. W. Sayers et al., 2009) of biomedical references has been used to do gene prioritization. Many methods for gene prioritization using literature data are based on co-occurrence analysis of keywords and extract gene names from abstracts (Krallinger, Valencia, & Hirschman, 2008). ‘Génie’ algorithm is based on Naive bayes classifier and take advantage of linking orthologues genes study in many different species (Fontaine et al., 2011). Primary Sclerosing Cholangitis (PSC) is an Idiopathic, Heterogeneous, cholestatic liver disease that is characterized by persistent, progressive, biliary inflammation and fibrosis (Lazaridis & LaRusso, 2016). Three related MESH terms for indirect characterization of PSC symptomatology were used to process in ‘Génie’ algorithm and trigger gene related to the disease with the following exact terms: ‘biliary inflammation’, ‘biliary fibrosis’, ‘biliary stasis’. These respective analyses allowed to collect a common set of 525 ranked genes (workflow, [Figure 1](#) and [Supplemental Table 1](#)). NR1H4 alias FXR Farnesoid X receptor was found as the best ranked gene at cross of these three independent text mining analyses

(**Supplemental Table 1**). This text mining results allowed to give us a restrictive gene list (525) to investigated downstream omics analyses in context of PSC disorder as it is highlight graphically on the workflow of the article (**Figure 1**). Starting omics analyses with reduced size gene sets allowed to drastically eliminate background noise and False Discovery Rate in these experiments as it is shown with Gene Set Enrichment Analysis (GSEA) procedure (Subramanian et al., 2005).

Abnormalities in physiology of hepatobiliary system during primary sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is a chronic hepatic syndrome with fibro-inflammatory affection of the bile ducts. In order to test our txt mining PSC symptom related gene set, a bioinformatics investigation was performed on transcriptome study GSE61256 (**Figure 1**) (Horvath et al., 2014) which is composed of liver biopsy samples from PSC (n=14) patients as compared to distinct control groups such as: PBC (n=11), normal control (n=38), normal obese (n=24), NAFLD (n=23), NASH (n=24). Data from GSE61256 were reduced in dimension with the 525 PSC symptom related genes but only 507 of them were find provided in these type of experiments. Unsupervised principal component analysis revealed an individual stratification of PSC samples as compared to every other control groups and especially as compared to PBC control which could harbored also these three phenotypes (p-value=6.89E-4, **Figure 2A**). With less importance, these genes also discriminates PBC samples from other liver control groups in the second map of PCA analysis (**Supplemental Figure 1**). These results suggested that in its entirety PSC symptom related gene set obtained by text mining seems to be specific to predict liver sample transcriptome of PSC as compared to divers control groups. Effectively, starting from these 507 molecules supervised 'Linear Model from Microarray' (LIMMA) algorithm for differential expression analysis allowed to characterized a significant expression profile of PSC liver samples as compared to all other pooled control groups (**Figure 2B** and **Supplemental Table 2**). Among the best up regulated genes, FOXP3 was found the best one followed by NR0B2, TNFRSF1A and FGF19. A distinct trait of expression of up regulated for PSC samples could be observed on the right of expression heatmap performed with up regulated genes (**Figure 2C**). Functional enrichment performed with these PSC up regulated genes on Mouse Phenotype database allowed to characterized were found mainly implicated in abnormal liver physiology and abnormal

hepatobiliary system physiology (**Figure 2D**). As PSC is a hepatic disorder affecting bile ducts a functional enrichment network was built on affection of hepatobiliary system. On this hepatobiliary system phenotype network we could observed that some of the top up regulated genes in PSC are present such as: FOXP3, TNFRSF12A, TNFRSF1A, LCN2 and NR0B2 (**Figure 2E**). Starting from PSC symptom related gene found by text mining we could predict with liver samples, a PSC specific up regulated network implicated in hepatobiliary system phenotype.

Hepatic regulation of immune response and intracellular receptor signaling under FXR dependency

In PSC symptom related genes found by text-mining we could observed that NR1H4 alias Farnesyl X receptor (FXR) was the best ranked gene associated to the literature in relations with input symptom MeSH. FXR is a nuclear receptor implicated in bile acide metabolism and have been widely study in hepatocyte biology such as whole gene ChIP-sequencing experiments (Zhan et al., 2014). Liver transcriptome study were also performed on hepatic functional studies targeting FXR: such as GSE54557 dataset which investigate liver samples of *Mus musculus* with or without liver FXR knock-out reversed of not by GW4064 agonist treatment (Zhan et al., 2014). Data from GSE61256 were reduced in dimension with the 525 PSC symptom related genes and Pavlidis Template Matching (PTM) algorithm was used to understand FXR regulation dependency: FXR liver knock-out reversed by GW4064 FXR agonist (**Figure 3A** and **Supplemental Table 3**): 91 genes were found significantly regulated through FXR dependency in liver samples. These significant genes allowed to significantly stratified experimental samples of FXR liver KO from wildtype ones (WT) and reversion by FXR agonist was obtained only in wildtype samples (p -value=1.66.E-4, **Figure 3B**). Molecules with positive regulation following FXR liver dependency were selected to draw an expression heatmap (**Figure 3C**) which implicated a protein-protein interaction (PPI) network mainly implicated in regulation of immune response (nodes in green, **Figure 3D**) and in intracellular receptor mediated signaling pathway (in blue, **Figure 3D**). Concerning intracellular receptor signaling, three main blue crosstalk could be observed on the PPI network (**Figure 3D**): NR1H4, NR1I2 and PPARGC1A which are closely connected. Concerning immune response we could observed (**Figure 3C**) a liver FXR regulation dependency of CD274 alias PDL1 immune checkpoint. These results suggest that starting

from PSC symptom related gene list we could predict a hepatic expression profile under FXR regulation dependency and so confirming its potential functional importance in the pathology.

Nrb02 is the best predictive marker regulated in liver of primary sclerosing cholangitis under FXR dependency

In order to evaluate FXR dependency in PSC related human liver expression profile that we identified we investigated to cross the human study signature (**Supplemental Table 2** and **Figure 2**) with liver FXR functional signature (**Supplemental Table 3** and **Figure 3**). This investigation allowed to highlight 34 common regulated molecules between the two studies (**Figure 4A**). Proceeding supervised machine learning by leave one out cross validation algorithm (pamr) between human liver PSC samples and other liver control samples (GSE61256), it could possible to defined a predictive molecular ranking (**Supplemental Table 2**) with a minimal misclassification error of 8.9 percent between samples (**Figure 4B**). Inside these best molecular ranking to predict human PSC liver we could observed some molecules with an FXR dependent regulation (in pink, **Figure 4C**), such as: NR0B2, CYP7A1, DGAT2, NR1H4 (alias FXR), TNFRSF1A, BCHE, KLF6 and CEBPA. NR0B2 at the top of PSC prediction with FXR dependency was investigated by univariate analysis stratified on gender of the patients. Effectively, NR0B2 was found up regulated in PSC samples and more sensitively in samples of female gender (**Figure 4D**). In a biological and clinical multivariate model, we could observed that up regulation of NR0B2 was significantly up regulated in PSC liver samples but independently of the gender, the age and body mass index (BMI) of the patients. These results suggest that the nuclear receptor NR0B2 is the best predictive marker up regulated in PSC liver which harbored an FXR dependent regulation is its regulation is independent of the age, gender and BMI of the patients.

Up regulation of Nrb02 in cholangiocyte compartment of Abcb4^{-/-} liver

Abcb4^{-/-} (Mdr2) mice are widely used as model for sclerosing cholangitis because it recapitulates the progressive fibrosing cholangitis aspect of human PSC and also develop intrahepatic malignancy (Fickert et al., 2004, 2014). Single cell transcriptome performed in liver of wild type and Abcb4^{-/-} mice models have been provided in GSE168758 dataset (Reich et al., 2021, p. 5). With 4 replicates of liver in groups WT and Abcb4^{-/-} a single cell normalized object was built with 46.087 cells which individually expressed a minimum of

300 genes. After dimension reduction and clustering 15 cell communities were identified and classed in five main cell types: hepatocytes, cholangiocytes, endothelial cells, macrophages and lymphocytes (**Figure 5A** and **Supplemental Figure 2**). Wild type livers harbored more hepatocytes as compared Abcb4^{-/-} livers (in red, **Figure 5B**) and Abcb4 livers harbored more cholangiocytes than wild type livers (in blue, **Figure 5B**). Sox9 is a transcription factor implicated in the biliary development (Antoniou et al., 2009). Epcam and Sox9 expressions follow CK19 expression during human intrahepatic biliary tree formation through several developmental stages involving an initial transition of primitive hepatocytes into cholangiocytes (Vestentoft et al., 2011). Sox9 was found over expressed in Abcb4^{-/-} livers as compared to wild type ones (**Figure 5C**) and especially in cholangiocyte compartment (**Figure 5D**) which correspond to cell clusters : 0, 5 and 11 (**Supplemental Figure 3A**). Similarly, an overexpression of Nr0b2 was found in Abcb4^{-/-} livers as compared to wild type ones (Figure 5E). Expression of Nr0b2 was found detected in hepatocyte and cholangiocyte cell compartment in both liver genotypes (**Figure 5F**). Overexpression of Nr0b2 in liver Abcb4^{-/-} livers concerned cell clusters 0, 5 and 11 (**Figure 5G** and **Supplemental Figure 3B**) which were confirmed as expressing Sox9 and Epcam cholangiocytes markers (**Supplemental Figure 3A** and **3C**). Absence of Nr0b2 regulation was observed in hepatocyte compartment of Abcb4^{-/-} (cluster 1, **Figure 5G**). These results suggest that Nr0b2 nuclear receptor was found up regulated in cholangiocyte compartment of the Abcb4^{-/-} liver: mice model of sclerosing cholangitis.

Metabolic regulation during cell trajectory of Abcb4^{-/-} cholangiocytes

Nr0b2 alias small heterodimer partner is a nuclear receptor identified as a key transcription regulator affecting divers functions implicated in metabolism such as: bile acid metabolism, lipid metabolism, glucose and energy homeostasis (Zhang, Hagedorn, & Wang, 2011, p. 2010). Nr0b2 was found as best predictive marker of PSC in liver with FXR regulation dependency but its overexpression in Abcb4^{-/-} mice model affect cholangiocyte but not hepatocyte cell compartment. Starting from single cell transcriptome of GSE168758 dataset, a random down sampling subset of Abcb4^{-/-} cholangiocytes was selected to build a single cell trajectory based on alternative expression of Nr0b2 and Sox9. With an affected cholangiocyte compartment comprising in total 1316 cells, 238 cells were characterized as Sox9 Nr0b2 double negative, 51 cells were characterized as negative for Sox9 and positive for Nr0b2, 406

cells were characterized as positive for Sox9 and negative for Nr0b2, and 621 cells were characterized as Sox9 and Nr0b2 double positive (**Figure 6A**). The alternative expression of Sox9 and Nr0b2 reflect a cell heterogeneity in *Abcb4*^{-/-} the cluster heterogeneity of cholangiocytes clusters 0, 5 and found previously found at whole liver level (**Supplemental Figure 4A and 4B**). Pseudotime transformation of single cell transcriptome in this affected compartment (**Figure 6** and **Supplemental Figure 4C**) reflect a cell trajectory with progressive modification of Sox9 (**Supplemental Figure 4D**) and Nr0b2 (**Supplemental Figure 4E**) expressions. Identification of most significant regulated genes on this cell trajectory (**Supplemental Table 4**) allowed to identified three distinct regulated gene clusters (**Figure 6C**). Expressions of Sox9 and Nr0b2 were found closely regulated on the trajectory of the pseudotime green gene cluster (**Figure 6C**). Among the pseudotime green cluster, expression of *Alb*, *Gsta3*, *Id2* and *Tmem45a* were found closely regulated with Nr0b2 and Sox9, especially *Gsta3* very near Nr0b2 pseudotime regulation (**Figure 6C** and **Supplemental Figure 4F**). Protein-protein network performed with genes belonging to green pseudotime gene cluster with functional inference of Gene Ontology Biological Process database allowed to identified a main functional enrichment of positive regulation of metabolism (False Discovery Rate p-value=5.2E-23, **Figure 6D**). This metabolic functional enrichment allowed to mainly implicated sulfur compound metabolism, glutathione derivative biosynthesis, cellular detoxification and monocarboxylic acid metabolism (**Figure 6E**) which share some main regulated molecules (**Figure 6F**). These results suggest that heterogeneity of Nr0b2 expression inside *Abcb4*^{-/-} cholangiocyte affected compartment defined a cell trajectory implicating an important regulation of metabolism with detoxification process.

DISCUSSION

Primary sclerosing cholangitis is a chronic, fibro-inflammatory disorder affecting intra/extrahepatic bile ducts without precise etiology and efficient therapy. The resulting cholestasis may progress to cirrhosis and liver failure (Karlsen, Folseraas, Thorburn, & Vesterhus, 2017). Enterohepatic circulation have been proposed to participate to the pathophysiology of this disease because it could be diagnose a preponderance of inflammatory bowel disease in PSC patients (Boonstra et al., 2012) and also it have been discovery that the gut microbiota of PSC patients is distinct from those inflammatory bowel disease patients and healthy controls (Sabino et al., 2016). Progress remains to be made in the understanding of the physiopathology of this disease in order to elucidate why some of these

patients have a higher risk of developing cholangiocarcinomas (Rizvi et al., 2015). Few liver transcriptome experiments were available in PSC disease (Horvath et al., 2014): experiments in which it might be interesting to observe cellular mechanisms consecutive to the symptoms of PSC disorder. The integration of biomedical text mining into high-dimensional omics data such as transcriptome data drastically reduces the error of positive false discovery (Desterke et al., 2021). With the aim of increasing the authenticity of discovery of these mechanisms in human liver transcriptome samples from PSC, a biomedical text-mining pipeline has been developed based on a triad of symptoms characterizing PSC: biliary inflammation, biliary fibrosis and biliary stasis (Lazaridis & LaRusso, 2016). The intersection of these text-mining researches have made it possible to link 525 genes to the symptomatic of PSC disorder. The best literature associated gene by text-mining was NR1H4 alias FXR Farnesoid X receptor a nuclear receptor implicated in bile acid metabolism. Nuclear receptors (NRs) are a unique family of transcription factors (TFs) that are being recognized as key regulators of multiple functions in almost all aspects of mammalian development, metabolism and physiology (Gronemeyer, Gustafsson, & Laudet, 2004). FXR is highly expressed in liver and is used as bile acid sensor by regulating genes that are critically involved in bile acid homeostasis, including bile acid biosynthesis, conjugation, and entero-hepatic circulation (Sinal et al., 2000). PSC symptom related genes found by biomedical text mining were used to analyzed human liver transcriptome and predicted a stratification of PSC samples as compared to samples from different controls: healthy normal liver, obese healthy donors, NAFLD, NASH and PBC. A PSC expression profile was able to be identified by differential expression analysis which highlighted important over expression of distinct molecules. FOXP3 was found as the best overexpressed gene in liver of PSC patients. FOXP3 transcription factor characterized the phenotype of regulatory T-lymphocyte immune cell sub population (Sakaguchi, Miyara, Costantino, & Hafler, 2010) and bile acid metabolites have been shown to be implicated in the control regulatory T-lymphocyte cell differentiation (Hang et al., 2019). In genome of PSC patients, polymorphisms found in IL2RA gene affected FOXP3+ regulatory T-cell subpopulation of these patients (Sebode et al., 2014). Among best up regulated genes found in PSC it was found NR0B2 alias small heterodimer partner (SHP). NR0B2 has been identified as key transcription regulator implicated in divers biological function such as: bile acids; cholesterol and lipid metabolism, glucose and energy homeostasis (Zhang et al., 2011). NR0B2 alias Small heterodimer partner (SHP) is a unique nuclear receptor (NR) distinct from other conventional NRs in both its structure and function. The presence of a putative ligand-binding domain (LBD) classifies SHP as a member of the NR

family, although the endogenous ligand has not been identified (Seol, Choi, & Moore, 1996) and NR0B2 is known as common heterodimer partner of FXR implicated in bile acid metabolism (Goodwin et al., 2000). Among best up-regulated genes found in PSC liver, FGF19 is implicate in bile acid homeostasis and effectively it is a target of bile acids via FXR in enterocyte and recirculate in portal blood to bind to FGFR4 receptor on hepatocyte (Inagaki et al., 2005). Among best up regulated molecules in liver of PSC, it was found TNFRSF12A which is a receptor from TNF superfamily. TNFRSF12A is also named TWEAK receptor and TWEAK/Fn14 signaling have been associated to promote cholangiocarcinoma niche formation and progression (Dwyer et al., 2021). Through liver functional analysis, FXR regulation dependency was used to build a liver protein-protein interaction network which mainly implicated immune response and nuclear receptor signalling. Through immune response functionality, CD274 (alias PDL1) was found regulated under liver FXR regulation. Effectively, some clinical trials in cancer therapy under pembrolizumab (anti-PDL1) highlighted risk to developed sclerosing cholangitis (Tahboub Amawi, Tremaine, & Venkatesh, 2020). In next step, human PSC gene signature was investigated with the FXR regulation dependency. NR0B2 was found as the best PSC predictive up regulated gene under FXR regulation and this relation is well known to be implicated in regulatory cascade of bile acid metabolism drive by nuclear receptors which repressed CYP7A1. CYP7A1 catalyzes the rate limiting step in bile acid biosynthesis. NR0B2 is known to repress CYP7A1 via activity inhibition of liver receptor homolog 1 (LRH-1) (Goodwin et al., 2000). In liver from PSC, CYP7A1 was confirmed to be down regulated as compared to liver samples from controls. Among best PSC predictive genes under FXR dependency, DGAT2, Diacylglycerol O-Acyltransferase 2 (Brandt, McFie, & Stone, 2016) implicated in biosynthesis of triglycerides was found repressed in PSC liver and effectively portal blood and bile lipidomics of PSC patients was found peculiar as compared to similar samples from disease controls and non-disease controls especially with increase of free fatty acid detection (Tietz-Bogert et al., 2018). NR0B2 alias SHP was found as the best predictive marker of PSC under FXR regulation dependency and its up regulation in PSC liver was found independent of the age, the gender and Body Mass Index (BMI) of the patients. Mdr2^{-/-} alias Abcb4^{-/-} mice model is widely used as a model of sclerosing cholangitis. It recapitulates the progressive fibrosing cholangitis aspect of human PSC. At single cell level in liver of Abcb4^{-/-} mice, expression of Nr0b2 was detected in hepatocyte and cholangiocytes cell compartments but it's over expression as compared to wide type cells was observed only the cholangiocytes which highly expressed Sox9. Based on alternative expression of Sox9 and Nr0b2, single cell trajectory was

built with in *Abcb4*^{-/-} cholangiocyte cell compartment. Affected cholangiocytes highlighted a cell trajectory cluster comprising a network of molecules implicated in metabolism: sulfur component metabolism, glutathione derivative biosynthesis and monocarboxylic acid metabolism. N-acetylcysteine therapeutical option have been already tested in PSC, by its antimucolytic action it potentially reduce bile viscosity and improved clinical and laboratory parameters of PSC patients in a small study (Ozdil, Cosar, Akkiz, Sandikci, & Kece, 2011). On Nr0b2 cell trajectory of affected cholangiocyte, *Gsta3* Glutathione S transferase was found with similar pseudotime expression meaning their closed regulation during cell trajectory of this affected cell compartment. Glutathione S-transferases (GST) like *GSTA3* acts as antioxidant enzymes mainly in liver tissue through glutathione peroxidase activity toward phospholipid hydroperoxides (Yang, Sharma, Zimniak, & Awasthi, 2002). *GSTA3* belongs to the GST α -class, which converts lipid peroxides to glutathione conjugates (Johansson & Mannervik, 2001, p. 3-3). It has been shown that glutathione S-transferase A3 have a role in inhibiting hepatic stellate cell activation and rat hepatic fibrosis (H. Chen et al., 2019). Also, glutathione S-transferase A3 knockout mice harbors liver injury, oval cell proliferation and cholangiocarcinogenesis in (Crawford et al., 2017). Inhibitor of DNA binding 2 (*ID2*) was found also closely regulated on Nr0b2 cell trajectory of *Abcb4*^{-/-} cholangiocytes. *ID2* is a member basic Helix Loop Helix transcription factor family. *ID2* like other ID proteins lacks DNA binding domain and so transcription of downstream cell cycle targets like p16, p21 (Benezra, Davis, Lockshon, Turner, & Weintraub, 1990). *ID2* like *ID1* and *ID3* proteins is frequently overexpressed in all biliary tract cancer (BTC) subtypes. Also, ID protein expression is deregulated in many tumors including pancreatic cancer a malignancy somehow related to bile tract cancers. During bile tract cancer, for subgroup of patients who had received chemotherapy, if nuclear expression of *ID2* is negative these patients presented a better overall survival as compared those who were nuclear positive (Harder et al., 2013). With closed pseudotime expression on Nr0b2 cell trajectory of *Abcb4*^{-/-} cholangiocyte cell compartment, it was found the membrane molecule *Tmem45a*. *Tmem45a* is transmembrane molecule of 275 amino acids, predicted to have five to seven transmembrane domains and localized in the trans Golgi apparatus. This protein is over expressed in many cancers: breast cancer, liver cancer, renal cancer, glioma, head and neck cancer, ductal cancer and ovarian cancer: it could be supposed to act as an oncogene (Flamant et al., 2012; Guo et al., 2015; Lee et al., 2012; Manawapat-Klopfer et al., 2016; Sun et al., 2015; Wrzesiński et al., 2015). During breast and cervical tumors, there was found a higher level of expression for *TMEM45A* suggesting this molecule could be a biomarker of aggressiveness in these

malignant pathologies (Manawapat-Klopfer et al., 2016). TMEM45A have been implicated in the proliferation, migration and invasion of glioma cancer cells (Guo et al., 2015; Sun et al., 2015). TMEM45A also confers chemoresistance in hypoxia condition for the cell death induced chemotherapeutic agents of breast cancer (Flamant et al., 2012).

Conclusion:

In this work we performed integration of biomedical text-mining related to PSC symptom in omics data such as human transcriptome of PSC liver, FXR functional liver transcriptome and liver single cell transcriptome of the *Abcb4*^{-/-} model of PSC. This integrative work allowed to confirmed major implication of *Nr0b2* and its associated nuclear receptors like FXR in a metabolic cascade that could influence immune response. TNFRSF12A/TWEAK receptor, was found up regulated in PSC liver independently of FXR regulation and TWEAK signaling is known for its implication in pre-conditioning niche of cholangiocarcinoma. At single cell level, *Nr0b2* up regulation was found in cholangiocytes but not in hepatocytes. In this affected cell compartment cell trajectory defined on *Nr0b2* expression, highlighted several metabolic pathways of detoxification like sulfur, glutathione derivative and monocarboxylic acid metabolisms. On this cell trajectory it was discovered some molecules potentially implicated in carcinogenesis like: *GSTA3*, *ID2* and mainly *TMEM45A* a transmembrane molecule considered as oncogene in several cancers.

DATA AVAILABILITY

R bioinformatics code for single cell analyses performed with Seurat 4 and Monocle 2 packages on dataset GSE168758 are accessible on internet at the following address: www.github.com/cdesterke/pssc (accessed on 2021, July 10th).

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CONTRIBUTIONS

CD and CF : design of the experience, CD and CF : written manuscript, CD : data analysis,
CF : supervisor and correction of the manuscript

ABBREVIATIONS

Abcb4: ATP Binding Cassette Subfamily B Member 4

BMI: body mass index

BTC: biliary tract cancer

DEGs: differential expressed genes

FDR: False Discovery Rate

FXR: Farnesoid X Receptor, alias NR1H4

GO-BP: Gene Ontology Biological Process database

GSEA: Gene Set Enrichment Analysis

GW4064: Farnesoid X Receptor agonist

ID2: inhibitor of DNA binding 2

KO: knock-out

LIMMA: LInear Model from Microarray

MeSH: Medical Subject Headings

NAFLD: Nonalcoholic fatty liver disease

NASH: Nonalcoholic steatohepatitis

NR: Nuclear receptor

Nr0b2: Nuclear Receptor Subfamily 0 Group B Member 2, alias SHP: Small Heterodimer Partner

PBC: primary biliary cholangitis

PPI: Protein-protein interaction

PSC: primary sclerosing cholangitis

PTM: Pavlidis Template Matching

t-SNE: t-distributed stochastic neighbor embedding

UMAP: Uniform Manifold Approximation and Projection

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FIGURE LEGENDS

Figure 1: workflow of bioinformatics analyses: this figure describes the workflow of the bioinformatics process performed on data used in this work.

Figure 2: Abnormal hepatobiliary system physiology in liver biopsies of Primary sclerosing cholangitis liver biopsy: from A to E: investigations on transcriptome dataset GSE61256; A/ principal component analysis performed with 507 detected symptom related genes on liver biopsy transcriptome from distinct group of diseases and controls, PSC: primary sclerosing cholangitis, PBC: primary biliary cholangitis, NAFLD: Nonalcoholic fatty liver disease, NASH: Nonalcoholic steatohepatitis; B/ Volcanoplot of differential expressed genes (DEGs) between PSC liver and other liver biopsies, C/ Expression heatmap of significant up regulated genes in PSC liver samples; D/ Functional enrichment performed on Mouse Phenotype database with genes up regulated in PSC liver samples; E/ Functional enrichment network with PSC up regulated genes and implicated in hepatobiliary mouse phenotype.

Figure 3: Hepatic regulation of immune response and intracellular receptor signaling under FXR dependency: from A to D: investigations on transcriptome dataset GSE54557; A/ qqplot of p-values obtained by Pavlidis Template Matching (PTM) algorithm with symptom related genes for liver FXR regulation dependency; B/ Principal component analysis performed with PSC symptom related genes under liver FXR regulation dependency, KO: knock-out, GW4064: FXR agonist; C/ Expression heatmap for PSC symptom related genes found positively correlated to hepatic FXR regulation; D/ Protein-protein interaction network based on PSC symptom related genes up regulated in PSC liver samples with colored function inference of Gene Ontology Biological Process (GO-BP) database: in green enrichment of immune response function and in blue intracellular receptor signaling function.

Figure 4: Nrb02 is the best predictive marker regulated in liver of primary sclerosing cholangitis under FXR dependency: A/Venn diagram merging FXR liver regulation dependency of PSC related genes found up regulated in PSC human liver biopsies; B/ Supervised machine learning misclassification plot by class obtained with PSC symptom related genes to stratified PSC liver samples from other control samples in GSE61256; C/ Ranked predictive scores obtained by machine learning on GSE61256 dataset with PSC symptom related genes, FXR hepatic regulation dependency is highlighted in pink for concerned genes; D/ Boxplot of Nr0b2 expression regulation through liver group samples and stratified on gender (GSE61256); E/ Multivariate model based on Nr0b2 expression: exponential coefficients and their confident intervals (95 percent) were drawn for each covariates.

Figure 5: Up regulation of Nrb02 in cholangiocyte compartment of Abcb4^{-/-} liver: from A to G: investigations on whole liver single cell transcriptome dataset GSE168758; A/ Uniform Manifold Approximation and Projection (UMAP) dimension reduction with identification of the distinct cell compartments in whole liver samples: colors reflect 15 distinct cluster cell communities; B/ UMAP with genotype stratification: WT: wildtype, Abcb4^{-/-}: Abcb4 knock-out; C/ Violinplot of Sox9 expression in whole liver stratified on genotypes; D/ Sox9 feature plot stratified on genotypes: blue for positive expression; E/ Violinplot of Nr0b2 expression in whole liver stratified on genotypes; F/ Nr0b2 feature plot

stratified on genotypes: blue for positive expression; G/ violin of Nr0b2 expression stratified on cluster cell communities and genotypes.

