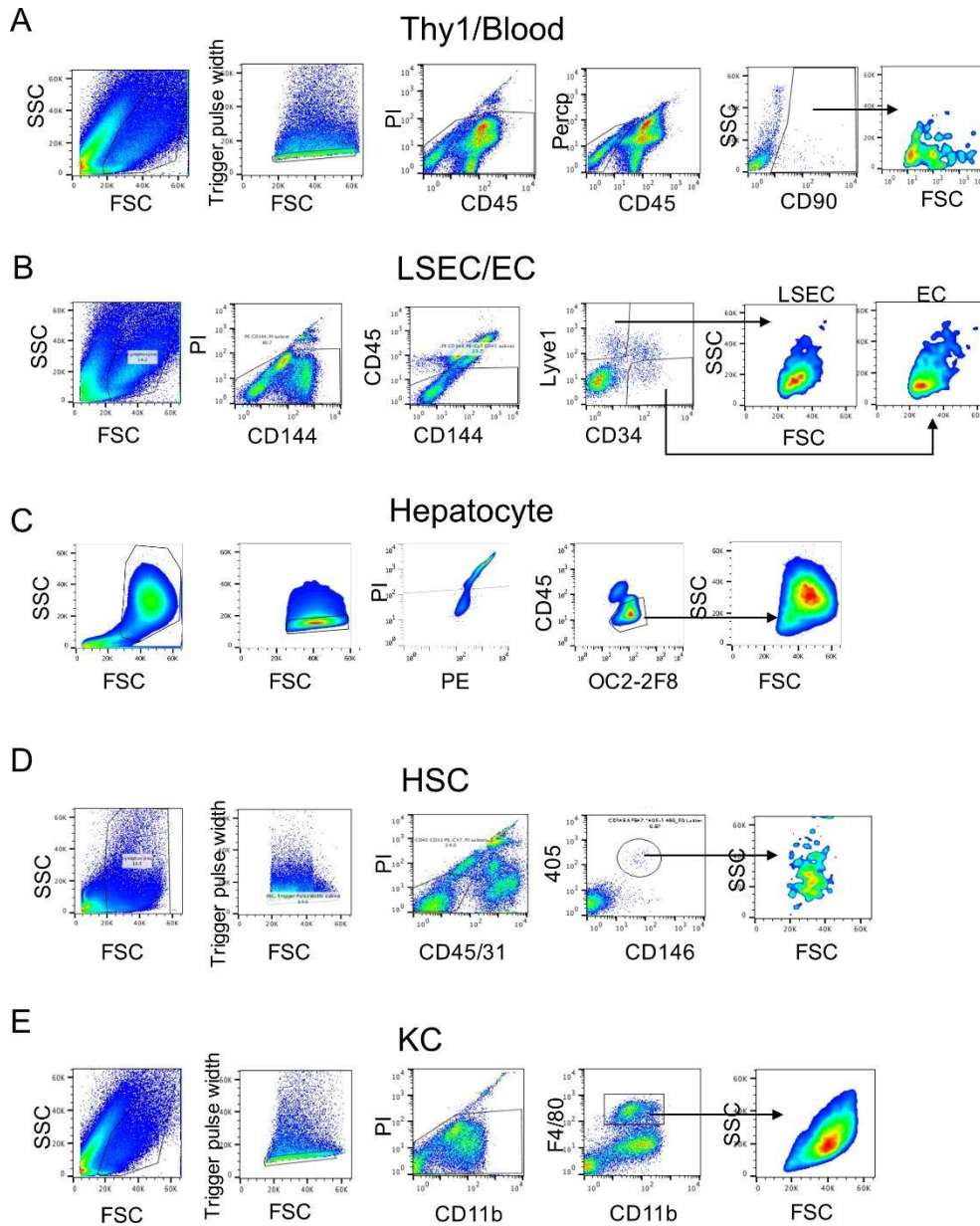


Figure S1 FACS strategy for isolating liver cells

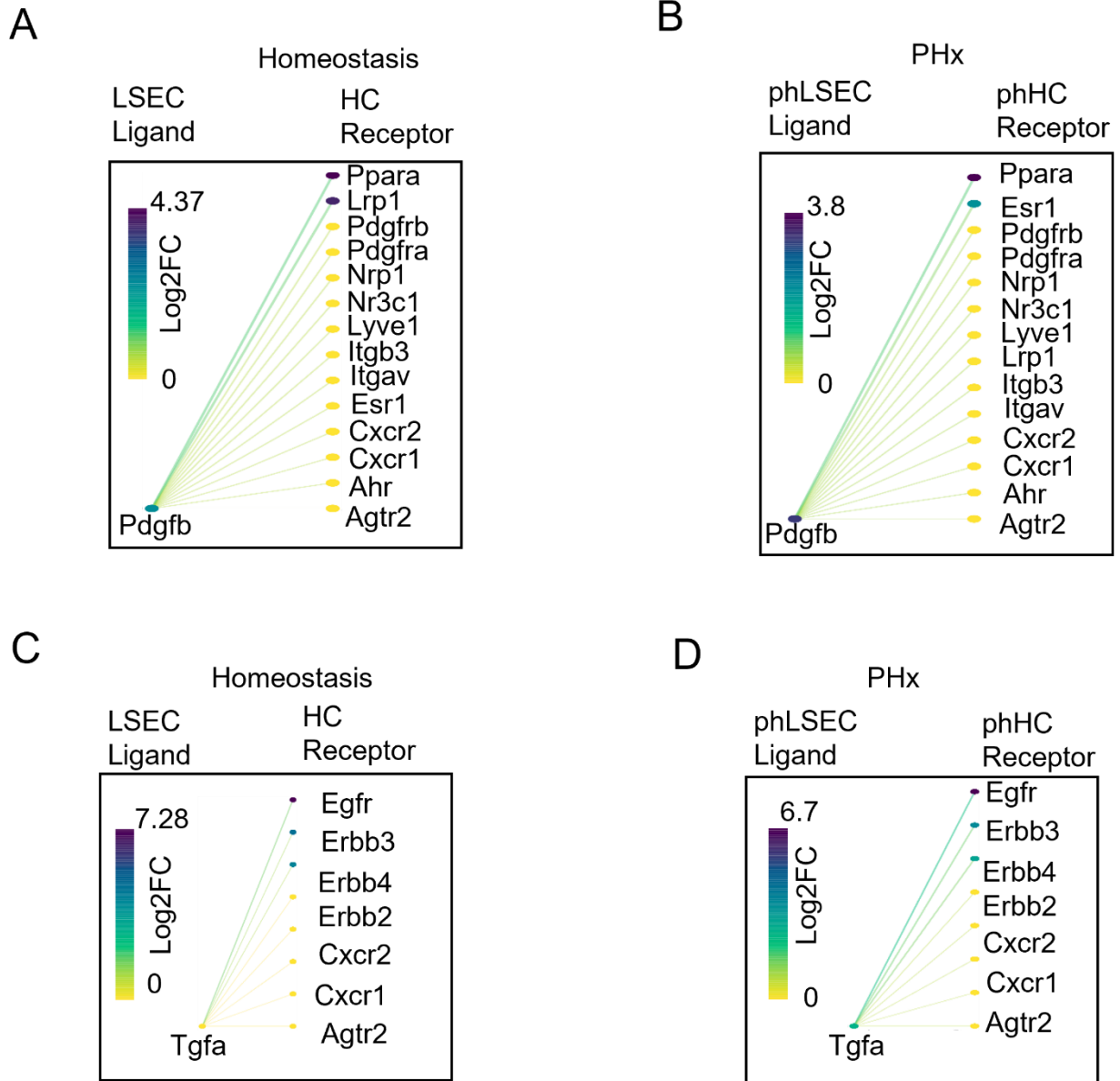


Single cell suspension was labelled with antibodies to isolate liver cell populations

Cells were sequentially gated based on cell size (forward scatter [FSC] versus side scatter [SSC]) and singlets (FSC versus trigger pulse width). Dead cells and debris were gated out with propidium iodide (PI) positivity. (A) Blood cells were isolated with CD45 positivity and Thy1 cells were isolated with CD45⁺CD90⁺. (B) LSEC and EC were isolated with CD45⁺

CD144⁺Lyve1⁺CD34⁻ and CD45⁻CD144⁻Lyve1⁺CD34⁺. (C) Hepatocytes were first gated with bigger FSC vs SSC, singlets followed by CD45⁻OC2-2F8⁺. (D) Hepatic stellate cells (HSC) were isolated by CD45⁻CD31⁻Violet⁺CD146⁺. (E) Kupffer cells (KC) were isolated with CD11b⁺F4/80⁺.