Figure 6: metabolic regulation during cell trajectory of Abcb4^{-/-} cholangiocytes: from A to F: downsampling of Abcb4^{-/-} identified cholangiocytes in liver single cell transcriptome dataset GSE168758; A/ Pie chart of cell stratification depending of alternative expression of Nr0b2 and Sox9 in cholangiocyte of Abcb4^{-/-} liver samples; B/ Abcb4^{-/-} cholangiocyte single cell trajectory identified on alternative expression of Nr0b2 and Sox9; C/ Pseudotime expression heatmap of genes found significantly regulated on Nr0b2-Sox9 single cell trajectory of Abcb4^{-/-} cholangiocytes: green cluster follow Sox9 and Nr0b2 pseudotime expression; D/ protein-protein interaction network identified on pseudotime green cluster: blue color characterized network inference of positive regulation of metabolism process; E/ Barplot of functional enrichment performed on pseudotime green cluster with Gene Ontology Biological Process database, FDR: False Discovery Rate; F/Functional enrichment network performed with best metabolism function enriched on pseudotime green cluster.

SUPPLEMENTAL MATERIAL

Supplemental Figures

Supplemental Figure 1: Stratification of PSC and PBC liver transcriptomes by unsupervised analysis: Second principal map of principal component analysis performed on liver transcriptomes of dataset GSE61260 with PCS related genes found by text mining.

Supplemental Figure 2: Single cell heterogeneity of clusters identified in WT and Abcb4^{-/-} livers: A/ whole liver UMAP dimension reduction with summary of the cell cluster indentifications; B/ Cldn7 featureplot which identified cholangiocyte cell subgroup; C/ Apoc4 featureplot which identified hepatocyte cell subgroup; D/ Kdr featureplot which identified endothelial cell subgroup; E/ Cd68 featureplot which identified macrophage cell subgroup; F/ Cd8a featureplot which identified T-lymphocyte cell subgroup; G/ Ms4a1 Kdr featureplot which identified B-lymphocyte cell subgroup.

Supplemental Figure 3: Single cell differential expression of Sox9, Nr0b2, Epcam in cholangiocyte clusters of WT and Abcb4^{-/-} livers: A/ Violinplot of Sox9 expression in cholangiocyte cluters 0-5-11 stratified on phenotype wildtype versus Abcb4^{-/-}; B/ Violinplot of Nr0b2 expression in cholangiocyte cluters 0-5-11 stratified on phenotype wildtype versus Abcb4^{-/-}; C/ Violinplot of Epcam expression in cholangiocyte cluters 0-5-11 stratified on phenotype wildtype versus Abcb4^{-/-};

Supplemental Figure 4: Pseudotime transformation of cholangiocyte cell trajectory in Abcb4^{-/-} livers: A/t-SNE plot of Abcb4^{-/-} cholangiocyte with group stratification based on alternative expression of Sox9 and Nr0b2; B/ t-SNE plot of Abcb4^{-/-} cholangiocyte with group stratification identified in Seurat clustering: clusters 0-5-11; C/ pseudotime tree with group stratification identified in Seurat clustering: clusters 0-5-11; D/ pseudotime tree with expression of sox9 as dot size and group stratification as dot color; E/ pseudotime tree with expression of Nr0b2 as dot size and group stratification as dot color; F/ pseudotime expression plot for markers found closely regulated with Nr0b2 on pseudotime cell trajectory

Supplemental Tables

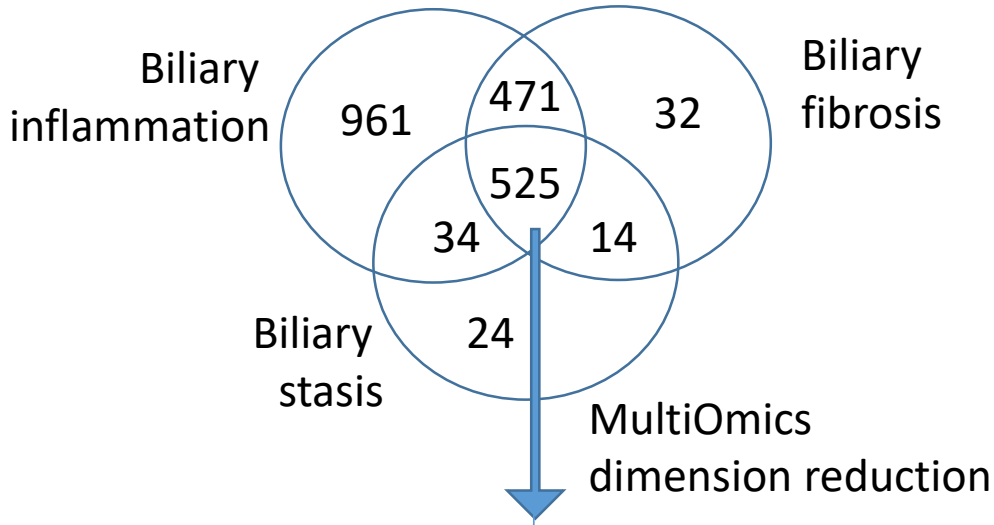
Supplemental Table 1: Textmining table of the common 525 ranked genes found in Pubmed with symptom keywords: this table describes the 525 ranked genes obtained by text mining with 'Génie' algorithm against the three MESH terms: biliary inflammation, biliary fibrosis, biliary stasis, respective ranks, p-values and collected PMID identifiers for each gene and each MESH term are presented

Supplemental Table 2: Symptoms related genes found differentially expressed in liver from primary sclerosing cholangitis patients: Differential expressed gene analysis results (logarithm Fold Change, Average Epression and Adjust p-values) are presented with respective machine learning predictive score for supervised sample categories of GSE61256 dataset: PSC versus other liver samples)

Supplemental Table 3: Pavlidis Template Matching for FXR dependency in liver transcriptome: Pavlidis template analysis results to describe FXR regulation dependency of PSC genes in liver samples of GSE54557 dataset. For each gene R-Pearson correlation coefficient and its respective p-value are presented in this table.

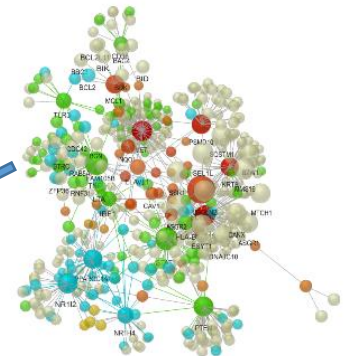
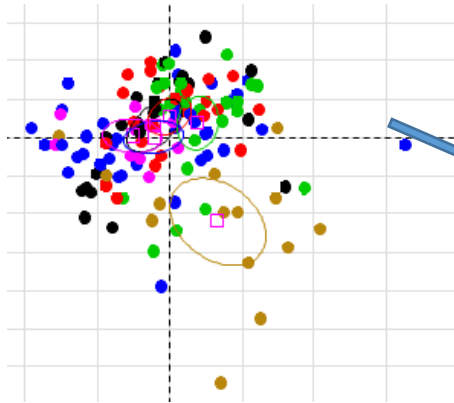
Supplemental Table 4: Best one hundred genes found to be significant pseudotime trajectory of Abcb4^{-/-} cholangiocytes : Best one hundred ranked genes found as significant on pseudotime cell trajectory of cholangiocytes Abcb4^{-/-} based on alternative expression of Nr0b2 and Sox9 in GSE168758

525 genes related to PSC symptomatology (textmining)



Transcriptome
GSE61256
Homo sapiens
PSC and other liver
diseases

Transcriptome
GSE54557
Mus musculus
FXR K liver

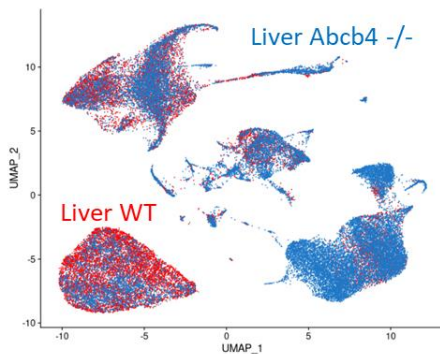


Intersection
and supervised
machine learning

Single cell functional
validation

Single Transcriptome
Mus musculus
Liver ABCC4 knock-out

Whole liver heterogeneity



Cholangiocyte trajectory

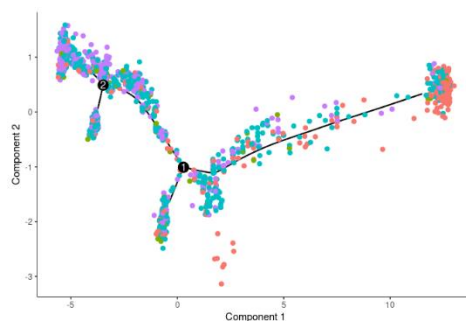


Figure 1

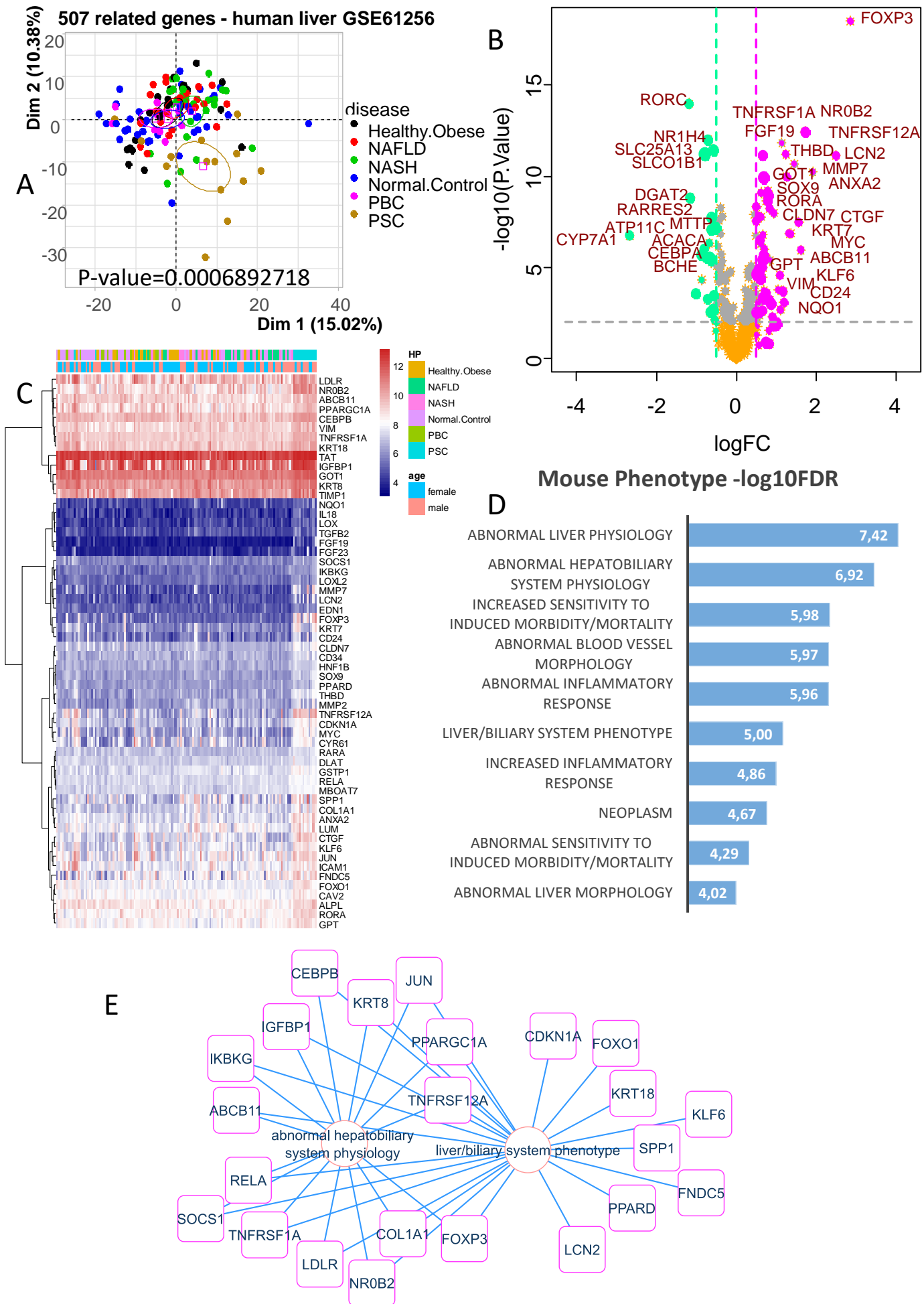
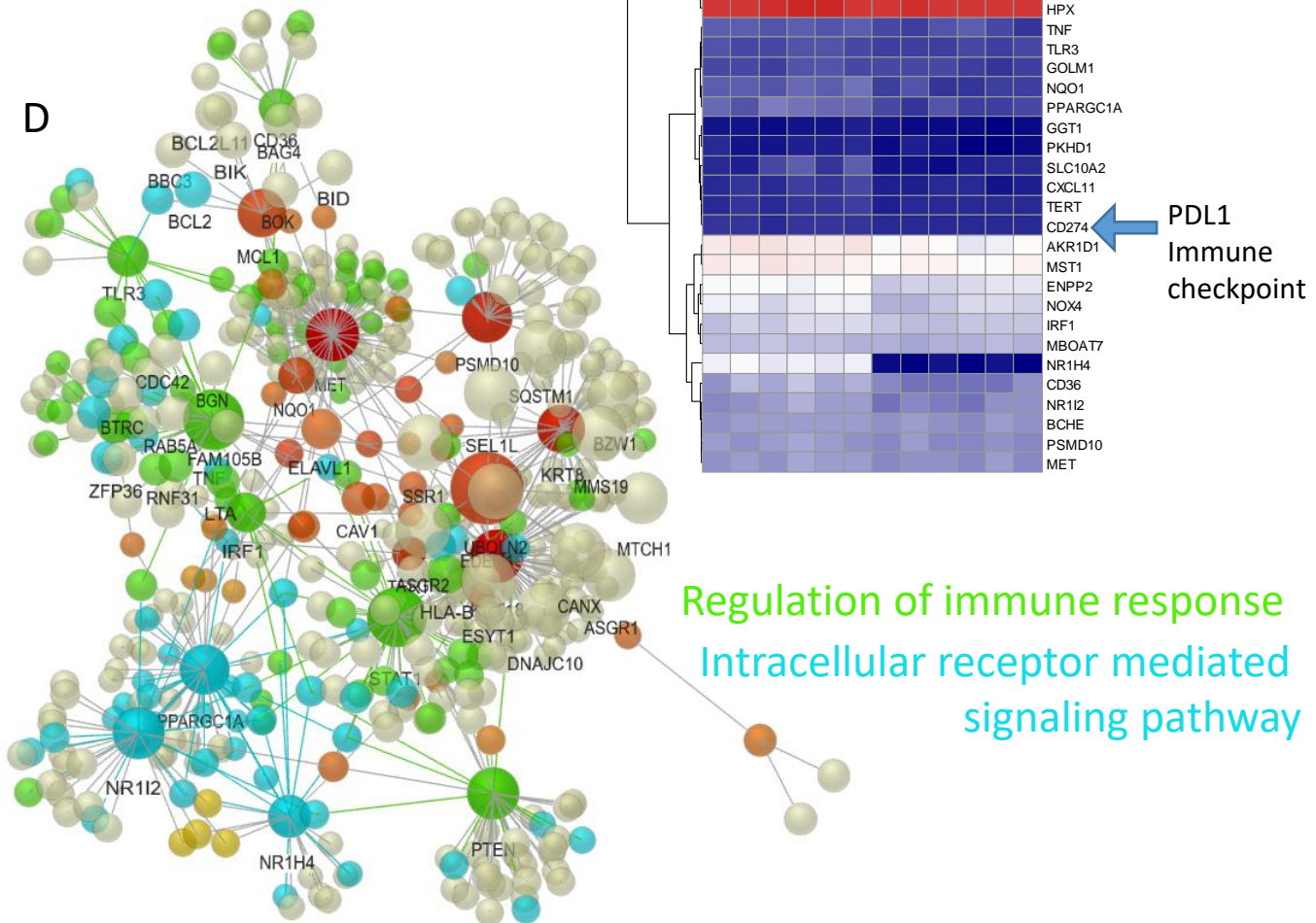
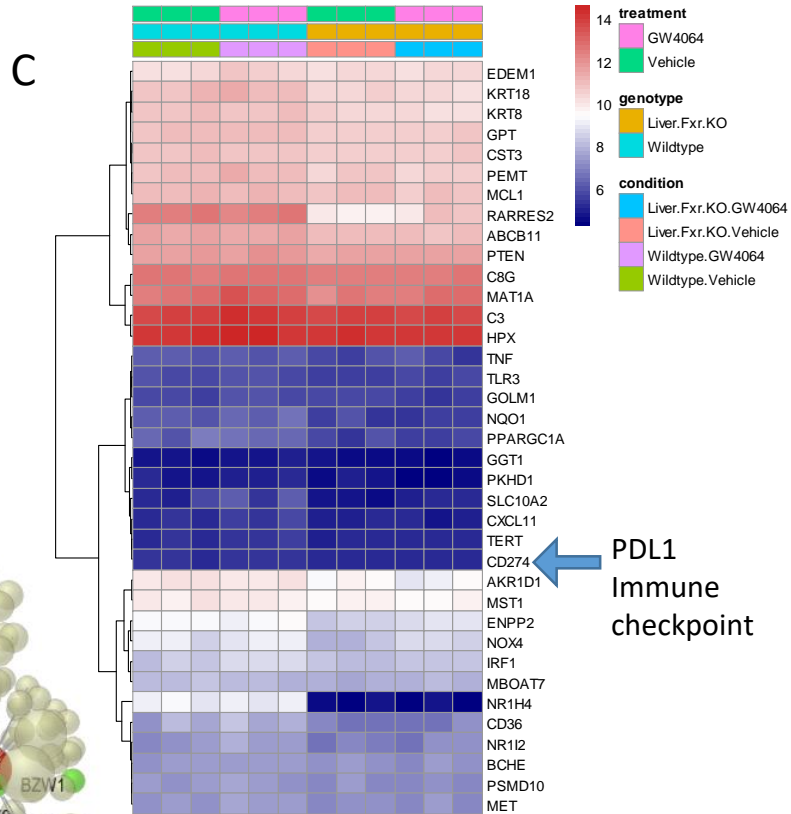
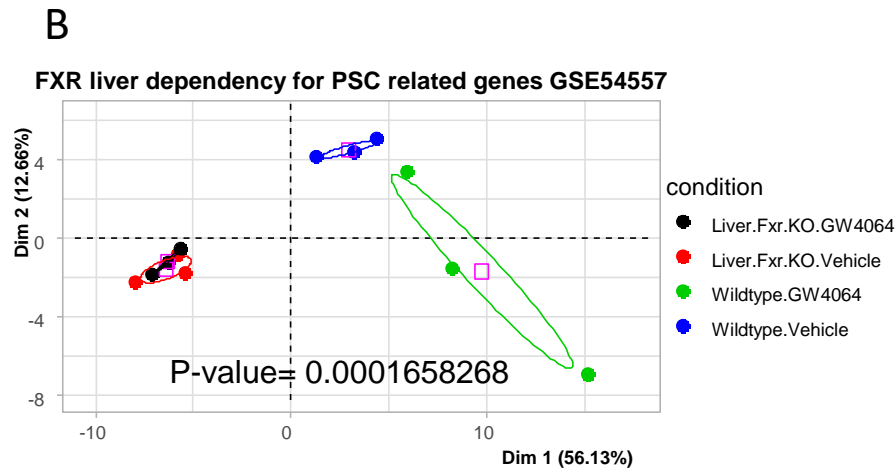
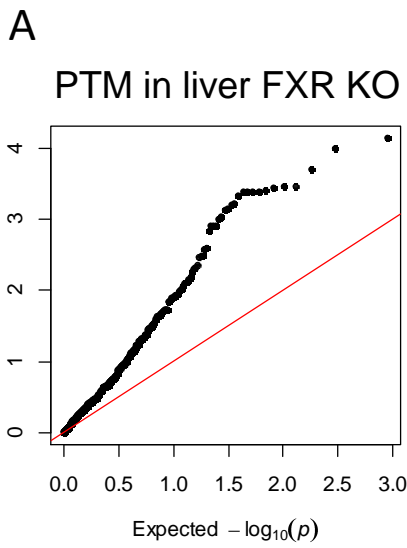
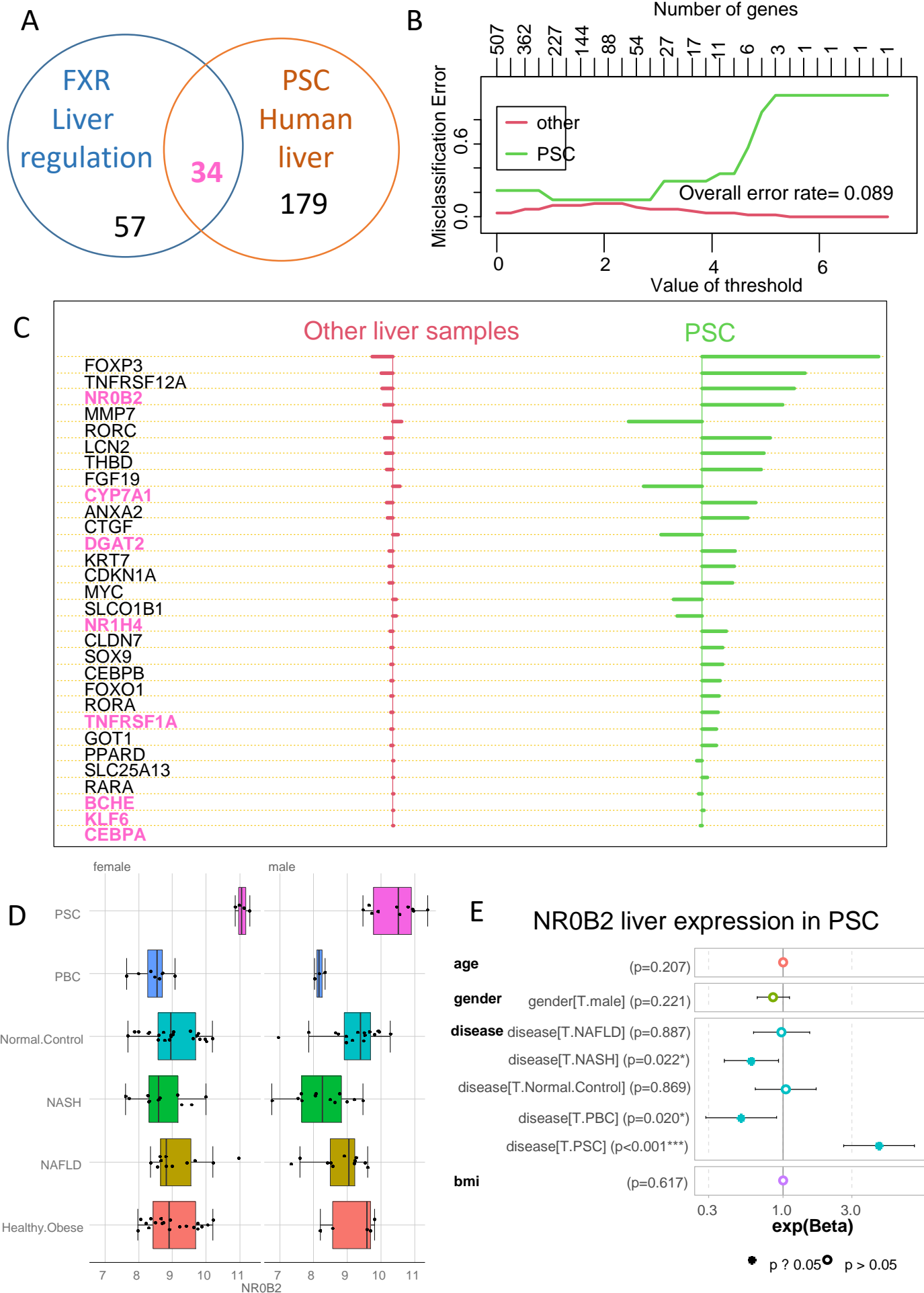


Figure 2



Topology DifNET database : liver specific network

Figure 3



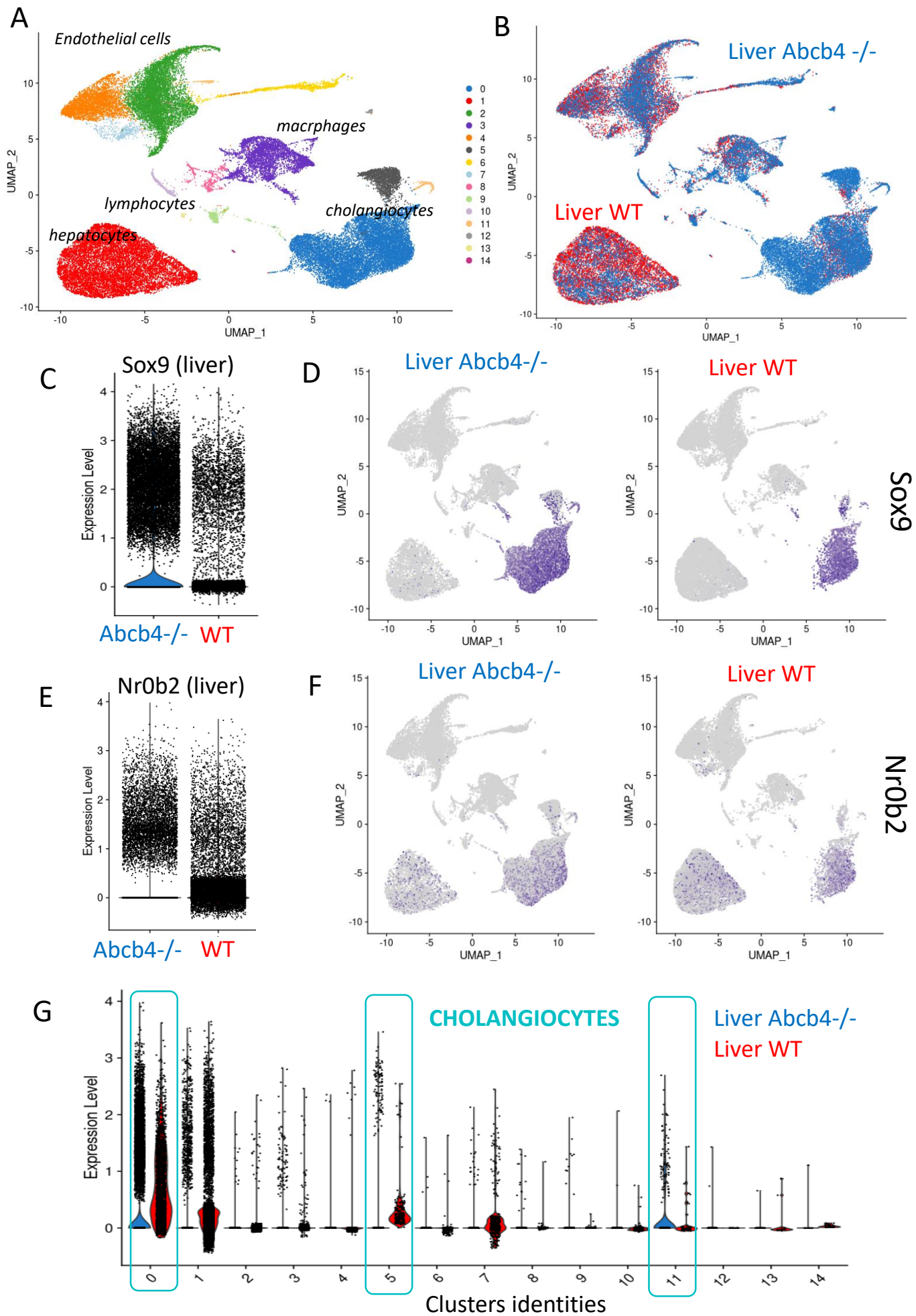
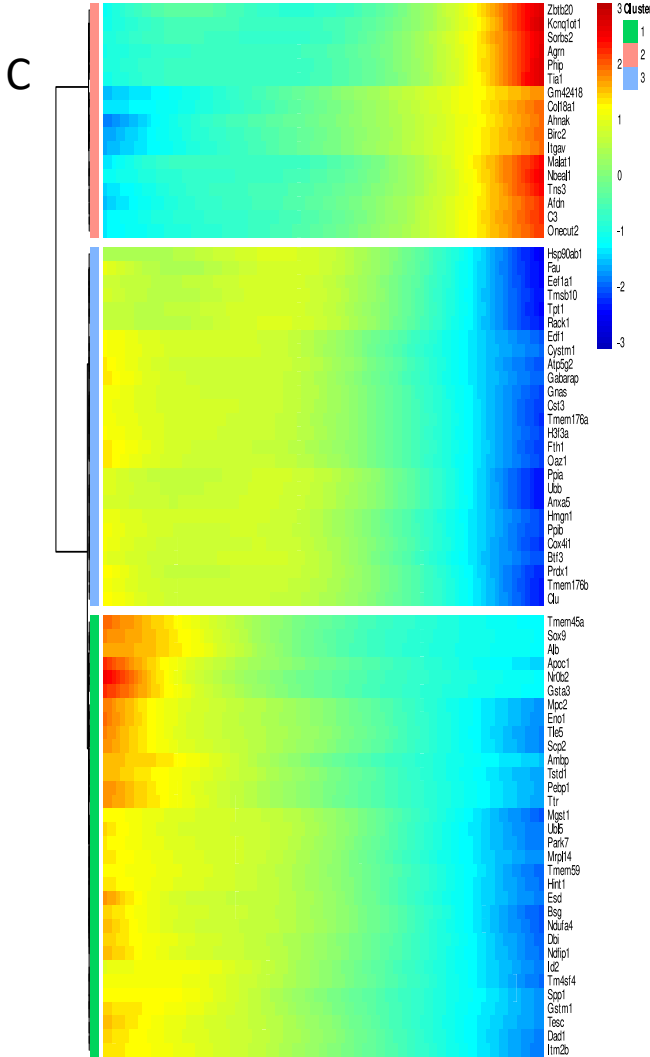
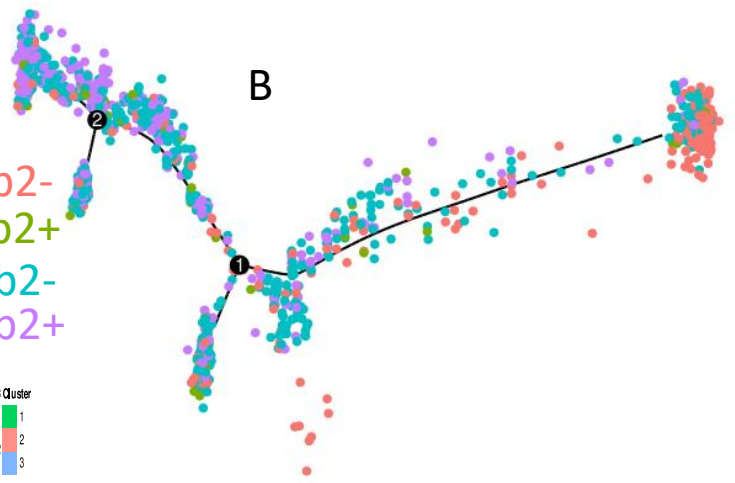
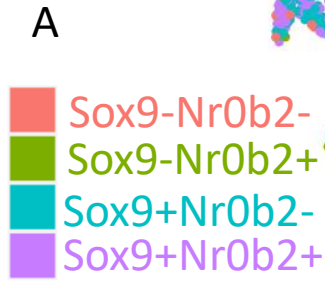
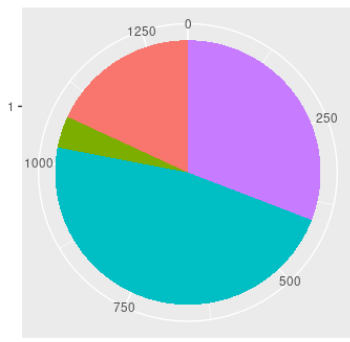
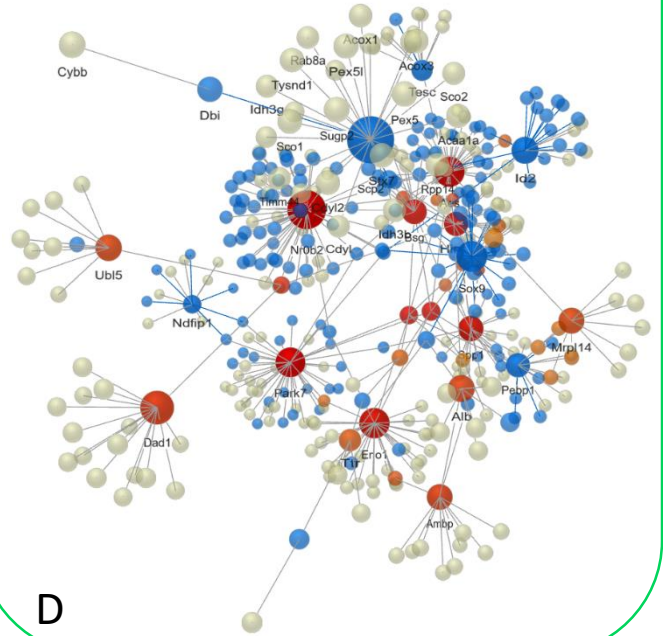


Figure 5



Positive regulation of metabolic process
GO-BP (FDR p-value = 5.2×10^{-23})



Nr0b2 cluster (-logFDR GO-BP)

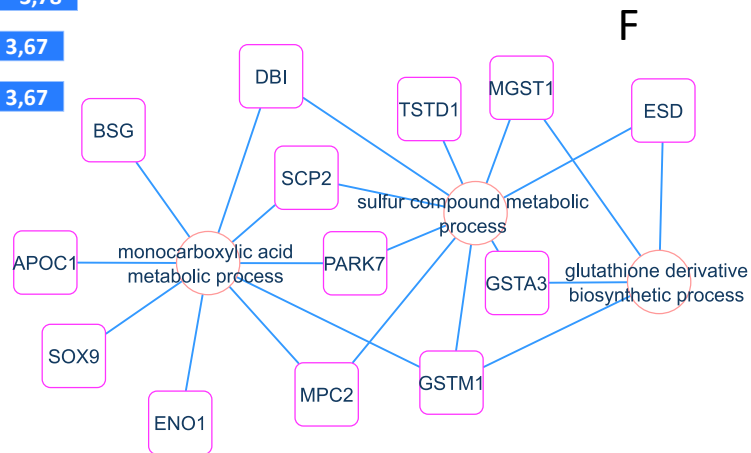
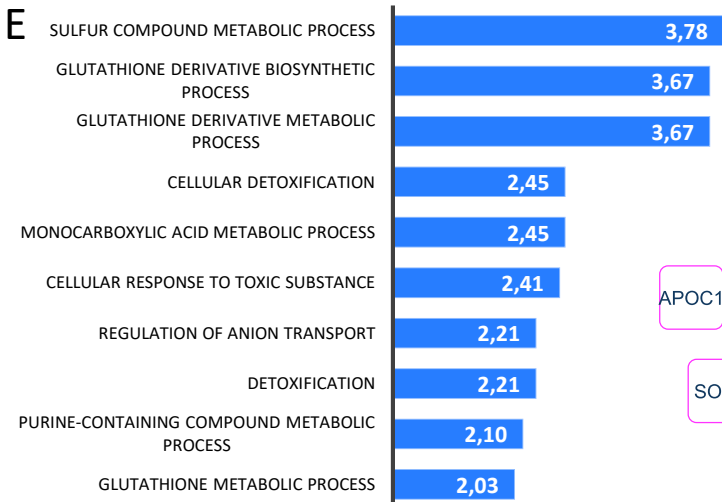
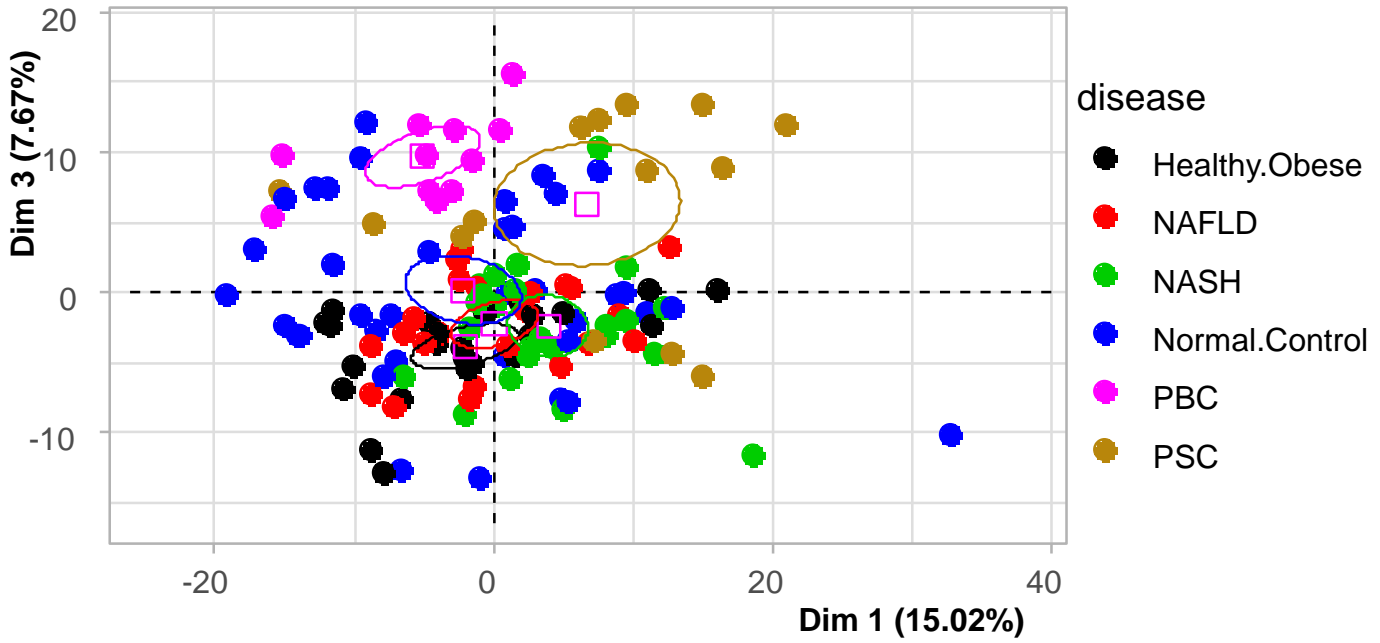
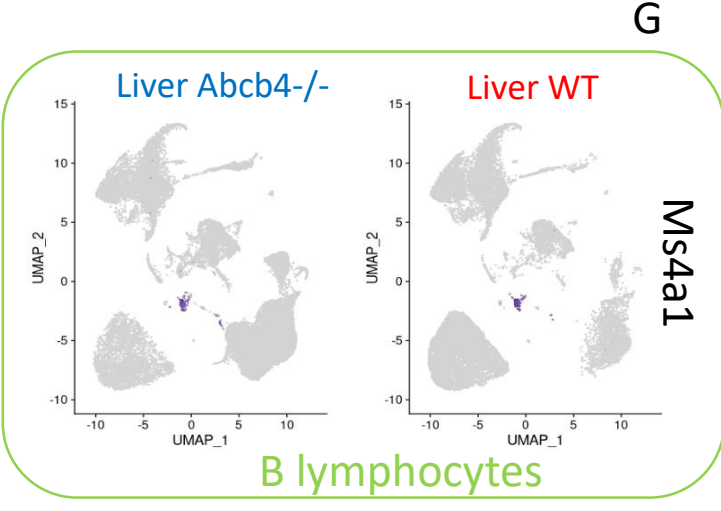
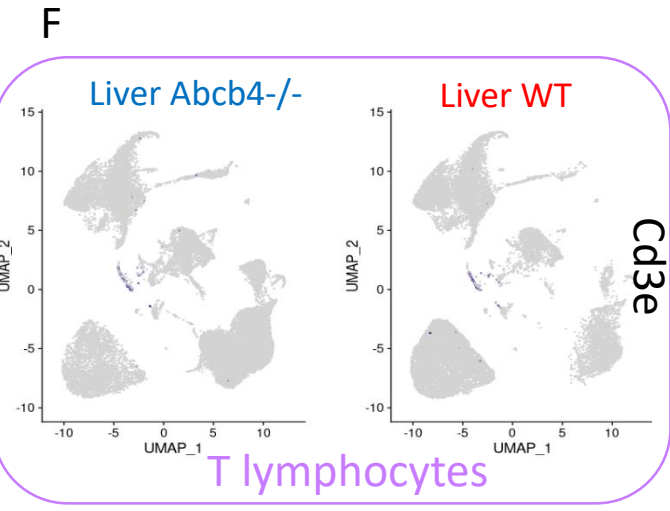
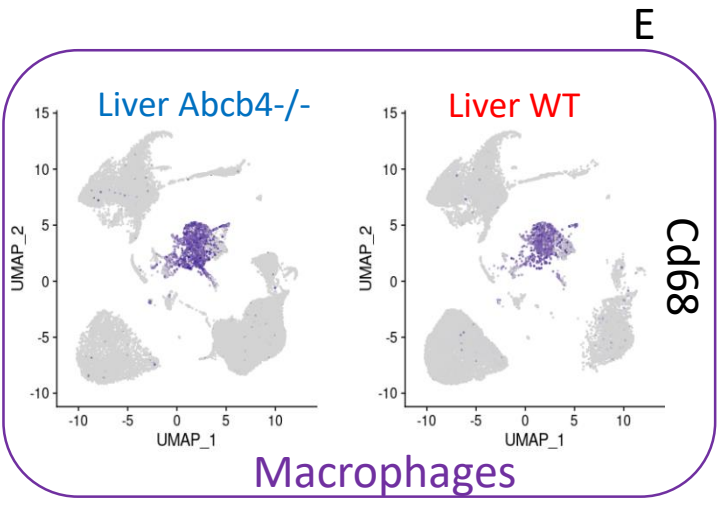
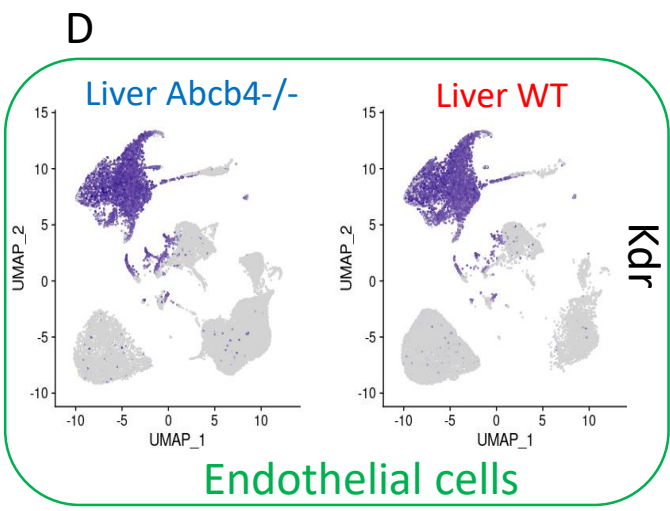
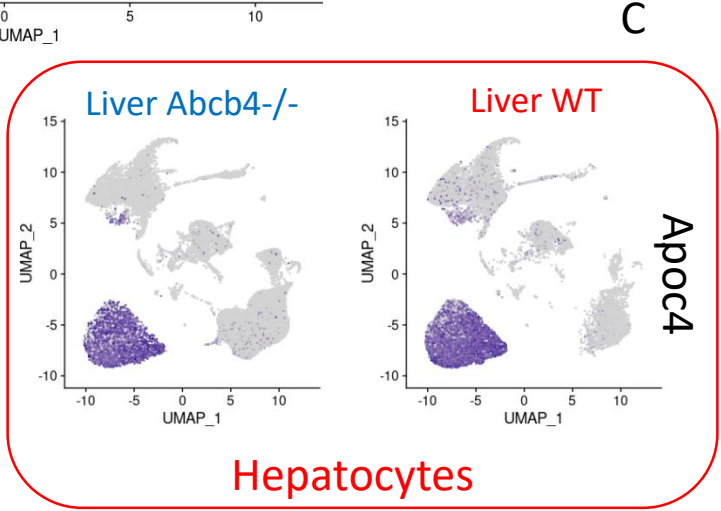
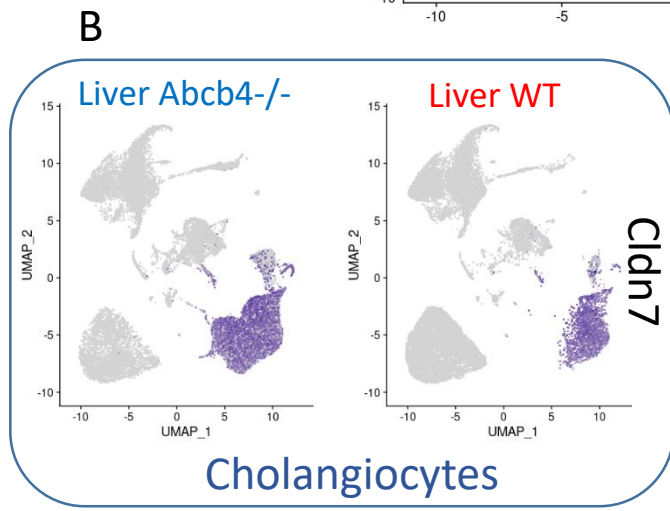
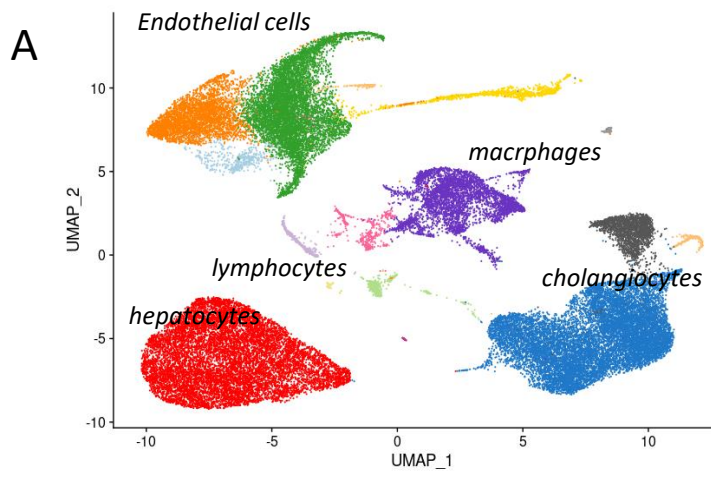


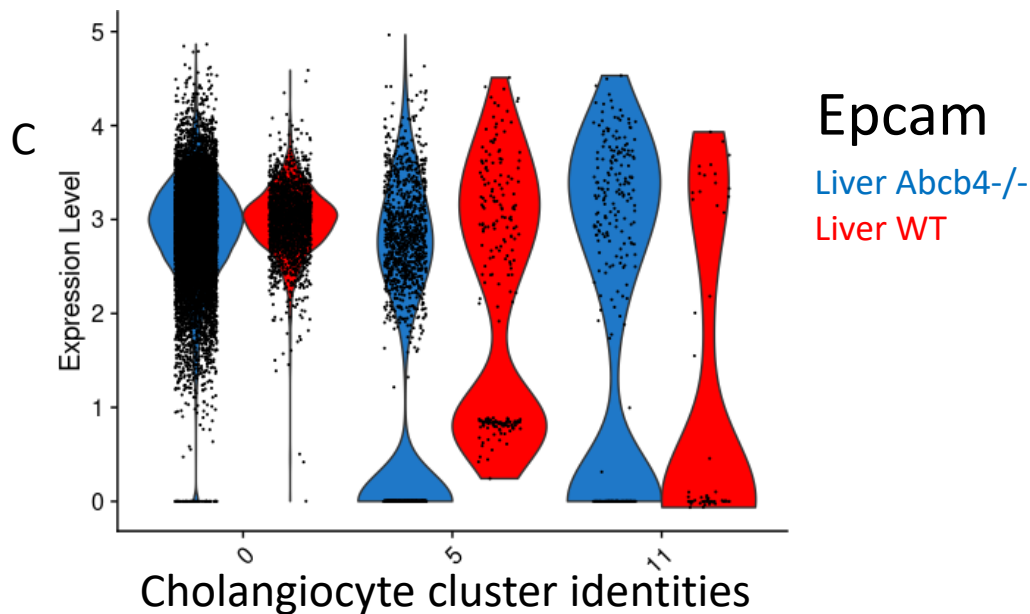
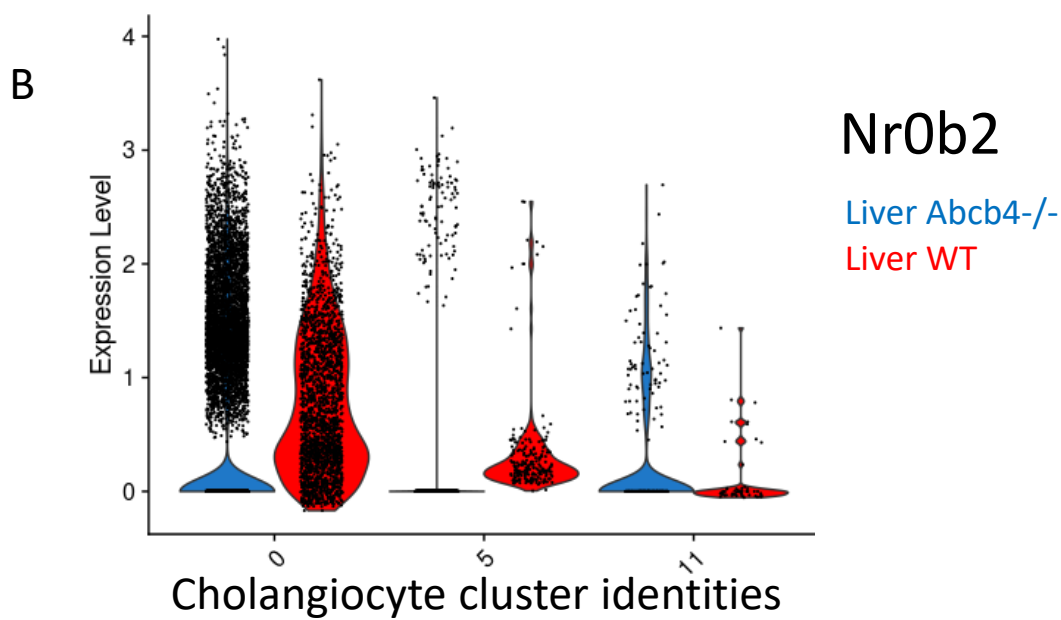
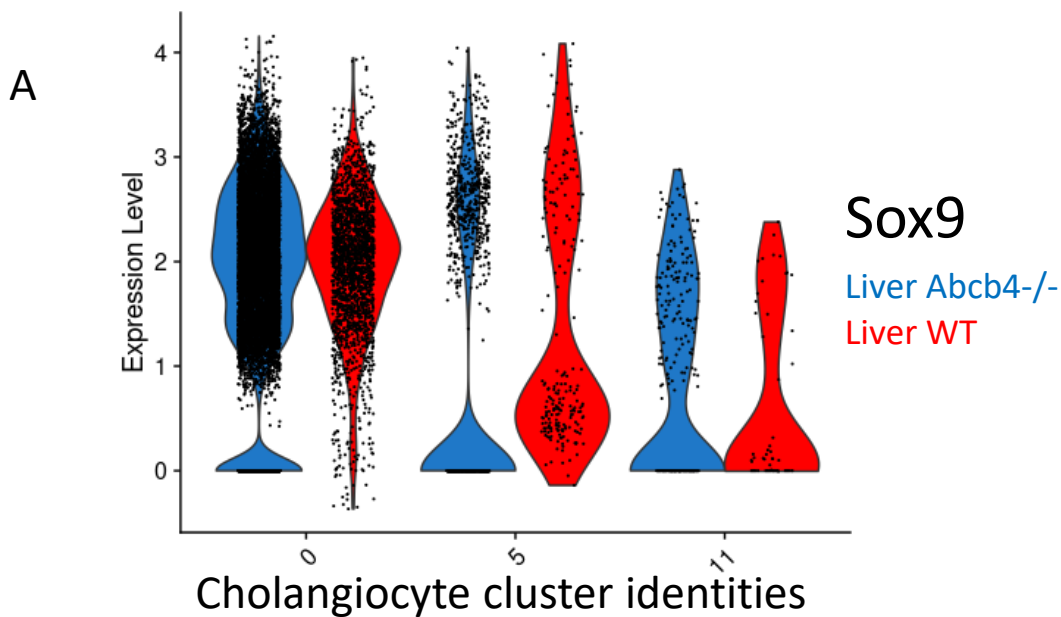
Figure 6

507 related genes - human liver GSE61260



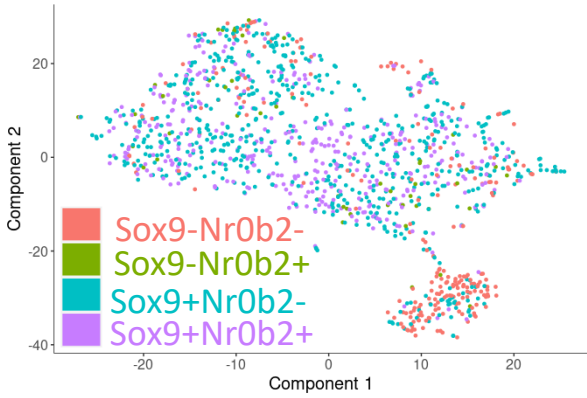


Supplemental Figure 2

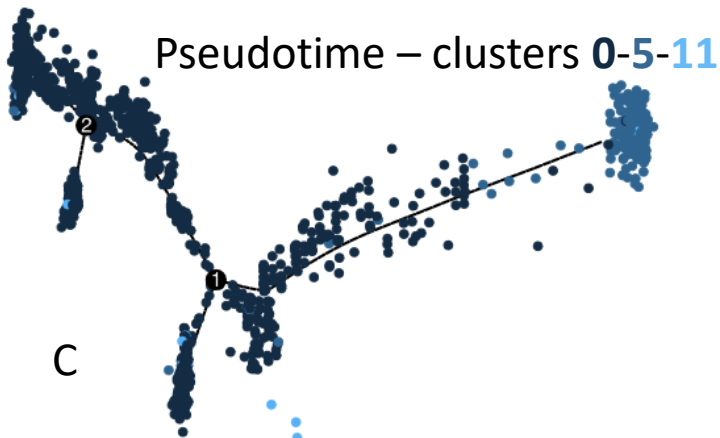
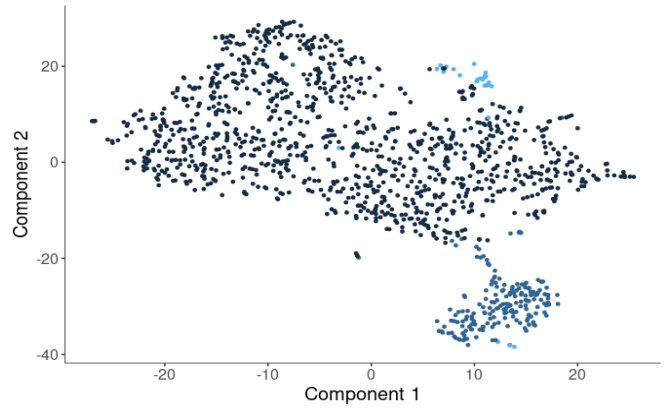
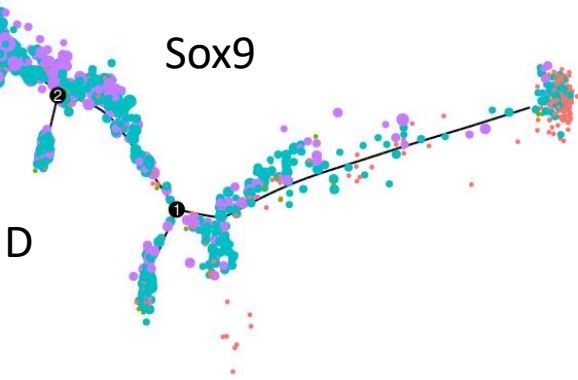
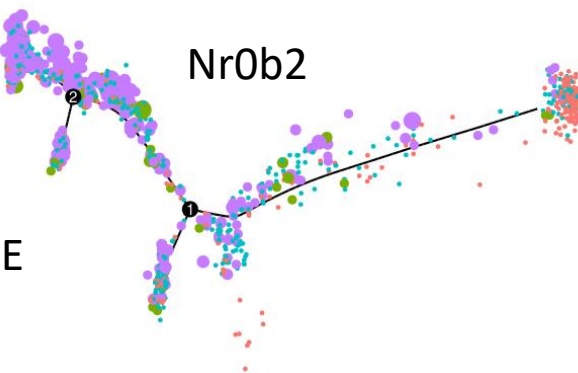
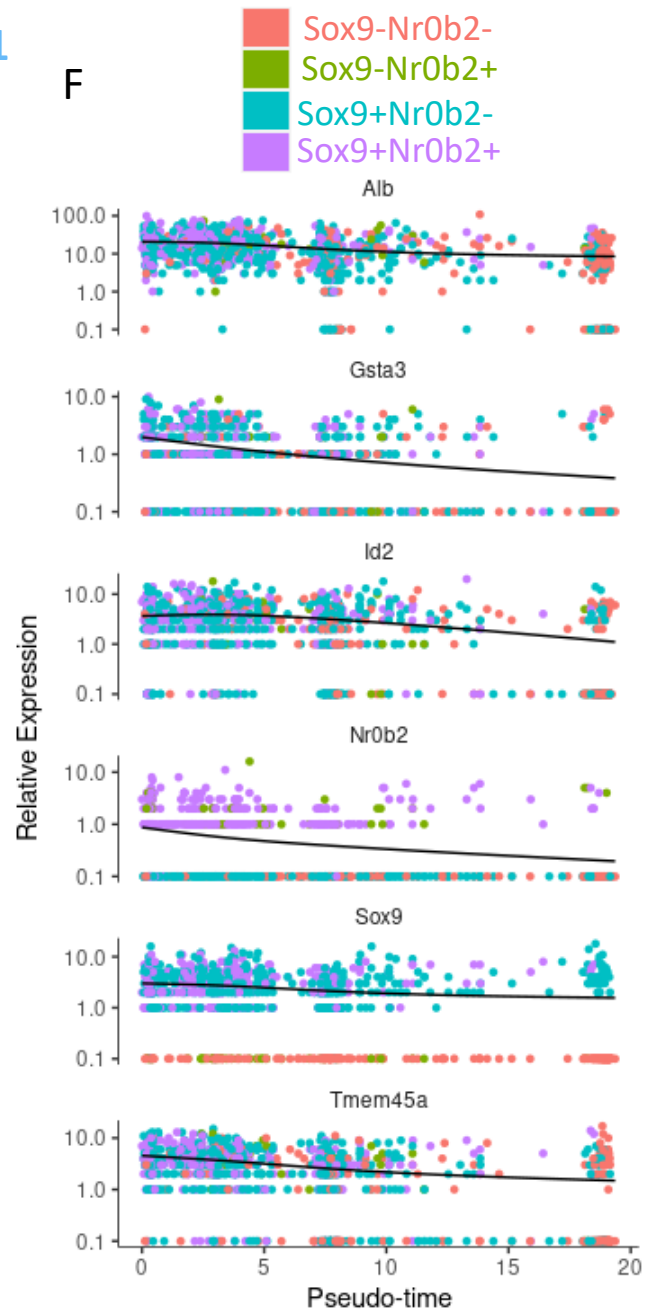


A

T-SNE stratification Nr0b2-Sox9

**B**

T-SNE- cholangiocyte clusters 0-5-11

**C****D****E****F**

SUPPLEMENTAL MATERIALS

Supplemental Tables

Supplemental Table 1: Textmining table of the common 525 ranked genes found in Pubmed with symptom keywords: this table describes the 525 ranked genes obtained by text mining with 'Génie' algorithm against the three MESH terms: biliary inflammation, biliary fibrosis, biliary stasis, respective ranks, p-values and collected PMID identifiers for each gene and each MESH term are presented

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Supplemental Table 1

gene	Genel D	n.total.pu bmed	Homo logs	ranking_me an	Rank.biliary. fibrosis	Rank.biliary.infla mation	Rank.biliary .stasis	n_pos.biliary. fibrosis	n_pos.biliary.infla mation	n_pos.biliar y.stasis	FDR.biliary.f ibrosis	FDR.biliary.infla mation	FDR.biliary .stasis
NR1H4	9971	486	10	1.66666666 666667	1	3	1	108	153	157	7.785e-144	4.838e-210	6.278e-212
ABCB4	5244	295	11	5.66666666 666667	4	10	3	77	82	104	1.455e-118	2.618e-127	7.063e-161
ABCB1 1	8647	203	10	8.33333333 333333	5	18	2	58	62	101	6.742e-98	8.01e-106	2.523e-176
TGFB1	7040	6275	9	11	6	8	19	202	339	113	1.35e-79	8.031e-138	5.692e-40
IFNL3	28261 7	527	10	12	2	27	7	100	69	65	5.873e-129	1.062e-87	7.138e-79
PNPLA 3	80339	262	8	17	3	42	6	80	45	53	3.532e-128	8.692e-70	1.284e-79
IL6	3569	6198	7	17.3333333 333333	15	1	36	117	551	79	7.473e-45	1.318e-230	9.478e-27
TLR4	7099	4840	11	18.3333333 333333	18	4	33	96	389	69	7.342e-43	1.276e-188	2.147e-27
GPBAR 1	15130 6	114	7	20	10	38	12	29	38	29	3.938e-54	1.874e-73	5.339e-52
IL17A	3605	2099	8	21.3333333 333333	14	6	44	64	225	42	6.968e-45	1.34e-170	2.905e-26
TNF	7124	8701	8	21.6666666 666667	17	2	46	141	656	95	6.731e-43	4.088e-218	2.117e-25
HMOX 1	3162	1990	10	22.6666666 666667	24	26	18	56	122	61	4.269e-40	2.293e-92	3.275e-41
ATP8B 1	5205	88	10	23	8	57	4	32	28	46	1.662e-64	1.792e-56	8.701e-94
NFE2L2	4780	2172	9	24.6666666 666667	26	19	29	56	141	50	2.393e-38	7.63e-103	2.115e-31
PPARA	5465	1457	11	26.6666666 666667	28	39	13	43	85	56	4.818e-35	3.185e-73	9.144e-44
HNF4A	3172	832	11	29	21	52	14	41	55	44	2.884e-42	1.805e-58	5.653e-43
KRT19	3880	403	8	30	11	56	23	39	42	29	9.56e-52	8.678e-57	1.599e-35
CFTR	1080	1992	10	30.3333333 333333	19	40	32	59	97	43	2.537e-42	1.324e-72	1.13e-27
HFE	3077	1015	7	30.6666666 666667	7	76	9	71	49	61	5.66e-70	7.329e-48	8.847e-57
CXCL10	3627	820	7	31	22	36	35	39	69	29	2.846e-40	1.139e-74	4.507e-27
CTGF	1490	939	9	32	12	45	39	50	64	30	1.096e-49	1.983e-65	1.42e-26
SPP1	6696	1677	7	32.6666666 666667	23	34	41	52	97	38	2.93e-40	7.601e-79	2.141e-26
HGF	3082	1121	10	37.3333333 333333	20	58	34	46	58	33	2.584e-42	7.407e-55	2.58e-27
AFP	174	546	8	38.3333333 333333	9	82	24	51	38	31	2.869e-62	3.469e-46	2.538e-34
STAT3	6774	3858	10	41	44	14	65	57	208	42	3.088e-28	1.073e-112	6.706e-18
TNFRSF 1A	7132	1812	10	44	55	9	68	36	165	26	4.091e-26	2.034e-132	3.815e-16
CRP	1401	2117	29	44.3333333 333333	31	47	55	48	88	33	7.068e-33	1.43e-63	1.183e-19
NR1H3	10062	684	9	46	67	41	30	22	62	30	2.516e-23	1.918e-71	2.504e-30
NR1H2	8856	551	10	46	34	89	15	28	37	38	1.032e-32	8.953e-45	6.609e-43
IL22	50616	475	10	47.6666666 666667	38	23	82	25	71	14	1.799e-30	1.242e-93	1.848e-14
KRT18	3875	449	10	48	16	102	26	34	31	29	4.062e-43	9.082e-40	3.146e-34
IL10	3586	4840	10	48.6666666 666667	40	5	101	68	377	35	1.365e-29	1.34e-182	4.496e-12
NOS2	4843	2636	12	48.6666666 666667	57	30	59	42	125	36	2.348e-25	5.07e-82	4.009e-19
HNF1B	6928	446	10	50.3333333 333333	25	101	25	31	31	29	3.015e-39	7.463e-40	2.701e-34
NLRP3	11454 8	1166	24	51.6666666 666667	65	12	78	27	120	20	1.863e-23	1.076e-115	6.692e-15
CYP7A 1	1581	237	10	51.6666666 666667	66	79	10	16	30	37	2.027e-23	9.997e-47	3.093e-55
FAS	355	2660	10	54.3333333 333333	42	65	56	48	82	37	3.898e-29	2.025e-52	1.224e-19
LCN2	3934	811	7	55.3333333 333333	33	84	49	32	43	25	1.037e-32	1.429e-45	5.63e-23
ABCC2	1244	479	13	55.3333333 333333	30	128	8	28	28	50	2.54e-34	5.953e-35	4.028e-61
PPARG	5468	3417	9	56	73	44	51	42	116	47	8.096e-22	1.115e-65	3.058e-22
ALB	213	855	9	57.3333333 333333	27	107	38	37	38	29	1.797e-37	3.52e-39	1.285e-26
SMAD3	4088	1507	12	59.3333333 333333	32	66	80	41	62	22	8.859e-33	9.906e-52	1.251e-14

SERPIN A1	5265	633	20	60	29	124	27	31	31	32	1.051e-34	2.458e-35	1.171e-33
FGF19	9965	239	10	61.33333333333333	37	125	22	21	23	26	2.533e-31	3.706e-35	2.871e-37
IFNG	3458	4209	7	62	59	16	111	52	212	31	3.346e-24	3.914e-109	1.484e-11
ADIPO Q	9370	2651	10	62.33333333333333	56	68	63	43	79	35	6.114e-26	1.745e-50	1.961e-18
ONECU T1	3175	193	8	62.66666666666667	36	109	43	20	24	18	1.448e-31	4.602e-39	2.526e-26
SLC10A 1	6554	111	9	67	53	137	11	15	18	29	8.911e-27	3.412e-33	2.415e-52
MMP9	4318	4106	12	67.33333333333333	49	55	98	57	115	32	3.536e-27	2.165e-58	3.148e-12
CD14	929	961	7	74	75	53	94	23	58	16	2.189e-21	1.955e-58	1.7e-12
TIMP1	7076	945	6	74	39	93	90	31	43	17	9.862e-30	6.334e-43	1.391e-13
SREBF1	6720	836	12	74.33333333333333	63	113	47	24	36	27	1.047e-23	2.58e-37	8.283e-25
MMP2	4313	2608	10	75.33333333333333	46	97	83	45	65	28	1.853e-27	1.854e-41	3.359e-14
IL1B	3553	4025	8	75.66666666666667	84	7	136	43	295	27	3.072e-20	2.541e-158	4.81e-10
CXCR3	2833	507	9	76.33333333333333	48	73	108	23	39	12	3.037e-27	1.116e-48	1.014e-11
LEPR	3953	2229	10	78.33333333333333	70	69	96	34	72	23	4.802e-22	3.904e-50	2.706e-12
LDLR	3949	1935	9	79	116	60	61	24	72	30	3.442e-16	8.426e-54	1.727e-18
HAMP	57817	365	5	80.33333333333333	72	103	66	17	29	15	6.472e-22	1.311e-39	2.632e-17
JAG1	182	1196	12	80.66666666666667	51	151	40	31	35	33	6.015e-27	2.696e-31	1.504e-26
NR1I3	9970	281	8	82.33333333333333	79	126	42	15	24	20	9.475e-21	4.278e-35	2.115e-26
PDCD1	5133	924	9	85	52	63	140	28	52	13	6.332e-27	6.571e-53	6.449e-10
NROB2	8431	259	10	85.66666666666667	76	165	16	15	20	30	2.904e-21	1.292e-29	1.322e-42
LGALS3	3958	923	10	86	45	108	105	29	39	15	6.047e-28	4.444e-39	8.58e-12
SIRT1	23411	1802	10	87.33333333333333	106	94	62	24	56	29	8.926e-17	9.553e-43	1.723e-18
LEP	3952	3609	8	87.66666666666667	94	92	77	37	81	35	2.41e-18	1.353e-43	5.221e-15
NOTCH 2	4853	669	10	87.66666666666667	69	130	64	21	31	19	2.417e-22	1.217e-34	4.353e-18
CHI3L1	1116	409	9	88.33333333333333	35	117	113	25	28	11	4.92e-32	8.239e-37	1.713e-11
NFKB1	4790	4419	9	88.66666666666667	98	17	151	40	212	27	1.452e-17	6.239e-106	0.0000000 02375
SERPIN E1	5054	1808	12	89	62	110	95	33	51	21	9.107e-24	1.178e-38	1.815e-12
COL1A 1	1277	1616	9	89	41	142	84	38	41	22	3.107e-29	2.441e-32	4.425e-14
CCL13	6357	1262	5	89.33333333333333	125	24	119	19	101	16	2.16e-15	1.887e-93	6.502e-11
HMGB 1	3146	904	8	89.66666666666667	60	32	177	25	76	11	5.299e-24	1.431e-79	0.0000000 3828
IL18	3606	1496	7	92	99	21	156	23	112	15	1.533e-17	1.452e-96	0.0000000 03399
ICAM1	3383	1864	7	97.33333333333333	121	59	112	23	72	20	9.59e-16	8.539e-55	1.473e-11
CCR5	1234	1824	11	99	86	83	128	28	60	18	8.811e-20	1.055e-45	2.896e-10
CCL5	6352	958	8	100.33333333333333	74	43	184	23	67	11	2.076e-21	4.027e-68	0.0000000 6536
KRT8	3856	633	11	102	54	199	53	24	23	22	2.218e-26	1.005e-25	5.607e-22
TNFRSF 1B	7133	1050	8	103.33333333333333	107	35	168	19	78	12	1.089e-16	5.251e-77	0.0000000 2066
TLR3	7098	1093	12	104	112	80	120	19	49	15	2.077e-16	2.004e-46	7.33e-11
TLR2	7097	2916	13	106.33333333333333	127	13	179	28	179	19	2.528e-15	5.61e-113	0.0000000 4105
VEGFA	7422	6064	7	106.66666666666667	50	96	174	72	106	30	4.766e-27	1.096e-41	0.0000000 3062
CCL2	6347	1332	7	107	91	54	176	23	66	13	1.595e-18	2.18e-58	0.0000000 3428
PTGS2	5743	3482	10	107.33333333333333	95	49	178	36	109	21	3.416e-18	7.622e-61	0.0000000 4118
PKHD1	5314	103	8	107.33333333333333	47	221	54	15	13	12	3.056e-27	7.226e-24	1.048e-19
CXCL8	3576	2063	5	108	68	20	236	34	135	13	5.628e-23	7.742e-101	0.0000028 77
MIF	4282	975	8	109.66666666666667	128	15	186	17	109	11	2.97e-15	1.065e-112	0.0000000 7688
CD163	9332	222	7	110.33333333333333	82	106	143	14	25	8	1.211e-20	3.136e-39	9.321e-10

SMAD7	4092	532	10	111.666666 666667	83	127	125	18	29	11	1.485e-20	5.273e-35	2.453e-10
MBL2	4153	845	13	112.666666 666667	43	203	92	29	25	16	5.815e-29	3.259e-25	2.662e-13
CCR2	72923 0	1068	10	114	138	50	154	17	61	13	1.128e-14	5.149e-59	0.0000000 0317
ABCC3	8714	247	26	120.333333 333333	93	251	17	13	15	29	1.954e-18	4.307e-22	1.214e-41
MET	4233	1475	10	124.666666 666667	92	145	137	24	39	16	1.64e-18	5.444e-32	4.881e-10
IL33	90865	637	6	126.333333 333333	139	11	229	14	97	8	1.33e-14	2.894e-117	0.0000019 03
FASLG	356	1399	10	126.333333 333333	113	140	126	21	39	16	2.178e-16	9.092e-33	2.568e-10
TGFBR 2	7048	983	10	129	77	163	147	23	31	13	3.44e-21	7.308e-30	0.0000000 01268
APOE	348	6483	8	129.666666 666667	184	74	131	36	128	37	5.905e-12	1.302e-48	3.32e-10
C5	727	485	9	131.333333 333333	135	136	123	13	27	11	7.391e-15	1.739e-33	9.485e-11
IKBK	8517	567	9	132	129	133	134	14	29	11	3.044e-15	3.038e-34	4.434e-10
CTNNA 1	1499	5958	13	134	64	144	194	63	82	28	1.118e-23	4.129e-32	0.0000001 199
CEBPA	1050	898	9	134.333333 333333	90	243	70	20	23	19	7.217e-19	1.601e-22	7.18e-16
IL4	3565	2440	7	138.333333 333333	115	31	269	27	118	13	2.734e-16	2.004e-80	0.0000138 6
PTEN	5728	3558	12	139.333333 333333	80	173	165	41	55	22	9.762e-21	3.845e-29	0.0000000 1814
IL6ST	3572	518	10	143	163	91	175	12	36	9	2.686e-13	1.96e-44	0.0000000 3432
SLC10A 2	6555	125	13	144	134	270	28	9	12	19	7.195e-15	6.821e-21	1.377e-31
UGT1A 1	54658	715	22	148.333333 333333	81	343	21	20	16	38	1.135e-20	1.201e-16	6.787e-39
CYP2E1	1571	845	7	149.333333 333333	183	192	73	13	26	18	4.978e-12	2.711e-26	2.693e-15
CD274	29126	1011	10	152	117	88	251	18	46	9	5.441e-16	7.31e-45	0.0000059 58
SOCS1	8651	639	10	153.333333 333333	160	70	230	13	43	8	1.909e-13	8.999e-50	0.0000019 39
GPT	2875	189	15	153.333333 333333	13	442	5	28	9	53	1.773e-45	9.366e-14	6.163e-88
STAT1	6772	1574	10	156.333333 333333	167	81	221	18	57	12	4.518e-13	2.047e-46	0.0000010 43
IFNAR1	3454	957	11	157.333333 333333	161	99	212	15	41	10	2.122e-13	1.34e-40	0.0000005 109
SLCO1 B3	28234	174	6	158.666666 666667	152	293	31	9	12	19	1.291e-13	3.657e-19	9.145e-29
KRT7	3855	165	9	159	103	287	87	11	12	10	3.313e-17	1.954e-19	5.957e-14
ANGPT 2	285	621	10	159.666666 666667	104	147	228	16	28	8	4.699e-17	6.074e-32	0.0000015 82
TNFSF1 0	8743	946	10	160.333333 333333	158	112	211	15	38	10	1.845e-13	1.229e-37	0.0000004 629
IGF1	3479	3110	10	161.333333 333333	97	246	141	33	40	23	1.115e-17	2.104e-22	6.685e-10
TNFAIP 3	7128	463	9	163.666666 666667	174	119	198	11	29	8	1.472e-12	1.084e-36	0.0000002 01
FAH	2184	163	17	164.666666 666667	123	285	86	10	12	10	1.473e-15	1.696e-19	5.328e-14
EDN1	1906	1574	10	165.666666 666667	96	256	145	24	28	16	6.104e-18	8.575e-22	0.0000000 01115
IL1RN	3557	1296	8	166	173	29	296	16	93	9	1.425e-12	9.991e-85	0.0000353 3
C3	718	1180	21	167	131	132	238	18	38	10	6.014e-15	2.36e-34	0.0000028 88
FGF21	26291	429	6	169	168	264	75	11	17	14	6.786e-13	2.609e-21	5.121e-15
ENPP2	5168	247	11	169	85	333	89	14	12	11	5.236e-20	2.207e-17	9.608e-14
IL1R1	3554	846	11	170	146	37	327	15	69	7	4.269e-14	8.857e-74	0.0000999 1
CAV1	857	1621	10	170	198	182	130	16	35	17	2.815e-11	2.794e-27	3.005e-10
RBP4	5950	430	9	171.666666 666667	124	303	88	13	15	13	1.773e-15	1.326e-18	9.266e-14
NAMPT	10135	578	15	172.666666 666667	170	188	160	12	23	10	9.036e-13	1.432e-26	0.0000000 06631
PPARG CIA	10891	1286	9	173.333333 333333	210	200	110	14	30	17	7.303e-11	1.005e-25	1.212e-11
IL13	3596	1096	7	174	101	28	393	20	89	7	2.464e-17	6.904e-87	0.0004115
TP53	7157	12916	9	175.333333 333333	108	148	270	79	140	39	1.237e-16	8.161e-32	0.0000145 2
NOS3	4846	3360	8	177	120	224	187	31	44	20	9.299e-16	1.011e-23	0.0000000 8043
CNR2	1269	480	11	178	175	237	122	11	19	11	2.144e-12	4.038e-23	8.578e-11

GOLM1	51280	115	6	178.666666 666667	78	326	132	12	10	7	8.372e-21	1.585e-17	3.532e-10
DDIT3	1649	532	8	181.333333 333333	216	175	153	10	24	10	9.492e-11	1.231e-28	0.0000000 03176
NR1H2	7376	933	10	181.666666 666667	263	100	182	11	40	11	0.00000000 1364	5.977e-40	0.0000000 509
FABP1	2168	312	9	181.666666 666667	144	353	48	11	12	19	2.596e-14	3.352e-16	4.589e-24
CPS1	1373	189	12	183	109	336	104	11	11	9	1.417e-16	4.597e-17	8.482e-12
CD36	948	873	14	184.333333 333333	211	170	172	12	29	11	7.477e-11	3.561e-29	0.0000000 2784
KEAP1	9817	535	10	185	217	211	127	10	21	11	9.962e-11	8.808e-25	2.559e-10
SLC4A2	6522	195	14	186.333333 333333	111	339	109	11	11	9	1.967e-16	6.441e-17	1.071e-11
AHSG	197	367	10	188	132	282	150	12	15	9	6.065e-15	1.396e-19	0.0000000 02071
RETN	56729	656	5	188.333333 333333	202	129	234	11	31	8	4.881e-11	6.844e-35	0.0000023 13
RELA	5970	2194	10	191	260	64	249	16	75	13	0.00000000 1227	9.1e-53	0.0000051 32
LYZ	4069	1250	10	191.666666 666667	206	22	347	14	101	8	5.237e-11	8.402e-94	0.0001554
HP	3240	520	7	193.333333 333333	105	265	210	15	18	8	6.026e-17	3.131e-21	0.0000004 557
SMAD2	4087	1072	10	195.333333 333333	150	209	227	16	27	10	1.087e-13	7.387e-25	0.0000013 07
HLA- DRB1	3123	2535	4	195.333333 333333	61	401	124	39	24	22	6.928e-24	1.976e-14	9.53e-11
CDKN1 A	1026	2488	7	200.666666 666667	156	202	244	23	40	14	1.726e-13	2.35e-25	0.0000044 51
TIMP3	7078	470	9	200.666666 666667	246	212	144	9	20	10	5.252e-10	1.387e-24	0.0000000 01042
HIF1A	3091	4151	9	201.333333 333333	137	116	351	33	75	15	8.425e-15	6.417e-37	0.0001752
MAPK8	5599	2419	13	202.333333 333333	276	169	162	16	45	18	0.00000000 4064	3.324e-29	0.0000000 1354
IFNL4	10118 0976	61	-	203.333333 333333	71	437	102	11	7	7	5.167e-22	7.526e-14	4.791e-12
ANXA1	301	530	10	209.666666 666667	264	152	213	9	26	8	0.00000000 1375	3.245e-31	0.0000005 185
CDH1	999	3239	14	209.666666 666667	143	210	276	28	45	15	2.107e-14	7.922e-25	0.0000174 7
SOX9	6662	1727	10	210.333333 333333	164	278	189	19	27	14	2.951e-13	4.922e-20	0.0000000 978
ACTA2	59	1372	12	211	110	262	261	21	26	10	1.56e-16	1.906e-21	0.0000096 32
TIMP2	7077	652	10	212	162	308	166	13	17	10	2.414e-13	2.104e-18	0.0000000 1968
CD40	958	1130	9	213	196	121	322	14	39	8	1.56e-11	5.816e-36	0.0000835 4
EPCAM	4072	381	10	213.333333 333333	100	273	267	14	16	6	1.809e-17	9.388e-21	0.0000131 7
IL12B	3593	1145	10	215.666666 666667	220	194	233	13	29	10	1.506e-10	4.335e-26	0.0000022 69
CXCL9	4283	160	4	216.333333 333333	181	316	152	8	11	7	3.048e-12	7.658e-18	0.0000000 03128
AHR	196	1062	10	216.666666 666667	207	135	308	13	36	8	6.643e-11	6.529e-34	0.0000566 3
TLR7	51284	680	10	220	253	118	289	10	33	7	8.251e-10	8.578e-37	0.0000282 4
FN1	2335	1314	9	220.666666 666667	87	277	298	24	24	9	1.506e-19	4.729e-20	0.0000390 1
ATP7B	540	371	12	221.333333 333333	133	481	50	12	10	19	6.836e-15	1.321e-12	1.144e-22
SOCS3	9021	889	11	222.666666 666667	190	46	432	13	62	6	8.806e-12	1.155e-64	0.000894
ACE	1636	2786	11	224	130	354	188	27	28	18	4.101e-15	3.371e-16	0.0000000 8158
AREG	374	305	9	224.666666 666667	142	290	242	11	14	6	2.06e-14	2.906e-19	0.0000040 34
EGR1	1958	1049	10	225.333333 333333	186	266	224	14	23	10	6.432e-12	3.909e-21	0.0000010 93
TLR9	54106	1359	9	226	256	51	371	13	67	8	9.316e-10	8.884e-59	0.0002566
VDR	7421	2181	11	226	141	335	202	23	26	15	1.653e-14	4.369e-17	0.0000002 738
TNFRSF 12A	51330	164	7	226.666666 666667	89	90	501	12	26	3	5.849e-19	1.862e-44	0.003109
GFER	2671	136	10	228.666666 666667	204	302	180	7	11	6	5.088e-11	1.294e-18	0.0000000 4615
AGT	183	1702	9	230.666666 666667	102	358	232	24	22	12	2.889e-17	3.663e-16	0.0000021 66
FGFR4	2264	411	10	231.666666 666667	225	356	114	9	13	11	1.796e-10	3.491e-16	1.788e-11
MMP3	4314	915	14	232.666666 666667	151	312	235	15	19	9	1.221e-13	3.409e-18	0.0000028 61
NOTCH 1	4851	4375	12	233	188	257	254	28	47	19	6.88e-12	1.132e-21	0.0000063 65

APOA1	335	1300	11	233	213	347	139	14	20	15	8.231e-11	1.529e-16	6.237e-10
CXCR2	3579	627	10	233.333333 333333	154	86	460	13	39	5	1.57e-13	3.196e-45	0.001444
MKI67	4288	2213	7	236	179	372	157	20	24	18	2.58e-12	1.541e-15	0.000000 03964
FOXP3	50943	1865	7	236.333333 333333	157	160	392	20	41	9	1.733e-13	3.391e-30	0.0004015
MPO	4353	694	9	237	297	208	206	9	23	9	0.00000001 207	7.209e-25	0.0000003 4
PARP1	142	1587	15	237.666666 666667	284	179	250	13	35	11	0.00000000 482	1.492e-27	0.0000058 99
CP	1356	355	9	238.333333 333333	148	418	149	11	11	9	1.017e-13	3.599e-14	0.0000000 01562
MYD88	4615	2260	11	242	169	25	532	21	130	8	7.372e-13	1.297e-92	0.004696
F2	2147	1508	10	245	243	393	99	14	19	19	4.431e-10	1.345e-14	3.162e-12
MYC	4609	2950	11	245.666666 666667	226	255	256	20	38	15	1.92e-10	7.496e-22	0.0000068 38
CX3CR 1	1524	904	8	247.666666 666667	191	114	438	13	37	6	1.069e-11	2.945e-37	0.0009635
IL2	3558	1496	6	247.666666 666667	303	161	279	12	37	10	0.00000001 677	4.671e-30	0.0000187
TM6SF 2	53345	53	12	249	58	629	60	12	5	10	5.276e-25	6.239e-10	6.215e-19
HES1	3280	765	8	250	228	306	216	11	18	9	2.103e-10	2.01e-18	0.0000007 246
RXRA	6256	1035	11	251.666666 666667	275	351	129	11	18	14	0.00000000 3677	2.665e-16	2.959e-10
ARG1	383	425	17	252.333333 333333	231	242	284	9	18	6	2.34e-10	1.008e-22	0.0000231 1
TNFRSF 6B	8771	133	5	252.333333 333333	201	245	311	7	13	4	4.411e-11	2.087e-22	0.0000605 9
RARRE S2	5919	207	8	253	251	344	164	7	11	7	7.818e-10	1.228e-16	0.0000000 1735
ABCC4	10257	329	21	253.333333 333333	172	530	58	10	9	16	1.143e-12	1.088e-11	2.349e-19
SOD2	6648	1527	22	254.333333 333333	193	375	195	16	20	13	1.268e-11	2.383e-15	0.0000001 408
IL2RA	3559	772	7	255.666666 666667	316	193	258	9	25	8	0.00000002 768	4.125e-26	0.0000069 24
EGFR	1956	5823	10	256	119	157	492	43	77	15	9.039e-16	1.682e-30	0.002788
NR5A2	2494	288	11	257.333333 333333	356	345	71	6	12	13	0.00000017 18	1.329e-16	7.101e-16
SMPD1	6609	308	15	258.666666 666667	241	292	243	8	14	6	4.137e-10	3.306e-19	0.0000042 52
CNR1	1268	1249	10	258.666666 666667	240	319	217	13	21	11	3.777e-10	9.359e-18	0.0000007 25
GOT1	2805	223	20	259	118	622	37	11	7	19	8.127e-16	5.287e-10	9.687e-27
AGER	177	1248	7	259.333333 333333	205	48	525	14	69	6	5.158e-11	6.044e-63	0.004289
GPC3	2719	247	10	259.666666 666667	126	365	288	11	11	5	2.335e-15	8.061e-16	0.0000280 3
JUN	3725	1872	11	261.666666 666667	255	247	283	15	31	11	9.253e-10	2.36e-22	0.0000231
POSTN	10631	455	11	262	147	249	390	12	18	5	6.67e-14	3.245e-22	0.0003849
GNMT	27232	120	9	262.666666 666667	197	291	300	7	11	4	2.174e-11	3.263e-19	0.0000417 6
FOXA2	3170	1054	9	263	187	499	103	14	14	16	6.794e-12	2.546e-12	5.867e-12
TNFRSF 10A	8797	302	7	265.333333 333333	238	317	241	8	13	6	3.591e-10	7.702e-18	0.0000038 25
CD40L G	959	953	9	267.333333 333333	302	143	357	10	33	7	0.00000001 564	2.591e-32	0.0001922
ADAM TS13	11093	444	9	271	171	524	118	11	10	11	9.606e-13	6.911e-12	3.908e-11
NOX4	50507	496	10	273.666666 666667	358	259	204	7	18	8	0.00000021 19	1.409e-21	0.0000003 285
CYR61	3491	336	10	274.666666 666667	252	240	332	8	17	5	7.81e-10	4.835e-23	0.0001073
HLA- DQB1	3119	2160	11	276.666666 666667	140	445	245	23	21	13	1.388e-14	1.29e-13	0.0000044 46
MTOR	2475	3192	19	277.333333 333333	270	168	394	19	52	12	0.00000000 2098	3.103e-29	0.0004213
F3	2152	765	10	279	364	166	307	8	28	7	0.00000028 5	1.406e-29	0.0000563 8
CCND1	595	2374	10	279.333333 333333	189	350	299	20	26	12	7.611e-12	2.511e-16	0.0000404 8
CASP8	841	1154	11	279.666666 666667	332	236	271	10	26	9	0.00000007 973	3.793e-23	0.0000156 8
YAP1	10413	792	9	280.333333 333333	177	149	515	13	30	5	2.359e-12	2.106e-31	0.003709
MAPK1 4	1432	3060	22	282	395	123	328	14	61	13	0.00000085 34	1.731e-35	0.000101
IL23A	51561	525	7	285	368	67	420	7	41	5	0.00000030 1	1.051e-50	0.0006973

VCAM1	7412	879	8	285	390	131	334	8	34	7	0.0000007394	1.894e-34	0.0001243
CD44	960	1581	9	285.333333333333	282	233	341	13	30	9	0.000000004654	2.026e-23	0.0001379
G6PC	2538	208	11	288	88	731	45	13	6	18	2.193e-19	0.00000001227	9.569e-26
TGFBR1	7046	889	14	291.333333333333	136	307	431	16	19	6	7.775e-15	2.09e-18	0.000896
TERT	7015	1760	9	294.333333333333	165	479	239	19	18	12	3.982e-13	8.785e-13	0.000002925
FGL2	10875	99	10	295.666666666667	242	217	428	6	13	3	4.276e-10	4.277e-24	0.0008178
CFLAR	8837	480	10	298	355	238	301	7	19	6	0.00000001717	4.021e-23	0.00004344
DPP4	1803	606	19	298.666666666667	327	377	192	8	14	9	0.000000005561	2.528e-15	0.0000001177
HSPA5	3309	1303	23	303	279	434	196	12	17	12	0.000000004294	7.402e-14	0.0000001712
CLDN1	9076	351	10	303.333333333333	203	369	338	9	12	5	5.016e-11	1.286e-15	0.0001299
SPHK1	8877	465	12	306.666666666667	349	274	297	7	17	6	0.00000001412	9.532e-21	0.0000368
CBSL	102724560	246	22	308.333333333333	417	411	97	5	10	10	0.0000002115	2.723e-14	2.876e-12
TXNIP	10628	319	10	314	369	325	248	6	13	6	0.00000003014	1.518e-17	0.000005105
CST3	1471	605	9	316.333333333333	149	658	142	13	9	11	1.045e-13	0.000000001708	8.181e-10
IL21	59067	520	7	317	259	134	558	9	28	4	0.0000000001191	5.401e-34	0.006427
STAT6	6778	869	9	317.666666666667	454	72	427	7	47	6	0.000000655	1.018e-48	0.0008009
CXCL2	2920	370	8	317.666666666667	387	85	481	6	33	4	0.00000006809	3.112e-45	0.002085
STAT4	6775	533	10	318.666666666667	265	268	423	9	18	5	0.000000001438	4.752e-21	0.0007428
PDGFB	5155	683	10	319.333333333333	166	313	479	13	17	5	4.16e-13	4.37e-18	0.002047
PPARD	5467	694	11	320.666666666667	412	176	374	7	26	6	0.000000169	2.373e-28	0.0002713
HAVCR2	84868	340	6	321.666666666667	306	196	463	7	19	4	0.000000001946	7.837e-26	0.001571
LIPA	3988	129	23	323.333333333333	340	537	93	5	7	9	0.0000000106	1.331e-11	2.981e-13
IKKB	3551	894	10	324	463	75	434	7	47	6	0.0000007699	3.443e-48	0.0009164
BID	637	449	8	324.666666666667	345	337	292	7	14	6	0.0000000113	5.034e-17	0.00003071
IDO1	3620	551	11	326	566	197	215	5	22	8	0.000007577	9.02e-26	0.0000006876
TGFBR2	7042	738	10	328.333333333333	221	462	302	11	13	7	1.501e-10	3.842e-13	0.00004561
SLC40A1	30061	296	13	328.666666666667	235	511	240	8	9	6	3.108e-10	4.445e-12	0.000003419
STK11	6794	659	11	329.333333333333	182	443	363	12	13	6	3.743e-12	1.006e-13	0.0002105
PROM1	8842	609	11	329.666666666667	236	298	455	10	17	5	3.134e-10	7.222e-19	0.001277
CX3CL1	6376	436	7	331.333333333333	337	146	511	7	25	4	0.000000009498	5.715e-32	0.003642
KLF6	1316	224	10	331.333333333333	145	286	563	10	13	3	3.04e-14	1.779e-19	0.00687
ITGAV	3685	824	10	332	281	391	324	10	15	7	0.000000004434	1.105e-14	0.00008544
SCD	6319	427	11	332.333333333333	408	454	135	6	11	10	0.0000001477	2.389e-13	4.443e-10
ENG	2022	592	8	333	321	342	336	8	15	6	0.000000004749	1.19e-16	0.0001258
ANXA2	302	617	11	335	237	422	346	10	13	6	3.53e-10	4.701e-14	0.0001536
AGTR1	185	1558	9	335.666666666667	114	404	489	22	19	7	2.159e-16	2.238e-14	0.00264
F2R	2149	589	10	336	230	191	587	10	23	4	2.344e-10	2.139e-26	0.009659
FGF7	2252	342	10	336.333333333333	308	368	333	7	12	5	0.000000002012	9.5e-16	0.0001164
PLAUR	5329	694	6	337	298	340	373	9	16	6	0.000000001203	7.734e-17	0.0002721
GSK3B	2932	2095	12	338.666666666667	333	254	429	13	32	9	0.000000008466	7.505e-22	0.0008373
GGT1	2678	314	27	338.666666666667	122	827	67	12	6	14	1.046e-15	0.0000001226	8.074e-17
AQP1	358	663	14	340.333333333333	249	486	286	10	12	7	6.612e-10	1.501e-12	0.00002425
SELP	6403	743	9	341.333333333333	309	327	388	9	17	6	0.000000002056	1.609e-17	0.0003793
VWF	7450	1091	10	343.333333333333	250	466	314	12	15	8	7.195e-10	4.37e-13	0.00006704
ABC1	5243	2497	23	343.333333333333	342	521	167	14	20	18	0.00000001097	6.188e-12	0.00000002045

CTLA4	1493	1356	9	344.666666 666667	180	400	454	16	18	7	2.594e-12	1.819e-14	0.001271
CASP1	834	931	13	345	400	71	564	8	49	5	0.00000109 7	1.499e-49	0.006924
TREM1	54210	211	7	345	398	87	550	5	28	3	0.00000104 3	6.834e-45	0.005912
ENTPD 1	953	268	14	345	278	338	419	7	12	4	0.00000000 4206	5.76e-17	0.0006971
MAPK3	5595	2900	18	345.333333 333333	271	219	546	18	41	9	0.00000000 2231	6.258e-24	0.005833
MTTP	4547	313	12	347.333333 333333	363	594	85	6	8	12	0.00000027 42	1.904e-10	4.79e-14
C4B	721	377	12	348	214	564	266	9	9	6	8.894e-11	3.375e-11	0.0000124 5
REG3A	5068	113	5	350.333333 333333	430	171	450	4	16	3	0.00000333 4	3.78e-29	0.001153
TNFSF1 3B	10673	526	10	350.666666 666667	262	228	562	9	20	4	0.00000000 1299	1.145e-23	0.006656
SERPIN A12	14526 4	125	8	351.666666 666667	199	630	226	7	6	5	2.874e-11	6.754e-10	0.0000012 46
THBD	7056	419	10	353	227	330	502	9	14	4	2.105e-10	2.009e-17	0.003193
CALCA	796	390	6	354.333333 333333	320	383	360	7	12	5	0.00000004 717	4.259e-15	0.0002013
DLK1	8788	356	9	355	178	547	340	10	9	5	2.388e-12	2.107e-11	0.0001382
JAK2	3717	1649	10	356	287	427	354	13	19	9	0.00000000 7301	5.356e-14	0.0001814
FGA	2243	465	9	357	421	413	237	6	12	7	0.00000233 6	3.054e-14	0.0000028 85
VIM	7431	1063	9	357.333333 333333	208	555	309	13	13	8	6.685e-11	2.505e-11	0.0000568 2
PRF1	5551	670	20	358	291	311	472	9	17	5	0.00000000 9157	3.23e-18	0.001904
CXCL12	6387	1800	9	358.666666 666667	305	231	540	13	32	7	0.00000001 801	1.394e-23	0.005398
CLDN7	1366	164	9	361.666666 666667	224	361	500	7	10	3	1.728e-10	5.339e-16	0.003115
LBP	3929	191	6	363	730	252	107	3	14	9	0.0006853	4.681e-22	9.06e-12
CBS	875	556	22	363	450	506	133	6	11	11	0.00000605 2	3.482e-12	3.647e-10
SLCO1 B1	10599	283	5	364	352	671	69	6	7	13	0.00000015 68	0.00000002533	5.835e-16
CXCL3	2921	256	6	364.333333 333333	425	78	590	5	31	3	0.00000252 3	2.558e-47	0.009643
MMP1	4312	977	9	365	410	390	295	8	16	8	0.00000151 8	1.084e-14	0.0000328 5
SOX17	64321	232	9	365	268	546	281	7	8	5	0.00000000 1614	1.961e-11	0.0000211 8
ESR1	2099	4370	10	365.666666 666667	247	478	372	24	29	15	5.259e-10	8.288e-13	0.0002726
CXCL16	58191	195	7	366	389	174	535	5	18	3	0.00000072 27	1.115e-28	0.004831
SLC51A	20093 1	48	9	366.333333 333333	254	788	57	5	4	10	9.251e-10	0.00000005671	2.208e-19
NPC1	4864	458	19	367.333333 333333	418	593	91	6	9	13	0.00000215 7	1.743e-10	1.973e-13
S100A4	6275	438	10	367.666666 666667	286	304	513	8	15	4	0.00000000 5361	1.729e-18	0.00369
PDGFR B	5159	908	10	367.666666 666667	192	357	554	13	17	5	1.122e-11	3.507e-16	0.006318
HHEX	3087	453	10	368.333333 333333	346	465	294	7	11	6	0.00000011 95	4.371e-13	0.0000320 7
MCL1	4170	782	10	368.333333 333333	317	476	312	9	13	7	0.00000003 072	7.521e-13	0.0000637 7
CPT1A	1374	239	11	370.333333 333333	415	474	222	5	9	6	0.00000184 5	7.169e-13	0.0000010 61
CYP3A 4	1576	865	28	370.333333 333333	385	556	170	8	12	11	0.00000066 62	2.563e-11	0.0000000 257
PDCD1 LG2	80380	166	8	371	290	320	503	6	11	3	0.00000000 8068	1.141e-17	0.003208
PKD1	5310	481	8	371.666666 666667	176	540	399	11	10	5	2.179e-12	1.448e-11	0.0004881
ABCG8	64241	197	15	372	517	520	79	4	8	11	0.00002519	5.613e-12	9.074e-15
ANGPT 1	284	565	10	372.666666 666667	223	459	436	10	12	5	1.63e-10	2.581e-13	0.0009441
GSTP1	2950	1716	15	374.666666 666667	269	549	306	14	16	10	0.00000000 1884	2.209e-11	0.0000530 7
ADIPO R1	51094	380	20	375.333333 333333	392	381	353	6	12	5	0.00000078 46	3.16e-15	0.0001815
ADIPO R2	79602	254	13	377	423	299	409	5	13	4	0.00000244	8.735e-19	0.0005807
BCL2	596	2746	8	377.333333 333333	234	440	458	19	24	10	2.731e-10	8.159e-14	0.001356
CFH	3075	865	27	377.333333 333333	331	602	199	9	11	10	0.00000006 791	2.779e-10	0.0000002 194
CEBPB	1051	904	8	377.666666 666667	464	232	437	7	24	6	0.00000824 7	1.629e-23	0.0009657

SULT2A1	6822	120	14	379.333333 333333	261	771	106	6	5	8	0.00000000 1274	0.00000003253	9.129e-12
ITGB6	3694	177	10	380	295	497	348	6	8	4	0.00000001 164	2.496e-12	0.0001671
ALOX5	240	541	16	383.333333 333333	444	280	426	6	17	5	0.00000525 2	1.12e-19	0.0007904
TJP1	7082	779	11	385.666666 666667	371	527	259	8	12	8	0.00000031 98	8.457e-12	0.0000073 66
TNFAIP8L2	79626	74	9	386.333333 333333	546	227	386	3	12	3	0.00005425	1.079e-23	0.0003797
NPPB	4879	926	5	386.666666 666667	195	518	447	13	13	6	1.396e-11	5.254e-12	0.001072
CASP3	836	3210	10	387	497	360	304	12	30	14	0.00001658	4.309e-16	0.0000497 5
CYP7B1	9420	108	10	388.333333 333333	319	746	100	5	5	8	0.00000004 63	0.0000000198	4.106e-12
HNF1A	6927	640	10	389.666666 666667	482	539	148	6	11	11	0.00001249	1.416e-11	0.0000000 014
RORC	6097	363	8	391.333333 333333	480	220	474	5	18	4	0.00001219	6.82e-24	0.001968
EGF	1950	1046	10	391.333333 333333	244	457	473	12	15	6	4.675e-10	2.518e-13	0.001922
PLAU	5328	906	10	393.333333 333333	293	334	553	10	18	5	0.00000001 016	3.12e-17	0.006265
NQO1	1728	743	10	393.333333 333333	222	464	494	11	13	5	1.602e-10	4.152e-13	0.002905
NR3C2	4306	465	11	395.666666 666667	245	414	528	9	12	4	4.808e-10	3.047e-14	0.004483
IRF1	3659	572	10	396	458	288	442	6	17	5	0.00000698	2.702e-19	0.0009857
HSD11B1	3290	437	10	405.333333 333333	411	667	138	6	8	10	0.00000167 6	0.00000002259	5.425e-10
FGF2	2247	1553	10	406	350	380	488	11	20	7	0.00000014 78	3.151e-15	0.002597
COMM D1	15068 4	110	10	406.666666 666667	324	605	291	5	6	4	0.00000004 999	3.243e-10	0.0000304 5
FLT1	2321	1066	8	407.666666 666667	283	557	383	11	13	7	0.00000000 4789	2.58e-11	0.0003566
MST1	4485	178	10	408.333333 333333	376	500	349	5	8	4	0.00000047 62	2.595e-12	0.0001704
FOXO3	2309	947	10	411	301	363	569	10	17	5	0.00000001 481	6.651e-16	0.007392
APLN	8862	383	5	412.333333 333333	394	487	356	6	10	5	0.00000081 68	1.778e-12	0.0001868
SLC27A5	10998	38	6	412.333333 333333	325	754	158	4	4	5	0.00000005 241	0.00000002259	0.0000000 04069
DGAT2	84649	110	10	412.666666 666667	323	752	163	5	5	6	0.00000005 015	0.00000002154	0.0000000 142
SERPIN B3	6317	116	3	413.333333 333333	257	764	219	6	5	5	0.00000000 1054	0.00000002768	0.0000008 85
AKR1D1	6718	45	9	414.333333 333333	339	783	121	4	4	6	0.00000010 11	0.00000004375	7.688e-11
ITPA	3704	184	19	418.666666 666667	239	856	161	7	5	7	3.618e-10	0.0000002466	0.0000000 07813
PROX1	5629	732	10	420	357	412	491	8	14	5	0.00000020 96	2.803e-14	0.002733
BMP7	655	939	12	421.666666 666667	266	712	287	11	10	8	0.00000000 1438	0.000000005798	0.0000254 8
MAPK9	5601	539	9	422	560	387	319	5	13	6	0.00006903	9.625e-15	0.0000786 2
NOTCH3	4854	569	8	422.333333 333333	318	509	440	8	11	5	0.00000003 553	4.409e-12	0.0009662
MUC16	94025	255	3	425	334	648	293	6	7	5	0.00000008 956	0.000000001282	0.0000321 6
LECT2	3950	84	11	425.333333 333333	300	713	263	5	5	4	0.00000001 383	0.000000005817	0.0000114 5
ANGPT L2	23452	106	11	425.666666 666667	610	226	441	3	13	3	0.0001428	1.047e-23	0.0009729
MMP7	4316	558	10	426	451	394	433	6	13	5	0.00000616	1.453e-14	0.0008973
TGFA	7039	462	9	428.666666 666667	289	470	527	8	11	4	0.00000000 7988	5.328e-13	0.004384
CLU	1191	696	10	428.666666 666667	413	498	375	7	12	6	0.00000171 7	2.533e-12	0.0002749
SAA1	6288	343	13	429.333333 333333	626	198	464	4	19	4	0.000181	9.155e-26	0.00162
MACC1	34638 9	112	9	430.666666 666667	326	517	449	5	7	3	0.00000005 44	5.078e-12	0.001125
HBEGF	1839	334	8	432.666666 666667	304	533	461	7	9	4	0.00000001 734	1.236e-11	0.001474
CXCL11	6373	116	6	434.666666 666667	329	522	453	5	7	3	0.00000006 428	6.45e-12	0.001238
MAT1A	4143	137	14	436	348	645	315	5	6	4	0.00000013 99	0.000000001147	0.0000672 6
PTPN1	5770	541	10	436.333333 333333	562	566	181	5	10	9	0.00006997	4.248e-11	0.0000000 4796
CXCL13	10563	241	7	437.666666 666667	330	405	578	6	10	3	0.00000006 498	2.253e-14	0.008269
EPO	2056	792	10	440.666666 666667	373	435	514	8	14	5	0.00000035 95	7.43e-14	0.003716

LPIN1	23175	200	10	441.666666 666667	393	723	209	5	6	6	0.00000081 09	0.000000009831	0.0000003 949
HSD3B 7	80270	44	8	445	336	779	220	4	4	4	0.00000009 299	0.00000004011	0.0000009 871
CYP8B 1	1582	39	12	449	468	762	117	3	4	6	0.00000904 2	0.00000002489	3.2e-11
RORA	6095	428	9	449.666666 666667	515	456	378	5	11	5	0.00002508	2.439e-13	0.0002977
SCTR	6344	79	9	450.333333 333333	396	695	260	4	5	4	0.00000085 86	0.000000004369	0.0000090 45
NGF	4803	820	9	450.666666 666667	440	389	523	7	15	5	0.00000466	1.038e-14	0.004264
NCF1	65336 1	505	10	451.333333 333333	544	261	549	5	18	4	0.00005222	1.911e-21	0.005862
PCK1	5105	352	11	452	638	545	173	4	9	8	0.0001962	1.915e-11	0.0000000 282
VPS33 B	26276	75	11	458.666666 666667	388	873	115	4	4	7	0.00000071	0.0000003155	1.909e-11
CD1D	912	560	9	460	569	235	576	5	20	4	0.00008135	3.716e-23	0.008182
BLVRA	644	84	10	461	399	579	405	4	6	3	0.00000109 1	6.548e-11	0.000529
PLIN2	123	204	10	462.666666 666667	397	727	264	5	6	5	0.00000088 51	0.000000011	0.0000120 2
HMGC S1	3157	161	22	463.666666 666667	367	831	193	5	5	6	0.00000029 65	0.0000001309	0.0000001 181
CDKN2 A	1029	3062	9	465	328	493	574	16	23	9	0.00000006 382	2.246e-12	0.007832
CD69	969	183	30	465.666666 666667	504	373	520	4	10	3	0.00001932	1.561e-15	0.004127
TAT	6898	123	18	468	267	966	171	6	4	6	0.00000000 1446	0.000002082	0.0000000 2655
EPHX2	2053	264	13	468.666666 666667	563	426	417	4	10	4	0.00007287	5.291e-14	0.000661
ITGB2	3689	856	9	469.333333 333333	548	323	537	6	18	5	0.00005512	1.254e-17	0.005024
HLA-G	3135	819	5	472.666666 666667	438	659	321	7	10	7	0.00000464 5	0.000000001787	0.0000830 1
NOTCH 4	4855	335	6	473	619	469	331	4	10	5	0.000167	5.006e-13	0.0001061
EDNRA	1909	476	10	473.666666 666667	353	534	534	7	10	4	0.00000016 33	1.324e-11	0.004836
ACE2	59272	461	11	474	525	371	526	5	13	4	0.00003507	1.423e-15	0.004359
ABCG5	64240	210	12	480.666666 666667	752	609	81	3	7	11	0.0008793	3.563e-10	1.788e-14
HSP90 B1	7184	509	15	481	545	485	413	5	11	5	0.0000541	1.436e-12	0.0006139
PDGFC	56034	129	10	481.333333 333333	341	638	465	5	6	3	0.00000010 57	8.068e-10	0.001651
CCL25	6370	95	7	484	587	588	277	3	6	4	0.0001069	1.369e-10	0.0000178 1
CD34	947	524	9	485	307	832	316	8	7	6	0.00000001 969	0.0000001314	0.0000677 3
FECH	2235	229	20	488	409	909	146	5	5	8	0.00000151 8	0.0000006829	0.0000000 01166
DMBT1	1755	135	8	488.666666 666667	452	543	471	4	7	3	0.00000644 9	1.814e-11	0.001865
FGF23	8074	594	11	490	384	749	337	7	8	6	0.00000065 32	0.00000002088	0.0001278
ADH1C	126	316	10	492.333333 333333	456	701	320	5	7	5	0.00000656 4	0.00000005158	0.0000829 6
CYP27 A1	1593	179	18	497.666666 666667	716	703	74	3	6	11	0.0005771	0.00000005224	3.36e-15
LOXL2	4017	141	11	498.333333 333333	462	553	480	4	7	3	0.00000750 4	2.421e-11	0.00208
ADD3	120	93	10	499	311	914	272	5	4	4	0.00000002 233	0.0000007179	0.0000166 5
HAVCR 1	26762	180	3	501	299	852	352	6	5	4	0.00000001 269	0.0000002221	0.0001765
PGF	5228	415	9	502.333333 333333	680	328	499	4	14	4	0.0003464	1.773e-17	0.003099
ARNT	405	380	9	503.333333 333333	391	636	483	6	8	4	0.00000078 66	8.05e-10	0.002296
CYP1A 2	1544	639	8	504	799	433	280	4	13	7	0.001504	7.053e-14	0.0000195 3
BCL2L1 1	10018	832	6	505.333333 333333	539	448	529	6	14	5	0.00004795	1.368e-13	0.004497
APLNR	187	168	7	506	488	688	342	4	6	4	0.00001423	0.000000003654	0.0001385
MUC5 AC	4586	422	9	507.666666 666667	686	332	505	4	14	4	0.0003659	2.2e-17	0.00326
DKK1	22943	820	9	509.666666 666667	375	742	412	8	9	6	0.00000046 2	0.00000001947	0.0006083
PSMD1 0	5716	160	17	512.333333 333333	366	676	495	5	6	3	0.00000028 82	0.000000002778	0.002926
S1PR2	9294	225	10	516	535	624	389	4	7	4	0.00004103	5.609e-10	0.0003815
CD5L	922	63	6	516	524	656	368	3	5	3	0.00003477	0.000000001457	0.0002453

CES1	1066	146	20	520.666666 666667	677	562	323	3	7	4	0.0003341	3.044e-11	0.0000843 7
MERTK	10461	270	10	522	567	577	422	4	8	4	0.00007898	6.147e-11	0.0007126
ACACB	32	138	10	522	457	791	318	4	5	4	0.00000696 5	0.0000006381	0.0000686
ACOX3	8310	86	15	522	404	897	265	4	4	4	0.00000118 5	0.000005339	0.0000124 8
UCP2	7351	684	12	527.666666 666667	822	558	203	4	11	9	0.001882	2.722e-11	0.0000003 058
CD24	10013 3941	250	-	533	419	773	407	5	6	4	0.00000227 9	0.0000003445	0.0005485
IGFBP1	3484	434	11	541	335	778	510	7	7	4	0.00000009 262	0.00000003988	0.003587
CTH	1491	239	20	547.666666 666667	780	640	223	3	7	6	0.001239	8.299e-10	0.0000010 56
AGPAT 4	56895	51	10	548.666666 666667	503	800	343	3	4	3	0.00001908	0.00000007163	0.0001389
TGFB3	7043	549	9	550.666666 666667	446	634	572	6	9	4	0.00000568 1	7.745e-10	0.007658
ACACA	31	347	20	552	472	849	335	5	6	5	0.00000997 7	0.0000002138	0.000124
GLUL	2752	405	24	553.333333 333333	401	893	366	6	6	5	0.00000110 8	0.0000004978	0.0002369
PTPRO	5800	108	8	553.666666 666667	426	945	290	4	4	4	0.00000280 7	0.000001266	0.0000283 9
NOX1	27035	485	14	559.666666 666667	537	603	539	5	9	4	0.00004365	2.809e-10	0.00514
BHMT	635	159	10	561.666666 666667	477	1018	190	4	4	6	0.00001171	0.000005487	0.0000001 113
DGUOK	1716	68	12	562.333333 333333	378	1124	185	4	3	5	0.00000049 01	0.00002042	0.0000000 7057
LOX	4015	322	10	564	248	987	457	8	5	4	5.691e-10	0.000003322	0.001293
ALPL	249	530	12	564.666666 666667	215	1403	76	10	4	15	9.2e-11	0.000425	5.084e-15
PHB	5245	409	23	565.666666 666667	675	653	369	4	8	5	0.0003301	0.000000001385	0.0002461
XDH	7498	978	18	569.333333 333333	743	719	246	5	10	9	0.0008134	0.000000008313	0.0000046 65
F5	2153	1275	10	569.666666 666667	553	1001	155	7	8	14	0.00005947	0.000004151	0.0000000 03234
CAV2	858	182	10	570	502	853	355	4	5	4	0.00001898	0.0000002344	0.0001827
SREBF2	6721	357	10	572.666666 666667	885	619	214	3	8	7	0.003499	5.095e-10	0.0000005 474
GLS	2744	192	15	581.666666 666667	512	869	364	4	5	4	0.00002299	0.0000002997	0.0002197
ATP11 C	28641 0	46	10	583.333333 333333	490	1035	225	3	3	4	0.00001431	0.000006773	0.0000011 59
GC	2638	365	10	584.333333 333333	383	1025	345	6	5	5	0.00000063 6	0.000005863	0.0001533
MC4R	4160	652	10	585	615	781	359	5	8	6	0.0001535	0.00000004036	0.0002007
PDCD4	27250	350	15	588	881	415	468	3	11	4	0.00332	3.112e-14	0.001735
FOXO1	2308	1066	11	588.333333 333333	617	838	310	6	9	8	0.0001607	0.0000001478	0.0000577 7
OTC	5009	273	15	589.666666 666667	431	1179	159	5	4	8	0.00000340 7	0.00003964	0.0000000 04259
PON1	5444	1181	7	590.333333 333333	652	705	414	6	11	7	0.0002624	0.00000005273	0.00006134
HPX	3263	138	10	594	661	646	475	3	6	3	0.0002893	0.000000001196	0.001973
FABP4	2167	392	14	596.333333 333333	659	643	487	4	8	4	0.0002873	0.000000001013	0.002561
KLB	15283 1	72	9	596.666666 666667	543	865	382	3	4	3	0.00005023	0.0000002701	0.0003533
ENTPD 2	954	96	12	597.666666 666667	589	926	278	3	4	4	0.0001099	0.0000008052	0.0000185
MX1	4599	258	13	600.333333 333333	558	652	591	4	7	3	0.00006721	0.000000001381	0.009842
OCLN	10050 6658	410	9	603.666666 666667	676	765	370	4	7	5	0.0003325	0.00000002765	0.0002483
HLA-B	3106	1908	48	607.333333 333333	354	1071	397	12	9	9	0.00000017 04	0.00001072	0.0004669
CYP4B 1	1580	78	13	611.333333 333333	556	883	395	3	4	3	0.00006242	0.0000003658	0.0004345
SLC39A 14	23516	93	12	612.666666 666667	936	484	418	2	7	3	0.005236	1.439e-12	0.000695
ATF4	468	497	11	613.666666 666667	722	814	305	4	7	6	0.0006479	0.00000009446	0.0000521 6
MTHFR	4524	3355	20	618.333333 333333	382	1273	200	15	10	19	0.00000061 36	0.0001294	0.0000002 565
FUT2	2524	167	10	619	485	1033	339	4	4	4	0.00001399	0.000006566	0.0001365
ELOVL6	79071	122	14	619.333333 333333	435	964	459	4	4	3	0.00000447 6	0.00000202	0.001418
HMGCR	3156	483	24	623	719	949	201	4	6	8	0.0005837	0.000001288	0.0000002 727

AHCY	191	226	22	624.666666 666667	536	1120	218	4	4	6	0.00004168	0.00001995	0.0000007 781
TLR8	51311	258	11	625	800	483	592	3	9	3	0.00151	1.391e-12	0.009825
TTR	7276	745	10	629.333333 333333	310	1082	496	9	6	5	0.00000002 096	0.00001299	0.002928
ITGA1	3672	247	9	630	551	936	403	4	5	4	0.00005741	0.0000009615	0.0005287
ASS1	445	248	20	630	552	1155	183	4	4	7	0.00005823	0.00002783	0.0000000 5389
DLAT	1737	162	24	631	370	1026	497	5	4	3	0.00000030 32	0.000005862	0.003023
HLA- DQA1	3117	905	7	633	292	1168	439	10	6	6	0.00000001 01	0.00003506	0.0009671
TFF3	7033	209	8	634	749	608	545	3	7	3	0.0008706	3.453e-10	0.005801
FOXL1	2300	56	7	641	514	816	593	3	4	2	0.00002481	0.000000103	0.009944
EHHAD H	1962	83	12	644.666666 666667	564	1173	197	3	3	5	0.0000742	0.00003568	0.0000001 825
ERRFI1	54206	140	11	646.666666 666667	665	797	478	3	5	3	0.0003001	0.0000006804	0.002046
TYMP	1890	210	6	653	523	889	547	4	5	3	0.00003202	0.000000456	0.005862
SHBG	6462	337	9	657.333333 333333	872	845	255	3	6	6	0.003009	0.0000001812	0.0000068 16
SLC51B	12326 4	38	7	660.666666 666667	465	1445	72	3	2	8	0.00000840 2	0.0005655	8.532e-16
SLC25A 13	10165	143	8	661.666666 666667	669	1296	20	3	3	24	0.0003176	0.0001639	1.398e-39
GYS2	2998	71	9	663	878	859	252	2	4	4	0.00326	0.0000002569	0.0000060 66
CDK1	983	1289	13	666	557	905	536	7	9	6	0.00006312	0.000006245	0.004946
EZR	7430	681	11	671	628	908	477	5	7	5	0.000184	0.000006776	0.002029
INSR	3643	1129	11	679.666666 666667	1026	615	398	4	12	7	0.009237	4.228e-10	0.0004863
UTP4	84916	94	19	685.333333 333333	585	1196	275	3	3	4	0.0001039	0.00005084	0.0000171 9
SMN1	6606	597	11	687.333333 333333	466	999	597	6	6	4	0.00000873 7	0.000004075	0.009979
TRAPP C11	60684	72	15	687.666666 666667	542	1140	381	3	3	3	0.00005032	0.00002392	0.0003543
TNNI3	7137	513	8	687.666666 666667	362	1149	552	7	5	4	0.00000026 23	0.00002663	0.006178
PRDX4	10549	177	11	690.333333 333333	500	1055	516	4	4	3	0.00001708	0.000008093	0.003774
SLC2A2	6514	335	10	691.666666 666667	870	997	208	3	5	7	0.002964	0.000003983	0.0000003 668
APOB	338	1023	9	697	499	1215	377	7	6	7	0.00001678	0.00006544	0.0002817
LUM	4060	191	10	704.666666 666667	511	1072	531	4	4	3	0.00002256	0.00001075	0.00458
RPLP0	6175	338	22	705.666666 666667	624	1236	257	4	4	6	0.0001715	0.0000866	0.0000068 79
BCHE	590	303	11	706.333333 333333	596	1206	317	4	4	5	0.0001176	0.00005812	0.0000684 4
FOXA1	3169	421	9	707.666666 666667	938	903	282	3	6	6	0.0053	0.0000006153	0.0000220 5
GPX4	2879	261	12	713	561	1163	415	4	4	4	0.00006992	0.00003373	0.0006355
STK25	10494	87	11	721.333333 333333	573	1181	410	3	3	3	0.00008413	0.00004082	0.0005807
ITGB4	3691	399	10	723	922	757	490	3	7	4	0.004624	0.00000002326	0.002721
XBP1	7494	458	5	724.666666 666667	969	681	524	3	8	4	0.006521	0.000000003172	0.004271
LTPB3	4054	91	8	728	581	1187	416	3	3	3	0.00009496	0.00004648	0.0006542
GPX1	2876	705	11	730.666666 666667	643	1065	484	5	6	5	0.000211	0.000009709	0.00234
RARA	5914	802	9	735	683	1116	406	5	6	6	0.0003598	0.00001893	0.0005479
GSTT1	2952	1711	-	741.333333 333333	550	1152	522	8	8	7	0.00005706	0.00002724	0.004205
CYP3A 7	1551	189	10	748.666666 666667	510	1374	362	4	3	4	0.00002169	0.000353	0.0002077
NPC2	10577	171	12	751	706	1040	507	3	4	3	0.0005113	0.000007163	0.003472
HPD	3242	104	17	753.666666 666667	607	1219	435	3	3	3	0.0001356	0.0000675	0.0009319
ONECU T2	9480	59	8	764	845	1086	361	2	3	3	0.002341	0.00001376	0.0002052
SLC22A 1	6580	196	7	778.333333 333333	735	1393	207	3	3	6	0.0007344	0.0003875	0.0000003 539
DCLK1	9201	154	6	779	687	1321	329	3	3	4	0.0003856	0.0002005	0.0001022
TMEM 30A	55754	75	22	791.333333 333333	549	1634	191	3	2	5	0.0000562	0.001955	0.0000001 126

GLIS3	16979 2	74	10	800.333333 333333	386	1628	387	4	2	3	0.0000067 61	0.00191	0.0003787
PEMT	10400	138	16	808.666666 666667	662	1288	476	3	3	3	0.0002889	0.0001485	0.001969
NCOA1	8648	457	9	812	700	1345	391	4	4	5	0.000486	0.000253	0.0003918
NDOR1	27158	221	20	813	764	1114	561	3	4	3	0.001005	0.00001837	0.006629
SDC2	6383	230	10	822.666666 666667	771	1129	568	3	4	3	0.00112	0.00002119	0.00735
ADH1B	125	358	6	830.666666 666667	887	1261	344	3	4	5	0.00352	0.0001059	0.0001402
BCS1L	617	84	17	831	912	1177	404	2	3	3	0.004389	0.00003685	0.0005303
PF4	5196	238	6	831.333333 333333	778	1141	575	3	4	3	0.001227	0.00002397	0.008016
MBOA T7	79143	71	12	843	540	1610	379	3	2	3	0.00004844	0.001778	0.0003415
CYP2D 6	1565	929	9	852.333333 333333	929	1180	448	4	6	6	0.005094	0.00004001	0.001089
GALC	2581	181	11	868	720	1365	519	3	3	3	0.0005929	0.0003127	0.004007
PRDX3	10935	250	16	874	554	1483	585	4	3	3	0.00005986	0.000743	0.00908
NCAN	1463	103	8	874	605	1732	285	3	2	4	0.0001322	0.003465	0.0000239 2
ZNF26 7	10308	30	5	874.333333 333333	731	1386	506	2	2	2	0.0006932	0.0003656	0.003325
CCNG1	900	191	11	880.666666 666667	729	1383	530	3	3	3	0.0006862	0.0003617	0.004588
IFNL2	28261 6	34	2	897	751	1419	521	2	2	2	0.000869	0.0004599	0.004157
TJP2	9414	207	9	901	747	1415	541	3	3	3	0.0008486	0.000448	0.005685
AGXT	189	175	21	908	712	1960	52	3	2	15	0.0005427	0.008708	5.455e-22
FNDC5	25299 5	212	8	910.333333 333333	756	1424	551	3	3	3	0.0008993	0.0004774	0.005983
PRKCS H	5589	130	11	921.666666 666667	1028	1271	466	2	3	3	0.009253	0.000126	0.001686
ABCC1	4363	487	12	923	1002	1366	401	3	4	5	0.007505	0.0003169	0.0005147
SAAL1	11317 4	41	10	927.333333 333333	777	1462	543	2	2	2	0.001226	0.0006514	0.005815
ALMS1	7840	107	7	935	612	1749	444	3	2	3	0.0001464	0.0037	0.0009936
PARVB	29780	108	12	940	614	1761	445	3	2	3	0.00015	0.003744	0.001019
CCNA1	8900	250	16	953	793	1482	584	3	3	3	0.001389	0.0007435	0.009095
HMGC S2	3158	114	8	954.333333 333333	625	1786	452	3	2	3	0.0001732	0.004108	0.001178
EDEM1	9695	88	14	959	925	1684	268	2	2	4	0.004746	0.002607	0.0000135 4
DKC1	1736	260	22	967	803	1502	596	3	3	3	0.001539	0.0008225	0.009979
C8G	733	53	9	980	823	1535	582	2	2	2	0.001938	0.001039	0.009076
PCSK9	25573 8	505	10	981.666666 666667	1015	1382	548	3	4	4	0.008211	0.0003594	0.005873
HPSE2	60495	55	9	986.333333 333333	831	1540	588	2	2	2	0.002068	0.001116	0.009672
DHCR7	1717	173	12	986.333333 333333	495	1955	509	4	2	3	0.00001576	0.008536	0.003578
UGT1A 9	54600	179	7	1012.333333 333333	717	1970	350	3	2	4	0.0005763	0.009056	0.0001736

Supplemental Table 2

gene.symbol	logFC	AveExpr	adj.P.Val	pamrRank	other.score	PSC.score
FOXP3	2.85210795105714	5.55805130552239	1.53162271909194E-16	1	-0.2219	1.9022
RORC	-1.17587629229047	8.56628480147761	2.64335277207618E-12	5	0.1438	-1.2323
NR0B2	1.7169309115869	9.04411697635075	6.11261572747121E-11	3	-0.1582	1.3562
NR1H4	-0.712794012094047	8.8349269801194	1.28223642554479E-10	17	0.1074	-0.9205
FGF19	1.14023062745952	3.78925332470149	1.55433642960811E-10	8	-0.1332	1.142
SLC25A13	-0.558802832965476	10.2026380545746	3.34981321586864E-10	26	0.0925	-0.7931
THBD	1.24604327415952	6.36105013214179	3.79077853892621E-10	7	-0.1352	1.1589
SLCO1B1	-0.780172684142856	11.2512259610597	3.79077853892621E-10	16	0.11	-0.943
TNFRSF1A	0.661466204839285	9.28922832783582	3.79077853892621E-10	23	-0.1009	0.865
TNFRSF12A	2.48151812394762	7.08810014084328	3.79077853892621E-10	2	-0.1667	1.4289
LCN2	1.45198814049881	4.93861709934328	9.51260494528471E-10	6	-0.1403	1.2022
MMP7	1.91032866500952	5.11986373857463	2.49687091177077E-09	4	-0.1498	1.2841
ANXA2	1.25734785213333	7.56605700483582	3.99018536316181E-09	10	-0.1297	1.1117
GOT1	0.686823386523809	11.1131636585821	4.55583308289331E-09	24	-0.0994	0.8516
SOX9	0.793067253722618	6.26656025926866	2.19527748301191E-08	19	-0.104	0.8914
RARA	0.627855612294047	6.89608841800746	2.55434616107179E-08	27	-0.0925	0.7926
CEBPB	0.809975239821428	9.63041491653731	3.53432768007997E-08	20	-0.104	0.8913
DGAT2	-1.15189774165	9.57071199290299	4.30318075020949E-08	12	0.1196	-1.0248
PPARD	0.750035366583333	6.23324932888806	6.29204441123426E-08	25	-0.0992	0.8507
RORA	0.790360094770238	8.36343632343284	6.36224730667225E-08	22	-0.1016	0.8705
RELA	0.503990096264285	7.36045555814925	1.17940890961085E-07	48	-0.0801	0.6866
XBP1	-0.395305020821428	10.9471633776866	1.30238701430142E-07	73	0.0694	-0.5948
FOXO1	0.831022827163094	7.89966278085821	1.39805484811969E-07	21	-0.1021	0.8755
CLDN7	0.946410683592857	6.77095349418657	2.24157250467151E-07	18	-0.1067	0.915
PHB	0.443398718797618	9.92754586019403	2.65094396654188E-07	58	-0.0735	0.6296
MBOAT7	0.551692775039286	7.28846834633582	3.14688617923209E-07	42	-0.0826	0.7079
CES1	-0.351289752178571	12.6607570263433	3.17595031839151E-07	82	0.0636	-0.5452
HNF1B	0.62901710057619	6.47748342310448	3.17595031839151E-07	31	-0.0882	0.7557
RARRES2	-0.604635487913095	10.3010709824701	3.63739732241427E-07	35	0.0862	-0.7388
CYP2E1	-0.439273478297619	12.9584501285821	4.50228408045603E-07	60	0.0723	-0.6197
DLAT	0.505080317990475	7.14178310182836	4.92095343667422E-07	52	-0.078	0.6686
CTGF	1.56678735538571	7.54055372070895	5.41520853822938E-07	11	-0.1232	1.0557
MTTP	-0.517609129769048	10.4481300806866	1.00866274664432E-06	53	0.078	-0.6686
ATP11C	-0.639836200705952	8.95708644970895	1.25233878220911E-06	34	0.0864	-0.7402
HMGCS2	-0.403523366142856	12.3225090563433	1.99559977782949E-06	76	0.0671	-0.5752
KRT7	1.36808146231786	6.10623529244776	2.00699216806864E-06	13	-0.1141	0.9778
CDKN1A	1.33041751169524	6.96770206923881	2.07152670201502E-06	14	-0.1129	0.9681
IKBKG	0.664817888189285	5.46399046735821	2.21907558079244E-06	33	-0.0867	0.7431
CYP7A1	-2.67253765686309	8.30975828408209	2.48746689821013E-06	9	0.1321	-1.132
DGUOK	0.491759644992857	6.81336796500746	2.48746689821013E-06	57	-0.0744	0.638
CAV2	0.60108008992738	8.05232298273881	4.00879613719592E-06	45	-0.0815	0.6989
ACACA	-0.680500478763095	6.94508604124627	5.88260482557235E-06	36	0.0855	-0.7333

LOXL2	0.620960266333333	5.32455537790299	6.25199515796829E-06	44	-0.0819	0.7021
ADIPOR2	-0.453898547328571	8.76892005461194	8.37226729687356E-06	71	0.0696	-0.5962
CD34	0.699102314638095	6.59317781026866	0.0000117138790294528	37	-0.0849	0.7281
CEBPA	-0.793585411586904	8.71438031098507	0.0000117138790294528	30	0.0895	-0.7672
MYC	1.61424268134286	6.59621688223881	0.0000129018057208315	15	-0.1119	0.9589
HMGB1	-0.380865843883333	8.50804924604478	0.0000208511773604233	86	0.0619	-0.5305
ABCB11	0.696177024798809	9.13101949159702	0.0000212401768152683	39	-0.0834	0.7144
BCHE	-0.878162144288094	8.82505379848507	0.0000214145947787022	28	0.0913	-0.7823
EDN1	0.692519889665475	5.03712500848507	0.0000214145947787022	41	-0.0831	0.7119
AKR1D1	-0.741650069003571	10.2809911254702	0.0000303580307907452	38	0.0846	-0.7249
TNFSF10	-0.667743597348809	11.1823550280522	0.0000307854479784407	47	0.0809	-0.6934
KRT8	0.654853480961904	10.5257222183284	0.0000359426633022376	49	-0.0798	0.6843
FGF23	0.841346066421428	4.04483400198508	0.0000384695044367628	32	-0.088	0.7545
FAH	-0.361181739246428	10.4072904055821	0.0000401514486113887	96	0.0591	-0.5062
KLB	-0.627637080961904	7.70118748314925	0.0000471517350172316	54	0.0777	-0.6658
ESR1	-0.385321687365476	5.72605950378358	0.0000714244184943412	93	0.0604	-0.5178
ADAMTS13	-0.498702700491666	6.52675825677612	0.0000717181707249417	74	0.069	-0.5914
GLUL	0.375753703910714	9.95733887953731	0.0000719134634930595	95	-0.0595	0.5102
GPT	0.668178667007142	8.21614935632836	0.0000861610714178454	51	-0.0782	0.6703
CFLAR	-0.427687659375	7.91342681506716	0.000102837119225982	83	0.0632	-0.5417
ALPL	0.569195381269047	8.6299342456791	0.00010304013378728	59	-0.0725	0.6216
AGXT	0.297151385416666	11.6572566317164	0.000105781433871816	122	-0.0515	0.441
ADH1B	-0.420335135269047	11.6638200793358	0.000110152994436119	84	0.0624	-0.5352
SMPD1	0.358212088783333	8.2429873758209	0.000113652333728275	103	-0.0572	0.4904
GSTP1	0.543155824563095	7.42688227647015	0.000121066775940008	67	-0.0705	0.6046
HP	-0.141445180166667	13.4230204505224	0.000122277914061661	224	0.0311	-0.2662
PTPN1	0.322627943541666	7.27718730804478	0.000138886261048836	115	-0.0536	0.4594
GC	-0.159884606273809	12.7991564915672	0.00014083122763445	209	0.0339	-0.2903
HPD	0.291697116154761	12.2249192255224	0.000143360521398941	124	-0.0504	0.4323
TAT	0.54189327895238	12.4078977260448	0.000167627290450569	70	-0.0696	0.5966
CFH	-0.254308941535714	11.6732786213433	0.000175716233958485	142	0.0461	-0.3953
SOCS1	0.565960373196428	5.8146556351194	0.000175757524775664	65	-0.0708	0.6069
SLC22A1	-0.367494349690476	11.8327093847761	0.000180175195103295	104	0.0572	-0.49
KLF6	1.09118751625833	7.6004089331194	0.000180175195103295	29	-0.0898	0.7694
FABP1	-0.369297595261905	12.0579092829851	0.000207168264509191	105	0.0571	-0.4892
VIM	0.55934368475357	9.08367247161194	0.000225651610777606	68	-0.0697	0.5979
ADH1C	-0.469624440559524	11.8172474003582	0.000228414571329886	80	0.0643	-0.5512
LOX	0.660780969274999	4.41239920941045	0.000228617913598376	56	-0.0747	0.6403
CYP8B1	0.302114337555952	10.6197026276791	0.000229136827457663	123	-0.0508	0.4352
KRT18	0.600607857790475	9.40987241576119	0.000277167619946329	63	-0.0713	0.611
ANGPT2	-0.863459607657142	4.90330938798507	0.000295203370338608	46	0.0815	-0.6984
PKD1	-0.393824832654762	7.03502683654478	0.000295204972866838	99	0.0583	-0.4999
CTNNB1	-0.281363959194048	10.2481889333657	0.00032348008610387	133	0.0482	-0.4132
C5	-0.261539200333333	11.4438758942537	0.000324049273317314	143	0.0461	-0.3953
ACACB	-0.445772936514286	9.82315152892537	0.000376869108113019	87	0.0615	-0.5275

NOTCH3	0.458883079129762	5.96997005670895	0.000583931045345888	88	-0.0615	0.5268
GLIS3	0.451191169496428	6.15668248949254	0.000600717708196675	91	-0.0609	0.5219
CCL13	0.224525783110714	3.10549420581343	0.000925566956958317	169	-0.0408	0.3498
CD24	1.05736137905714	5.67967420664179	0.000925566956958317	43	-0.0819	0.7022
MMP2	0.689846856960714	6.24550500654478	0.00102984950506741	64	-0.0711	0.6094
SDC2	-0.270308771947619	10.3761006362537	0.00110120764979831	148	0.0454	-0.3894
TMEM30A	-0.290712684916666	9.18011395583582	0.00110305345197997	136	0.0474	-0.4059
JUN	1.17303463242976	8.14793930976119	0.00112165942195904	40	-0.0832	0.7128
IL6ST	0.309274613392857	10.386394966791	0.00112165942195904	131	-0.049	0.4198
CD14	0.355423840261904	11.0379942252239	0.00137233955989253	118	-0.0524	0.449
COL1A1	0.752719768015475	7.21903858666418	0.00138552343053512	61	-0.0721	0.6179
CD5L	-1.01720103627143	9.14099316156716	0.00147620108454795	50	0.0787	-0.6747
LTBP3	0.495092561020238	8.33054669987313	0.00147620108454795	89	-0.0611	0.5235
PPARGC1A	0.710520541098809	8.97196702512687	0.00179278027859444	69	-0.0697	0.5972
PNPLA3	-0.558192026590476	9.11620864879104	0.00179290263997411	81	0.0636	-0.5453
INSR	0.271565138574999	8.88289361308955	0.0018245483702322	151	-0.0447	0.3831
HFE	0.29582425065238	6.17992753289552	0.00199803740074926	138	-0.0467	0.4007
ITGB6	0.315041207470238	3.07936574197761	0.00204741735024337	132	-0.0483	0.4141
NQO1	0.620282626085714	4.60228334020149	0.00218518738575201	78	-0.0655	0.5617
FOXA2	0.403993981267856	7.25078328727612	0.00247122260364367	114	-0.0543	0.4656
TNF	-0.383799183407143	4.66795605690298	0.00247122260364367	116	0.053	-0.4542
IL18	0.609623117636904	4.28889905980597	0.00251975361629049	79	-0.0646	0.5533
TIMP1	0.676402594288095	10.2276795850448	0.00252653693756574	77	-0.067	0.5741
TJP1	0.293762043123809	8.68556554947761	0.00252653693756574	144	-0.0461	0.3948
JAK2	-0.425884876754762	6.24672368229851	0.00255144507601513	110	0.0555	-0.4757
VEGFA	-0.426501964159524	9.28195125231343	0.00257485937219156	111	0.0555	-0.4756
FGL2	-0.723646514135714	8.00708630266418	0.00266280571972731	75	0.0682	-0.5848
ICAM1	0.843361983080952	7.97919057812687	0.00278771748253761	62	-0.0714	0.612
RXRA	-0.294093300491667	9.91201777926866	0.00336376406690643	147	0.0455	-0.3901
ASS1	0.275900212464286	12.3274900635821	0.00353856675757111	155	-0.0438	0.3759
TGFB2	0.557219470588094	4.65288492359702	0.00361843748611693	90	-0.061	0.5226
SPP1	1.18662012062143	7.40273990243284	0.00385511488186322	55	-0.0764	0.6547
PON1	-0.280146381809523	11.3631959147015	0.00398822266767109	153	0.044	-0.3769
APOE	0.246712974892857	11.5550814497015	0.00409641825016325	168	-0.0409	0.3504
PRDX4	-0.291395728422619	8.68729633587313	0.0040997672914095	149	0.0448	-0.3844
LIPA	-0.494037271129762	9.61420247326119	0.0044476870927764	102	0.0574	-0.4916
LDLR	0.871278608734523	9.62877280828358	0.00471167065724233	72	-0.0695	0.5954
CDH1	-0.257189063504762	10.2019006687612	0.004841006742395	165	0.0415	-0.356
ANGPT1	0.360085246053571	3.64963814797761	0.00495916623493312	128	-0.0495	0.4241
MAPK8	-0.249568587133333	7.71696756263433	0.00572462069899759	171	0.0405	-0.3475
CTH	0.484650008519048	9.21078201878358	0.00615375995611532	107	-0.0558	0.4781
ALB	-0.0799170856785724	13.3152228429851	0.00618422974816703	331	0.0186	-0.1598
APOA1	-0.181764262773809	12.691742208806	0.00623940243539471	211	0.0334	-0.2859
C8G	0.362946827075	9.6169401146791	0.00626880806755297	130	-0.049	0.42
AHCY	0.343345867655952	9.6157913868806	0.00688417529055885	134	-0.0475	0.4069

FOXA1	-0.29987517700238	8.30017826334328	0.00756520968740015	152	0.0441	-0.3782
CYP3A7	-0.585310553890475	9.3497110701194	0.00756520968740015	97	0.059	-0.506
PDCD4	-0.335110342239285	7.31228748423134	0.00783271245971037	139	0.0466	-0.399
NGF	-0.242930225166666	4.66614034687313	0.00790099148020295	181	0.0393	-0.3366
CYR61	1.11199727061428	6.98450883791791	0.00802204656524097	66	-0.0706	0.6054
FGF7	0.249809154994048	3.36898810324627	0.00820346772822923	180	-0.0398	0.3411
ATF4	-0.261592290128571	8.19694160442537	0.00843982595587419	170	0.0408	-0.3493
ERRFI1	0.345652490738095	11.5810331546269	0.00847686520949062	137	-0.047	0.4026
SLCO1B3	-0.572666923472618	10.1374389161567	0.00882017175216568	100	0.0578	-0.4955
LUM	0.661474916894046	7.92533464956716	0.00921025519770478	92	-0.0605	0.5186
EHHADH	-0.254597385239286	10.319606094209	0.00921419768125727	177	0.0399	-0.3423
STAT4	-0.547082757755952	5.76226403647761	0.00929165599931861	106	0.0566	-0.4849
SELP	0.343737988308333	5.18001983334328	0.00929165599931861	141	-0.0465	0.3988
EPHX2	-0.298900827332142	9.21953272132836	0.0093950674748333	158	0.0434	-0.3719
CDKN2A	0.302636367315476	4.55011508298507	0.00942949780846537	157	-0.0436	0.374
ACTA2	0.394189685825	6.12645973420149	0.00959295226785569	129	-0.0494	0.4234
HMGCS1	-0.659752871669047	9.4010145443806	0.0103758468915622	94	0.0597	-0.512
PRKCSH	0.201252520648809	10.4791370199627	0.0104783744762407	204	-0.0346	0.2967
FN1	-0.135353179319048	8.72332516608955	0.0104783744762407	261	0.0268	-0.2301
VCAM1	-0.59920756902857	7.58338644573134	0.0104783744762407	101	0.0577	-0.4949
OCLN	0.464040920819046	9.26995547971642	0.0106873601683184	117	-0.0524	0.4494
STAT6	0.219761607486904	8.77380466438806	0.0107069499815171	193	-0.0364	0.3118
FECH	0.213801101482143	7.00353087088806	0.010917837764074	195	-0.0358	0.3065
HSPA5	-0.341240700869048	10.9544406180597	0.0109847712474079	145	0.0457	-0.392
NAMPT	0.522605490086904	10.3935425749328	0.0112832382211275	113	-0.0546	0.4679
XDH	-0.242462544878572	9.10421601727612	0.0114048938496317	186	0.0383	-0.3282
SIRT1	-0.283872815258333	6.95072090092537	0.0114048938496317	164	0.0416	-0.3569
MTHFR	-0.266473411285714	6.4599983634328	0.0120566722827458	175	0.0402	-0.3442
NR1H2	0.209216622476191	7.22433489976119	0.0124830505084972	202	-0.035	0.3003
GYS2	0.272765739207142	10.3460599562015	0.013434858339696	174	-0.0404	0.3462
CD69	0.579394236849999	4.36352608888806	0.013806945356894	108	-0.0556	0.477
KRT19	0.47701967012619	4.73806561	0.0140553973922545	121	-0.0518	0.4438
HAVCR1	0.237457976669047	2.96358434595522	0.015619688540108	192	-0.0372	0.3186
TNFAIP3	0.496494124146428	7.36031487935821	0.0163391131722684	120	-0.0519	0.4452
SCTR	0.318267912880952	3.98764098482836	0.016594402303981	160	-0.043	0.3685
FNDC5	0.906493419092856	7.89100666121642	0.0168577647474898	85	-0.0622	0.5328
SMAD2	-0.261492350883333	6.83299287102239	0.0171120181407762	183	0.0389	-0.3333
MAPK14	-0.19462833652619	7.63785294206716	0.0173178175229552	216	0.033	-0.2825
NPC2	0.247167416802381	9.4560049034403	0.0177761447781849	190	-0.0376	0.3226
RPLP0	-0.144646259190476	11.381380355597	0.0179801647224517	254	0.0273	-0.2344
RBP4	0.086938295178572	13.1588885617164	0.0182355384128878	324	-0.0191	0.1641
ABCB4	0.374419925466666	9.89013820420896	0.0190461256172034	146	-0.0457	0.3919
TP53	0.279512344282143	7.50218523481343	0.0194122184047791	179	-0.0398	0.3415
AGT	-0.161898926785715	11.7141416392537	0.0201264928129573	238	0.0292	-0.2503
FASLG	-0.174626354619048	4.1799887553209	0.0201264928129573	228	0.0306	-0.2623

ATP7B	-0.230170105420238	7.76245281003731	0.0203583393396195	194	0.0359	-0.3073
TGFB3	0.488930226833333	5.81335600967164	0.0220896511989663	125	-0.0501	0.4297
CD163	-0.543722463629761	7.8060080745	0.0221231857209349	119	0.052	-0.4457
APOB	-0.0689624926428569	12.8945403539552	0.0232760258453351	355	0.0159	-0.1367
SLC2A2	-0.172547587678572	11.7192592813433	0.0250690544867704	233	0.03	-0.2571
PDCD1LG2	-0.504650194617857	6.06897231327612	0.0264007459308898	127	0.0498	-0.4272
DKK1	0.206129870557143	2.56545417392537	0.0271643855849209	214	-0.0331	0.2837
HNF1A	0.263336276907143	6.83705366529851	0.0273382638371063	189	-0.0377	0.3229
TRAPPC11	-0.170224921713095	7.07221086032836	0.0285225944230309	237	0.0295	-0.2529
SERPINA12	0.324817773804762	3.64991878808955	0.0285225944230309	166	-0.0415	0.3554
AHR	-0.300898194492856	9.70732151155224	0.0299649963205464	178	0.0399	-0.3417
TXNIP	0.395622433838095	10.9647146473507	0.030928120668662	150	-0.0447	0.3834
VWF	0.438358827172619	4.96440029047761	0.030928120668662	140	-0.0465	0.3989
GPBAR1	0.197064517483333	4.53188852270149	0.0316773231581402	221	-0.0319	0.2734
IGFBP1	1.00551220627024	11.0371807237463	0.0332458882200971	98	-0.0585	0.5014
CNR1	0.141140503525	2.77966759973134	0.0332458882200971	268	-0.026	0.2229
SULT2A1	0.285791623584524	10.390915422903	0.0338583246583664	184	-0.0384	0.3296
TNFRSF10A	0.212698247448809	5.79385911536567	0.0338583246583664	215	-0.0331	0.2836
SERPINB3	0.285083344483333	2.81977852455224	0.0353548934615998	188	-0.0383	0.3279
VDR	0.239937650705952	3.95249142076866	0.0365550044839184	201	-0.035	0.3004
MAPK9	0.238878110765476	7.59497359064925	0.0371203219865998	203	-0.0349	0.2993
IL4	0.140509170517857	2.52856189371642	0.0377171430381646	270	-0.0257	0.2203
AGER	-0.192084730777381	5.13882168102985	0.0391211275734287	225	0.0309	-0.265
CCND1	0.205887967725	6.94957280497015	0.0393704683270882	220	-0.0321	0.2752
BCL2L11	-0.380125913370238	6.25483811727612	0.0410315106589983	161	0.0427	-0.3659
SERPINE1	0.934867324191666	9.16031041532089	0.0427513524728875	109	-0.0556	0.4762
HSP90B1	-0.146911343809524	11.5791771752985	0.0427513524728875	266	0.0262	-0.2246
HHEX	-0.256133971665476	7.77054767061194	0.0446200528280309	198	0.0355	-0.3047
S100A4	0.255227548883333	4.47852170792537	0.0448831690257445	200	-0.0355	0.3039
AREG	0.530584298516666	3.55755005392537	0.0457767247395846	135	-0.0474	0.4064
CXCL10	0.942670117776191	7.3499191106194	0.0457767247395846	112	-0.055	0.4715
TREM1	0.42598045447619	4.10301807428358	0.0462557149635531	154	-0.0439	0.3763
AQP1	0.41767792925	6.90573852835821	0.0493400270402151	159	-0.0433	0.3709
HES1	0.396285186980952	7.56781356671642	0.0495692202365003	162	-0.0424	0.3633
PPARA	-0.189075189498809	8.93218809236567	0.0495692202365003	232	0.03	-0.2573
TNFSF13B	-0.354265093641667	5.79875526766418	0.0497926208383706	172	0.0405	-0.3473
SREBF1	0.310045042410714	7.636426654	0.0500233469597791	187	-0.0383	0.328
ARNT	-0.153980971121429	9.02850370240298	0.0500233469597791	262	0.0266	-0.2281
F3	0.263545131889285	4.68796545684328	0.0509584519904039	199	-0.0355	0.304
CYP27A1	0.206513858914285	11.0086666866119	0.0525156138472724	222	-0.0313	0.2682
DDIT3	0.2415082974	6.77935393127612	0.0525156138472724	208	-0.0339	0.2905
IL6	0.309971382820238	3.19139126145522	0.0625745924349403	191	-0.0374	0.3202
TTR	-0.0991655703928571	12.9259340712687	0.0644387421541354	319	0.0197	-0.169
CYP4B1	0.131179569253571	3.09977601930597	0.0688462228323515	285	-0.0236	0.2019
CXCL9	0.816859002615475	6.16610278012687	0.0690820623568819	126	-0.05	0.4286

TYMP	0.260033099615476	6.89146193401493	0.0697183609568669	207	-0.0341	0.2924
PGF	0.18448740542619	4.56498826076866	0.0709882872284985	242	-0.0286	0.2456
ANXA1	0.45081395910119	8.16120718641791	0.0711786976088793	163	-0.0423	0.3624
CCL5	0.388904011129762	7.09366201279851	0.071333679474352	176	-0.0401	0.3439
CD40	0.167327239195238	5.34202885709701	0.0717683619684477	256	-0.0271	0.2322
ABCB1	0.23278200008333	7.88897849895522	0.0717908691470863	219	-0.0322	0.2761
IL1B	-0.511580559315476	4.79993909580597	0.0730153779543959	156	0.0437	-0.3749
EDEM1	-0.159685752582143	6.63149488313433	0.0730153779543959	264	0.0263	-0.2255
DCLK1	0.175224088592857	3.0205049033806	0.0758716903023264	252	-0.0276	0.2367
CXCR3	0.18637224645119	5.11040392793284	0.0769852944184032	245	-0.0285	0.2444
ELOVL6	-0.3749813521	8.22396675441045	0.0772940992602196	182	0.0391	-0.3348
CD274	0.357411451998809	4.51478436434328	0.0780447781274727	185	-0.0383	0.3283
ACOX3	0.156888872458332	7.62297875277612	0.0801207639578954	269	-0.0258	0.2211
PTEN	-0.134402819966667	9.95681642029851	0.0813948841113709	286	0.0235	-0.2015
ALMS1	-0.170677640939285	6.21532355338806	0.0832657141373954	260	0.0269	-0.2309
KEAP1	0.151940791645238	7.67551786535075	0.0853495585717802	275	-0.0252	0.2157
BID	0.194602931997619	7.85595109832836	0.085620507006878	241	-0.0288	0.2468
SERPINA1	0.103055869202381	11.254724796194	0.0856542834332554	318	-0.0198	0.1694
COMMD1	-0.137601224351191	7.52704110088806	0.0857096780411972	283	0.0237	-0.2032
STAT3	0.209690018028571	10.4353256262313	0.0862100400768974	235	-0.0298	0.2558
DHCR7	0.284562098415476	9.36775247943284	0.0862100400768974	206	-0.0344	0.2946
ADIPOR1	0.191472749452381	9.68186068494776	0.0887989765321462	246	-0.0284	0.2434
SHBG	0.480568337428571	7.58958372076866	0.0893097148513208	167	-0.0413	0.3543
NDOR1	0.175072007658333	5.2067996506194	0.0893097148513208	258	-0.027	0.2318
EGF	0.125533337628571	2.86032628663433	0.0954374839771327	295	-0.0222	0.1901
TIMP2	0.271035658210714	8.15563282639552	0.0969256867023045	213	-0.0331	0.2838
YAP1	0.161570296246428	8.64835466403731	0.098221715545508	271	-0.0256	0.2194
IDO1	-0.328622998986904	3.87342398989552	0.098221715545508	196	0.0357	-0.3061
NR3C2	-0.215097458623809	6.78796451295522	0.103127885535844	236	0.0295	-0.2531
NOS2	-0.194569433366666	3.98110194711194	0.105280947316144	251	0.028	-0.2402
ANGPTL2	-0.275274219159524	6.72562096047015	0.105463194574172	217	0.0329	-0.2819
CLU	0.0693577995119045	12.4916406741791	0.108304647261217	367	-0.0147	0.1263
GPC3	0.512841119634524	5.31033102949254	0.111554245576625	173	-0.0405	0.3468
GSK3B	-0.137874177335714	7.46675806475373	0.114349811811252	290	0.023	-0.1971
SAAL1	-0.150022636154762	5.9971179403209	0.115080288603776	280	0.0241	-0.2067
CAV1	0.296165605541666	7.88059622416418	0.117933442424765	212	-0.0333	0.2853
STK11	-0.160692945513095	6.67618493273881	0.11895388626582	277	0.0249	-0.2137
MAPK3	0.145204441910714	7.50368378120895	0.125894258987446	287	-0.0234	0.2007
TGFB1	0.244198324530953	6.84547973447015	0.126064216101296	230	-0.0304	0.2603
IL1R1	0.192638200670238	8.83740329843284	0.127981507661246	255	-0.0271	0.2325
CD36	-0.29121451007619	7.75465477335821	0.128233148879223	218	0.0326	-0.2791
SOD2	0.265434811330952	9.49430953559702	0.129811910314401	223	-0.0313	0.2681
CCR5	-0.131492114296429	4.06307426963433	0.129811910314401	298	0.022	-0.1886
F2R	0.254890826073809	6.99559991059702	0.129811910314401	227	-0.0307	0.2634
CX3CL1	0.247143020402381	6.96999823796269	0.139958465546539	234	-0.03	0.2569

CNR2	-0.117205103555952	4.05226015301493	0.141374057864564	310	0.0204	-0.1745
SLC10A2	0.0999517808821426	3.18354433735075	0.151459113436598	335	-0.0183	0.1569
PRF1	0.235214958685714	5.75763836277612	0.151459113436598	239	-0.029	0.2481
TNFRSF1B	0.223333672404762	6.97046291642537	0.157615693910426	250	-0.0281	0.241
ITGAV	0.227278641249999	7.82247797743284	0.158810396159408	247	-0.0283	0.2424
CLDN1	0.139624068309524	11.2481469380597	0.162008727646207	296	-0.0221	0.1897
SREBF2	-0.179000550334524	8.22397731265672	0.162360229992693	274	0.0252	-0.2159
CASP8	-0.113665133545238	6.37660966890298	0.163369092113311	320	0.0196	-0.1681
TGFBR1	0.119374812477381	7.37630218364179	0.163369092113311	312	-0.0202	0.173
CASP1	-0.244158751907143	5.46939866171642	0.163369092113311	240	0.0289	-0.2481
HPSE2	0.0831263427226189	3.14623096026866	0.163768573303158	354	-0.0161	0.1377
TJP2	-0.154997404096428	8.27195368088806	0.166586577460363	289	0.0233	-0.1994
CCR2	-0.213089317566666	4.26329921703731	0.170418843773816	257	0.027	-0.2318
CX3CR1	-0.211879217922619	4.653629488	0.170418843773816	259	0.027	-0.2312
SLC39A14	0.127777945749999	10.8066304938806	0.17150324119053	307	-0.0208	0.1785
FGFR4	0.166682351097619	8.00470888061194	0.17229780466976	281	-0.024	0.2057
G6PC	0.288528979145237	11.619212751	0.1760980783663	229	-0.0304	0.2605
GALC	0.186023178290476	6.6279125495	0.176163453750256	273	-0.0252	0.2161
TLR9	-0.13270733847619	4.59365414702239	0.177155913290023	305	0.0211	-0.1812
GPX1	-0.109928946414286	8.44892549989552	0.179834451234612	327	0.0189	-0.1622
TGFBR2	0.171188136304761	8.9557288409403	0.190231224079201	282	-0.0239	0.2048
CBS	0.128295453085714	9.88791037976119	0.192781995319782	308	-0.0205	0.1756
MCL1	0.235314505770238	9.53975323677612	0.196122627967702	253	-0.0274	0.2347
HGF	0.261932461539286	7.53382644174627	0.196122627967702	244	-0.0286	0.2449
NOTCH1	-0.1387250327	7.15521978606716	0.196740918342779	303	0.0213	-0.1825
BCL2	0.1286993198	5.70751113229105	0.198225286389254	309	-0.0204	0.1749
FABP4	-0.449404220294047	5.13765175227612	0.205702053492177	210	0.0336	-0.2879
CCNG1	0.185663284211905	9.61810877127612	0.208352366936575	279	-0.0243	0.2087
STK25	0.084766749902381	7.35963581698507	0.208352366936575	358	-0.0158	0.1351
ONECUT2	0.170794110372619	7.65557836062687	0.208949732544786	288	-0.0234	0.2003
MMP3	0.0909707818202379	2.92957249364925	0.208949732544786	350	-0.0165	0.1411
PKHD1	-0.276438520351191	5.91993493525373	0.209693475962963	243	0.0286	-0.2452
EGFR	-0.121949304735714	8.96002614031343	0.211357808808679	321	0.0195	-0.1675
IL21	0.104335899965476	2.5514004650597	0.211357808808679	338	-0.0178	0.153
HSD11B1	0.11619019525119	10.0581026695224	0.211357808808679	325	-0.019	0.1628
CTLA4	0.109909789064286	3.2164535249403	0.211357808808679	334	-0.0184	0.1576
SMAD3	0.127592652026191	7.70377691020149	0.211357808808679	313	-0.02	0.1714
IGF1	0.326322535358333	8.12989737785821	0.211357808808679	231	-0.0301	0.2581
APLN	-0.102836753347619	3.74141523772388	0.212003053367852	341	0.0177	-0.1513
HAVCR2	-0.237961266532143	5.37276937931343	0.222582536688757	263	0.0265	-0.2274
NR1I2	-0.166632535425	7.66076378105224	0.224065770025983	293	0.0227	-0.1943
CYP1A2	-0.28313390180119	11.7808542132388	0.22496398297865	249	0.0282	-0.2418
EGR1	0.747589413289285	9.59004463903731	0.235054695911498	197	-0.0356	0.3055
TLR8	-0.171409614666667	4.65925249246269	0.242392745217144	294	0.0226	-0.1937
UGT1A1	-0.102489450007143	9.01308145466418	0.247310905461416	342	0.0172	-0.1473

REG3A	0.133467041147619	2.79990174729851	0.252828291154336	316	-0.0198	0.1697
FLT1	-0.237908255620238	6.74477514278358	0.258782946612798	272	0.0255	-0.2187
AFP	-0.199647517222619	4.0060523261791	0.262492734490762	284	0.0237	-0.2031
IRF1	-0.26352706665	7.64717809604478	0.265991714468573	265	0.0263	-0.2252
GSTT1	0.833820031401191	8.61730183191045	0.266197466241779	205	-0.0346	0.2966
NCAN	0.102691167865476	3.68650149697761	0.266197466241779	347	-0.0169	0.1452
SPHK1	0.184743914127381	4.01439626162687	0.266197466241779	291	-0.0228	0.1953
MYD88	-0.129802364578572	8.52780406707463	0.267347156537808	323	0.0192	-0.1648
ITPA	-0.1322392035	5.50104385831343	0.267347156537808	322	0.0194	-0.1662
MERTK	0.160122157289285	8.29622230403731	0.267347156537808	302	-0.0213	0.1826
FGF2	-0.160881005464286	5.83553225599254	0.275232217128996	304	0.0212	-0.1817
MC4R	0.105325945832143	2.6260966348209	0.276202971884456	344	-0.017	0.1459
ENTPD2	0.0970627483130951	4.83897336041045	0.277335974668142	353	-0.0162	0.1391
CYP3A4	-0.143023909404762	12.4895699993284	0.277335974668142	314	0.02	-0.1712
LEPR	0.175409084345237	9.60490203632836	0.279419075785307	300	-0.0219	0.1878
PLIN2	0.230382429866667	9.84989155723881	0.28076292017958	278	-0.0244	0.2094
ADIPOQ	-0.0875764880904762	2.95894164739552	0.280888674273392	364	0.0152	-0.1303
LECT2	-0.182367950138096	10.9743902071418	0.285472503894445	297	0.0221	-0.1895
FAS	0.161121942872619	7.21225851566418	0.285472503894445	306	-0.0209	0.1794
SAA1	0.550468647434524	5.7036898824403	0.28654786350421	226	-0.0309	0.2649
LPIN1	0.12958469445	7.68710469047015	0.28654786350421	329	-0.0188	0.1611
AHSG	0.0701158422738088	12.1866152613433	0.28654786350421	383	-0.0132	0.1127
HMGCR	-0.259092783670237	7.98710285193284	0.29227731653174	276	0.0251	-0.2148
FUT2	0.0891472233190473	3.56091712447015	0.297355842987885	365	-0.0152	0.1299
FOXO3	0.121306599458333	5.87111874286567	0.301939775854683	337	-0.0179	0.1536
EPCAM	0.309355458965476	4.67690671298507	0.301939775854683	267	-0.0262	0.2245
CCL25	0.0956293862095236	4.52379241933582	0.302156502235437	359	-0.0157	0.1347
HAMP	-0.431387559064286	11.0124726403582	0.312901085563641	248	0.0282	-0.2419
IL13	0.105442766545238	3.72006392432836	0.321083769935639	352	-0.0164	0.1403
ABCG8	0.154304682946428	9.64191138191045	0.321083769935639	317	-0.0198	0.1695
TERT	0.0948066564452378	4.71526247304478	0.333562093631407	363	-0.0153	0.1311
PROM1	0.159735798022619	5.22548954691045	0.336653213057345	315	-0.0198	0.1697
ADD3	-0.110090956114286	6.95143279720896	0.349886768361213	351	0.0164	-0.1404
SCD	-0.213330354923809	8.37624559452985	0.350260348247919	299	0.0219	-0.1879
IL2	0.0491524252440475	2.25011532105224	0.356635212917085	410	-0.01	0.0854
NFKB1	0.100352818610714	7.88546330551493	0.357561495512231	361	-0.0155	0.1327
ABCG5	-0.131917433792858	8.80987566019403	0.357561495512231	340	0.0178	-0.1523
MET	0.120554924526191	9.27643885473881	0.359046828569645	346	-0.017	0.1455
TLR4	-0.152765451483333	7.89133981992537	0.359046828569645	326	0.0189	-0.1624
SLC10A1	0.121528358175	11.2909774914701	0.359404369356038	345	-0.017	0.1459
NLRP3	-0.118332463083333	4.46201101392537	0.366809507454208	348	0.0167	-0.1431
GLS	-0.150646619875	6.02480492828358	0.368058643569372	330	0.0186	-0.1598
IL1RN	0.214942461546428	7.65023188061194	0.373265985796418	301	-0.0213	0.1828
OTC	0.106640382798809	10.1604122555896	0.37599766726985	360	-0.0157	0.1345
S1PR2	0.0922209649309522	5.74624970197015	0.384498990443134	371	-0.0144	0.1236

IL22	0.0543084330476191	2.9151741595597	0.384498990443134	403	-0.0105	0.0896
DMBT1	0.0845033703749997	3.65100523396269	0.384498990443134	374	-0.0137	0.1177
IKBKB	0.0772845568023809	6.77484510491791	0.387750903199722	384	-0.013	0.1115
GNMT	0.280936135552381	9.46524956128358	0.38805644249187	292	-0.0227	0.1948
LEP	0.0857087122047618	3.5478975659403	0.388087330427783	373	-0.0138	0.1181
SOX17	0.106589959225	5.53803113167164	0.388087330427783	362	-0.0155	0.1326
CXCL12	-0.111780866516667	9.97350896202239	0.391568659346461	357	0.0158	-0.1353
NCOA1	-0.080937856961905	7.95899148352239	0.391568659346461	379	0.0133	-0.1138
ENTPD1	0.167044863817857	6.30885641128358	0.395567183599155	328	-0.0188	0.1611
CST3	0.086385095607143	10.8096642607463	0.396898572310403	375	-0.0137	0.1175
ALOX5	0.136468524459524	6.09480467422388	0.404146706721002	343	-0.0171	0.1466
HIF1A	0.151121192303571	8.91758396091045	0.409234521540082	339	-0.0178	0.1524
CYP2D6	-0.222738713478571	9.3346272346791	0.421232392298457	311	0.0202	-0.1735
FGA	-0.0388260664404764	13.0393234488806	0.421232392298457	428	0.0081	-0.0695
AGPAT4	0.0914595971928573	4.24822275075373	0.4212348572818	372	-0.0138	0.1187
PLAU	0.100661157939285	5.07097384817164	0.421472351618369	369	-0.0145	0.1246
TGFA	0.0881095774583333	4.85615553478358	0.429571470422862	377	-0.0135	0.1155
PRDX3	-0.0569396948214295	10.7652216979104	0.434813703444997	404	0.0104	-0.0891
ZNF267	-0.123962586186905	5.19406150728358	0.434813703444997	356	0.0158	-0.1358
DPP4	-0.13838759357381	9.16506212741791	0.443646830426147	349	0.0165	-0.1413
BMP7	0.0561859164559523	2.91524484213433	0.450352843065234	409	-0.0102	0.0874
ABCC3	0.0893495860500001	8.86576548082836	0.455216714351103	380	-0.0133	0.1137
HSD3B7	-0.089452823669048	8.07896378398507	0.45562631932361	381	0.0133	-0.1136
CFTR	0.209739445036904	4.84167986123881	0.475222332250368	332	-0.0185	0.1586
CASP3	-0.070398848836905	6.18460045579851	0.475222332250368	392	0.0115	-0.0982
GGT1	0.119194724119047	7.36955726029851	0.480187377253043	366	-0.0149	0.1274
CXCL11	0.219457129778571	3.87886159199254	0.484498693034177	333	-0.0185	0.1586
NPC1	0.0844065539595235	7.42727762437313	0.508472523069608	387	-0.0123	0.1054
FOXL1	0.0616966096261904	4.52959340845522	0.513533857843241	406	-0.0103	0.0884
PCSK9	0.102731149509523	6.55805648730597	0.519277503352977	378	-0.0134	0.1146
IFNAR1	0.0819329960773809	8.49252682097761	0.521228106277386	389	-0.012	0.1025
HNF4A	-0.0756019204071428	10.0572953539478	0.522335152762262	393	0.0114	-0.0981
ACE	0.0495026669345237	4.66737542913433	0.527628561033882	423	-0.0089	0.0764
MKI67	0.110711937842857	3.7686525801791	0.534318113564693	376	-0.0136	0.1163
JAG1	0.131583548903571	6.72281229098507	0.538201285972226	370	-0.0145	0.1243
SOCS3	0.272471747870238	5.83536710009701	0.542687042308827	336	-0.018	0.1545
TFF3	-0.140114686330952	5.22446113579104	0.544254299683263	368	0.0147	-0.1261
BLVRA	0.0704027081166667	5.06301931770149	0.548230314759976	398	-0.0107	0.0919
TNNI3	-0.0507539648166667	4.34253431177612	0.549791778087928	424	0.0089	-0.0761
SMN1	0.0654094731154761	7.15741881079104	0.554263601304626	408	-0.0102	0.0878
PF4	0.0521053760309524	4.4045767209403	0.563041920148878	422	-0.0089	0.0765
NOX4	0.0755691315071427	3.34589537324627	0.565901746571614	395	-0.0109	0.0935
ITGB2	-0.101710839771429	7.60105192555224	0.565901746571614	385	0.0125	-0.1075
NFE2L2	0.0881033284630956	9.37846987597015	0.567580708617001	390	-0.0117	0.1005
TM6SF2	0.11975204785119	8.85938945427612	0.578036862533456	382	-0.0132	0.1132

TIMP3	0.0845294905559521	7.91147952997015	0.592871153250506	394	-0.0112	0.0959
MUC16	0.0459310639083334	3.48160065196269	0.59514665295054	430	-0.008	0.0689
CD1D	-0.0593038453464285	7.17347000563433	0.59514665295054	416	0.0093	-0.0798
PDGFC	-0.0591987033642859	6.96931904749254	0.595167555015543	417	0.0093	-0.0796
ENG	0.102510142365476	8.99433384136567	0.603771060631101	388	-0.012	0.1026
C3	-0.015981004511905	13.2201415108955	0.605347225383798	467	0.0038	-0.0325
MMP1	0.0419823769023808	3.09025334586567	0.607262194143086	434	-0.0075	0.0643
NOTCH4	0.0750711177166667	5.90999465138806	0.611815239002884	407	-0.0103	0.088
CPT1A	-0.0974081698059529	9.51146226612687	0.611815239002884	391	0.0115	-0.0989
VPS33B	-0.0450952141059523	5.68389323711194	0.611815239002884	431	0.0078	-0.0667
ITGB4	0.0687910846047617	4.63095052520895	0.6143795983118	413	-0.0098	0.0839
CALCA	-0.0577232170547619	3.69455450311194	0.623619067148061	425	0.0088	-0.0759
BCS1L	-0.0466547899011903	6.71429301072388	0.635657416404078	432	0.0078	-0.0666
PROX1	0.0619064193357135	9.23217045380597	0.641123370656377	421	-0.009	0.0772
POSTN	0.132752088996428	5.84154263981343	0.64406690597194	386	-0.0123	0.1056
HPX	0.0303359404404764	12.5727448940299	0.644291067986128	450	-0.0059	0.0504
NR1I3	-0.0788091418630955	8.98290843135075	0.652489881810128	412	0.0099	-0.0852
PARVB	-0.0601179031107143	7.07163276237313	0.658703961796268	427	0.0087	-0.0742
ABCC4	0.0949384094202377	4.96712460280597	0.658703961796268	401	-0.0106	0.0911
MIF	0.106224119380953	9.48657328065672	0.670704121720404	396	-0.0109	0.0931
F5	-0.0412009969666672	10.656998543194	0.670704121720404	436	0.0069	-0.0594
IL12B	0.0350490620785714	3.16368775115672	0.670704121720404	448	-0.0063	0.0539
MAT1A	-0.0403209954523811	11.8518390998507	0.676246346074837	439	0.0068	-0.0583
ARG1	0.0492382114607145	10.4552084235746	0.684515667080014	433	-0.0075	0.0644
CPS1	0.0324284685476188	12.3506472061194	0.684515667080014	449	-0.0059	0.0504
CP	0.0272446989523811	12.5199615414179	0.684515667080014	455	-0.0053	0.045
TLR3	-0.0785155262476192	8.28718751685075	0.684515667080014	415	0.0093	-0.0801
PDGFRB	-0.0730218898642853	7.33472198947761	0.684515667080014	420	0.0091	-0.0776
MACC1	-0.0769609451761905	3.76545721026866	0.691602152564866	419	0.0092	-0.0785
MTOR	0.0437373633714286	8.07918388847761	0.696138231619637	438	-0.0069	0.0592
FGF21	-0.126446297010714	5.38644866307463	0.696138231619637	397	0.0108	-0.0928
CXCR2	0.100897255677381	3.59675890643284	0.70125571725802	411	-0.01	0.0853
IL33	0.0862045754333333	5.93547307774627	0.708065667747015	418	-0.0093	0.0796
UCP2	0.0939344193428567	7.22064413361194	0.710769481142648	414	-0.0095	0.0816
GOLM1	0.1277030018	7.28275777936567	0.719580125961173	405	-0.0103	0.0885
IFNG	-0.0454501675392858	2.93933436135821	0.726552366397051	442	0.0067	-0.0578
PSMD10	0.044296729377381	7.72669076241045	0.728396408512551	443	-0.0066	0.0568
ATP8B1	-0.0313892402666666	6.26486223090298	0.728396408512551	453	0.0054	-0.0467
CRP	-0.168345280091667	10.7246069782463	0.732071662198825	400	0.0107	-0.0917
CXCL13	-0.172342391705952	3.78729386747015	0.738313778877388	402	0.0106	-0.0907
CHI3L1	0.198500750617858	7.95947890741791	0.744073837965965	399	-0.0107	0.0919
PCK1	0.0732408992297616	11.8772930785896	0.745124619372517	429	-0.008	0.0689
TLR7	-0.0519510354178573	3.78061851865672	0.760342132965275	440	0.0067	-0.0578
DLK1	0.0570278788869047	4.67596630064179	0.760342132965275	435	-0.007	0.0603
F2	0.0266572272976187	11.7016734918657	0.760342132965275	460	-0.0047	0.0404

HBEGF	0.120511047189285	5.93074080894776	0.773122901700071	426	-0.0088	0.0757
APLNR	-0.0514710949142852	7.4508507861194	0.781012122472672	445	0.0064	-0.055
IL2RA	0.0579382513095237	4.70300065897015	0.781012122472672	441	-0.0067	0.0578
GPX4	-0.0281333474999994	11.3135517075373	0.781012122472672	461	0.0047	-0.0403
LBP	0.0383088840595237	11.648307168806	0.782854689934759	452	-0.0055	0.0475
LGALS3	-0.0523509998511903	5.53007165526119	0.782854689934759	446	0.0064	-0.0548
STAT1	0.0551642287833332	9.30439956110448	0.790732545259505	444	-0.0064	0.0551
SLC27A5	0.0389944527488097	10.1986881579104	0.803094215490467	454	-0.0054	0.046
MST1	-0.0344035276154769	9.91003401335075	0.805526028537823	458	0.005	-0.0429
MPO	0.0378422344226189	3.71581862657463	0.812671550517039	456	-0.0052	0.0442
IL17A	-0.0220524269964287	3.95805772851493	0.812671550517039	466	0.0038	-0.0328
CXCL2	-0.0820651115154758	8.45482374378358	0.812671550517039	437	0.0069	-0.0593
MBL2	-0.0641683111749999	10.7078374602612	0.813138873737447	447	0.0064	-0.0544
ACE2	-0.0518047316059521	5.63714470824627	0.817866191049633	451	0.0058	-0.0495
NR5A2	0.0258405146892853	8.94291250079104	0.833866297149495	465	-0.004	0.0344
CXCL16	0.0424238138833334	7.2954830328806	0.833866297149495	457	-0.0051	0.0437
ONECUT1	-0.0306621572535714	9.41820636785821	0.842423626623655	463	0.0043	-0.0368
EZR	0.0220529710809524	7.66777120388806	0.853461987704616	470	-0.0035	0.0302
NOTCH2	0.0164086490607144	8.84303240619403	0.860781670501423	477	-0.0029	0.0249
PTPRO	0.0194915775642856	3.88685132762687	0.870546941224976	474	-0.0031	0.027
CXCL3	0.0241803401166664	4.86635372457463	0.870546941224976	469	-0.0035	0.0302
TLR2	0.0385108976988094	5.40718882278358	0.870546941224976	462	-0.0043	0.0371
NPPB	-0.0174240505428569	3.61812246620896	0.871022564058828	476	0.0029	-0.025
BHMT	-0.024637113672619	11.8656515911567	0.878429860460012	472	0.0034	-0.0294
LYZ	0.0622068991047623	9.20094891223134	0.878429860460012	459	-0.0049	0.0417
TNFAIP8L2	-0.0182591335095236	4.83456712370149	0.888881577391701	478	0.0028	-0.0243
HMOX1	0.0432795220190472	8.24304956637313	0.890223932108496	464	-0.0041	0.0352
NCF1	0.0230657531785714	5.8379397805597	0.896614580372748	475	-0.0031	0.0265
NR1H3	-0.0138399287619049	7.15686303062687	0.90374031469662	481	0.0023	-0.0198
CYP7B1	-0.0169289319571433	8.37005425121642	0.914600977757212	480	0.0025	-0.0212
NOX1	-0.00896245997619049	3.18018607141791	0.914600977757212	490	0.0017	-0.0144
CD44	-0.0318211268511902	8.38638876986567	0.914600977757212	473	0.0032	-0.027
GFER	0.0133962262392853	5.51469317670149	0.914600977757212	484	-0.0021	0.0183
CCL2	0.0542809860059522	7.7686881395	0.914600977757212	468	-0.0036	0.0312
PTGS2	-0.0454644690511903	5.49191296875373	0.914600977757212	471	0.0035	-0.0297
PARP1	0.0151623832940476	7.74480460758955	0.914600977757212	482	-0.0022	0.0192
SLC40A1	-0.0151401280464287	10.3941305725522	0.914600977757212	483	0.0022	-0.0191
SMAD7	-0.012443632607143	6.13823056323134	0.927063725088991	486	0.0019	-0.0163
PDGFB	-0.0123636447619047	4.58011073725373	0.927063725088991	487	0.0019	-0.0162
MMP9	-0.0327138597226191	4.59747275806716	0.927063725088991	479	0.0028	-0.024
NOS3	-0.0127774251309522	5.56593831605224	0.933191773623727	488	0.0018	-0.0156
PPARG	-0.0126946449297621	7.12303202167164	0.933191773623727	489	0.0018	-0.0156
EPO	0.0173009869654761	5.22336722769403	0.933742644472953	485	-0.0021	0.0177
PDCD1	0.00992990592142844	4.29050097750746	0.937468992301964	494	-0.0015	0.0132
CDK1	0.0106335902773809	2.68010164712687	0.938594809746976	492	-0.0016	0.0134

AGTR1	-0.0124548317547619	8.31198545910448	0.94736599397164	491	0.0016	-0.0136
IL10	-0.0132236207738094	4.15915672359701	0.951217304177938	493	0.0016	-0.0134
PEMT	0.00863647137499999	11.0084380715299	0.952476659299077	496	-0.0013	0.0107
IL23A	-0.00416362960714275	4.12666963317164	0.952476659299077	498	0.0008	-0.0069
ENPP2	0.0182474916059518	8.02844441945522	0.965743200631755	495	-0.0014	0.0119
ABCC1	0.00694043438928573	6.06111009633582	0.965743200631755	497	-0.001	0.0082
CD40LG	0.00456193552499985	3.20529193410448	0.979077344016075	501	-0.0006	0.0055
MX1	-0.00604163464761933	6.53515132287313	0.979077344016075	500	0.0007	-0.006
PLAUR	0.00901187165595247	5.63332650088806	0.979077344016075	499	-0.0008	0.0066
EDNRA	-0.00533701776547612	6.46687138903731	0.979077344016075	502	0.0006	-0.0054
RETN	-0.00267083347738083	4.20917191438806	0.979077344016075	503	0.0004	-0.0038
SLC4A2	-0.00230366552380932	7.46496963219403	0.980741196117166	504	0.0004	-0.0032
CCNA1	0.00169430916190471	3.10310191264179	0.980741196117166	506	-0.0003	0.0026
DKC1	0.00231928933809521	6.29436516654478	0.980741196117166	505	-0.0004	0.003
ABCC2	0.00107757839404723	10.256582001709	0.988819475802519	507	-0.0002	0.0015

Supplemental table 3

gene symbol	PTM.R.values	PTM.p.Values
TNF	0.658481	0.019895649
NR1H4	0.8987596	7.051707E-5
TNFRSF1A	0.606782	0.036433317
MIF	-0.8562979	3.7723436E-4
IFNG	-0.62242836	0.03065831
ABCB11	0.85081524	4.5052322E-4
IL1RN	0.608279	0.035849635
IL1R1	0.582369	0.04693469
LDLR	0.6105657	0.03497096
CYP7A1	-0.64633787	0.023148783
TLR3	0.8164091	0.0011961266
STAT1	0.6501415	0.022091046
CD274	0.69797415	0.011598374
NR1I2	0.746237	0.0053126863
KRT18	0.8542353	4.0362534E-4
HIF1A	-0.57752514	0.049247243
C3	0.7234944	0.007823705
COL1A1	-0.6196485	0.03163258
CTNNA1	-0.57828486	0.04887935
MET	0.70211357	0.010909507
ANXA1	-0.58730876	0.044656325
NROB2	0.5881663	0.044268925
CD36	0.83506334	7.237027E-4
PTEN	0.65347886	0.021192333
KRT8	0.82332855	9.993713E-4
PPARGC1A	0.8274073	8.957106E-4
TIMP3	-0.8154762	0.00122478
PKHD1	0.66367006	0.018612774
CASP8	-0.5922592	0.04245258
CEBPA	-0.8422907	5.859107E-4
IGF1	0.58007735	0.048019014
NOX4	0.69428235	0.012239512
SLC10A2	0.80886513	0.0014432635
SPHK1	-0.6650197	0.018289283
KLF6	0.5804634	0.047835127
IRF1	0.83695173	6.8550755E-4
ADIPOR2	-0.72480935	0.007658131
TGFBR1	-0.8153795	0.0012277792
TIMP2	-0.7353816	0.0064204982
GOLM1	0.717523	0.008609553
ENPP2	0.7837536	0.0025568428
SLC4A2	-0.7578264	0.0042959247

RARRES2	0.8541692	4.0449417E-4
FABP1	-0.68153894	0.014655506
PDGFRB	-0.84134036	6.0276163E-4
CYP1A2	-0.6274603	0.028949907
GPT	0.85449815	4.0018465E-4
BCL2L11	-0.85782444	3.5858207E-4
NQO1	0.891083	1.002805E-4
MCL1	0.65469617	0.020871263
TERT	0.78323156	0.0025854032
AQP1	-0.6413803	0.024582073
CLU	0.6294113	0.028306369
MST1	0.71179026	0.009418075
CXCL11	0.8591084	3.4345628E-4
GSTP1	-0.69853413	0.011503345
VIM	-0.7176681	0.008589781
MERTK	-0.6456616	0.023340631
BLVRA	0.5798412	0.048131745
NPC1	-0.7495386	0.005006292
MTTP	-0.66207	0.019001702
SREBF2	0.6123078	0.034311987
CTH	0.6153943	0.033166353
FABP4	-0.75353557	0.0046534413
MAT1A	0.69206965	0.012636151
HPX	0.70675	0.01017455
MX1	-0.59253365	0.042332724
CST3	0.7293835	0.0071025416
PSMD10	0.73154086	0.0068512647
LPIN1	-0.6256573	0.02955394
G6PC	-0.6595853	0.019617384
DGAT2	-0.6934754	0.012383074
SLC27A5	0.6131261	0.034005534
CYP8B1	-0.66253716	0.018887538
AKR1D1	0.7719539	0.0032640218
GGT1	0.7714968	0.0032941196
HMGCS1	0.62166053	0.030925227
LUM	-0.6428049	0.024163788
TTR	-0.66472155	0.018360388
GSTT1	-0.6366131	0.026020017
BCHE	0.7080673	0.0099726245
PEMT	0.85449916	4.001714E-4
DCLK1	0.6461042	0.023214936
NCOA1	-0.5952546	0.04115723
GALC	-0.8746848	1.9648828E-4
ALPL	-0.6931997	0.012432414
CCNA1	-0.5844916	0.04594588

PRDX3	-0.8598483	3.349677E-4
C8G	0.7698487	0.0034043903
MBOAT7	0.6840867	0.014146564
EDEM1	0.68641347	0.013693266

Supplemental Table 4

gene symbol	num_cells_expressed	proportion positive	P-values	Q-values
Sox9	1027	78.0395136778116	7.19816577256051E-246	8.86526096548553E-242
Nr0b2	457	34.726443768997	7.80162701157387E-243	4.80424191372719E-239
Malat1	1310	99.5440729483283	1.76035519723752E-071	2.16805346091773E-068
Spp1	1303	99.0121580547113	5.39371002427612E-033	5.53574438824873E-030
Mgst1	1130	85.8662613981763	1.47597176822542E-031	1.39831294595879E-028
Tstd1	1014	77.0516717325228	2.3504283690298E-029	2.06770541378365E-026
Eef1a1	1229	93.3890577507599	1.22468548648441E-028	1.0055484301028E-025
Pebp1	1144	86.9300911854103	4.02906802976077E-027	3.10137511590835E-024
Fth1	1239	94.1489361702128	1.59753258665412E-026	1.09306729651289E-023
Bsg	1171	88.9817629179331	1.88253916849066E-026	1.22028170521742E-023
Ubb	1219	92.629179331307	8.97572503677164E-026	5.52725147764397E-023
Gm42418	1299	98.7082066869301	2.40003585125472E-025	1.40756388305015E-022
Ttr	1198	91.0334346504559	4.63013967737829E-025	2.59203637575414E-022
Sorbs2	1099	83.5106382978723	6.2231374271315E-025	3.33235480663268E-022
Mpc2	943	71.6565349544073	1.78839080918745E-023	8.81032848238105E-021
Tpt1	1211	92.0212765957447	2.76716898382304E-023	1.31078666172172E-020
Birc2	640	48.6322188449848	5.18588759305987E-023	2.28104969986162E-020
Dbi	1188	90.273556231003	8.89634465670118E-022	3.49103392867551E-019
Eno1	1013	76.9756838905775	9.07056558278793E-022	3.49103392867551E-019
Fau	1193	90.6534954407295	2.2382807335081E-021	8.35353500420782E-019
C3	1165	88.5258358662614	5.89060939166066E-021	1.96077689912683E-018
Anxa5	1241	94.3009118541034	1.17336272031784E-020	3.80293033248275E-018
Atp5g2	1060	80.5471124620061	3.55598889703684E-020	1.06818437209526E-017
Tmem45a	1092	82.9787234042553	9.19970538855949E-020	2.63496678059299E-017
Tmem176b	1243	94.4528875379939	1.30116534563943E-019	3.56114497708782E-017
Agri	422	32.0668693009119	5.40861819889119E-019	1.4172881220754E-016
Apoc1	979	74.3920972644377	7.18057911761755E-019	1.80481657984853E-016
Ppia	1199	91.1094224924012	2.38690303927379E-018	5.65328804455693E-016
Cox4i1	1157	87.9179331306991	3.66700241608377E-018	8.21141850117958E-016
Mrpl14	693	52.6595744680851	3.65807587824824E-018	8.21141850117958E-016
Tmem59	1078	81.9148936170213	6.07997019984648E-018	1.33715916038052E-015
Dad1	955	72.5683890577508	1.22868758853049E-017	2.60905454143819E-015
Oaz1	1118	84.9544072948328	1.66390966513063E-017	3.47334092131336E-015
Ndufa4	1117	84.8784194528875	2.3471410683842E-017	4.81789823303664E-015
Ndfip1	938	71.2765957446809	3.04424805295822E-017	6.04725145487637E-015
Gstm1	1068	81.1550151975684	3.99563738498861E-017	7.68910469273745E-015
Tle5	1086	82.5227963525836	4.11244014866789E-017	7.79212505707595E-015
Kcnq1ot1	444	33.7386018237082	1.34139849502433E-016	0.000000000000241456125018703
Gsta3	763	57.9787234042553	1.56486849650494E-016	0.000000000000275327434327927
Id2	1079	81.9908814589666	1.60027828590538E-016	0.000000000000277591934777614
Col18a1	525	39.8936170212766	2.3865223320723E-016	0.00000000000040263574049014
Clu	1308	99.3920972644377	2.386246313162E-016	0.00000000000040263574049014
Onecut2	1043	79.2553191489362	2.62852289518562E-016	0.000000000000437471459150083
Afdn	775	58.8905775075988	3.10321434495412E-016	0.000000000000509589171632732
Btf3	1064	80.8510638297872	4.5698036112189E-016	0.000000000000721560272766307
Ubl5	810	61.5501519756839	4.98414268966564E-016	0.000000000000777021536277494
Tns3	340	25.8358662613982	6.21310483604413E-016	0.000000000000933178038545359
Gnas	1105	83.9665653495441	8.09022339241375E-016	0.00000000000120047218434901
Hmgn1	1071	81.3829787234043	8.28106180554255E-016	0.00000000000121416139520312
Tmem176a	1155	87.7659574468085	9.30796209618464E-016	0.00000000000134866895501894

ltgav	406	30.8510638297872	1.23611514030828E-015	0.00000000000177023186837637
Park7	1019	77.4316109422492	1.51670376190678E-015	0.00000000000211516259636277
Phip	512	38.9057750759878	1.95567822990597E-015	0.000000000000267623700883577
Zbtb20	1134	86.1702127659575	3.01202663322541E-015	0.00000000000398883010911873
Tia1	383	29.1033434650456	4.40807968443344E-015	0.000000000000577552227590236
Edf1	994	75.531914893617	0.000000000000121470419875807	0.00000000000151378699336682
Ambp	1177	89.4376899696049	0.000000000000121683105182945	0.00000000000151378699336682
Ppib	1085	82.4468085106383	0.000000000000133471343504952	0.00000000000164383306660699
Tmsb10	1139	86.5501519756839	0.00000000000017399819163864	0.00000000000210094287080538
Tm4sf4	1257	95.516717325228	0.000000000000206759587053386	0.00000000000247228259626166
Cst3	1140	86.6261398176292	0.000000000000244009517551099	0.00000000000287166925463271
Rack1	1129	85.790273556231	0.000000000000244824027067583	0.00000000000287166925463271
H3f3a	1158	87.9939209726444	0.000000000000302081712786963	0.00000000000350091193403735
Rplp2	1107	84.1185410334347	0.000000000000304155226487493	0.00000000000350091193403735
Hint1	1062	80.6990881458967	0.000000000000325722449467062	0.00000000000371444230336698
Hsp90ab1	1243	94.4528875379939	0.000000000000329568107766566	0.00000000000372381726170003
Ahnak	454	34.4984802431611	0.000000000000361240236362452	0.00000000000404457704639996
Esd	866	65.8054711246201	0.00000000000042992116755536	0.00000000000477018837802867
Alb	1237	93.9969604863222	0.000000000000533275363098816	0.00000000000576124506309212
Prdx1	1176	89.3617021276596	0.000000000000550453645654987	0.00000000000589511921729288
Scp2	948	72.0364741641337	0.000000000000678746453288678	0.00000000000720641492991668
Nbeal1	458	34.8024316109422	0.00000000000106482357589854	0.000000000011138704752258
Itm2b	1204	91.4893617021277	0.00000000000109809295914124	0.0000000000113648007435156
Gabarap	978	74.3161094224924	0.00000000000171153306958712	0.0000000000175660344041958
Tesc	813	61.7781155015198	0.00000000000228189862389689	0.000000000023199144406452
Rps15a	1143	86.854103343465	0.00000000000229806399609219	0.000000000023199144406452
Cystm1	819	62.2340425531915	0.00000000000277847080048863	0.0000000000278208507144861
Atp5a1	1022	77.6595744680851	0.00000000000298869170958368	0.000000000029684457334865
Mgst3	574	43.6170212765957	0.0000000000033594717616705	0.0000000000330637385195228
Uqcrh	965	73.3282674772037	0.00000000000338261696448512	0.0000000000330637385195228
Atp5e	907	68.9209726443769	0.00000000000413607235844545	0.0000000000401101316272553
Spcs1	960	72.9483282674772	0.00000000000427869995695632	0.0000000000409405729229211
Son	805	61.1702127659575	0.00000000000432143104902545	0.0000000000409405729229211
Akr1a1	954	72.4924012158055	0.00000000000470313678377402	0.0000000000442166661289777
Gstt1	787	59.8024316109423	0.00000000000477629644427471	0.0000000000443156911359423
H2afv	965	73.3282674772037	0.0000000000095513615713678	0.0000000000877869918753477
Gm609	510	38.7537993920973	0.00000000000112124703209021	0.000000000102290951460912
Gng5	1079	81.9908814589666	0.00000000000133235499026606	0.000000000119775796059247
Myl6	1170	88.9057750759879	0.00000000000183397692982801	0.000000000163675796143202
Selenbp1	682	51.8237082066869	0.00000000000189327518882542	0.000000000167752354140819
B2m	1138	86.4741641337386	0.00000000000232533628988685	0.000000000201681984128496
Vps28	744	56.5349544072948	0.00000000000231200813012127	0.000000000201681984128496
A830018L16Rik	224	17.0212765957447	0.00000000000362271435796281	0.000000000307705862294276
Naca	1123	85.3343465045593	0.00000000000440331702141948	0.000000000371446934491797
Cd24a	1003	76.2158054711246	0.00000000000482931042720233	0.000000000404610797424652
Psma2	853	64.8176291793313	0.0000000000053866625747623	0.000000000448257983966738
Swi5	810	61.5501519756839	0.00000000000594324699257001	0.000000000486501171492006
Gstm5	694	52.7355623100304	0.00000000000596473505158274	0.000000000486501171492006
Etfb	859	65.273556231003	0.00000000000611738031878882	0.000000000495668789514495
Psenen	764	58.0547112462006	0.00000000000665385458286256	0.000000000535613549297617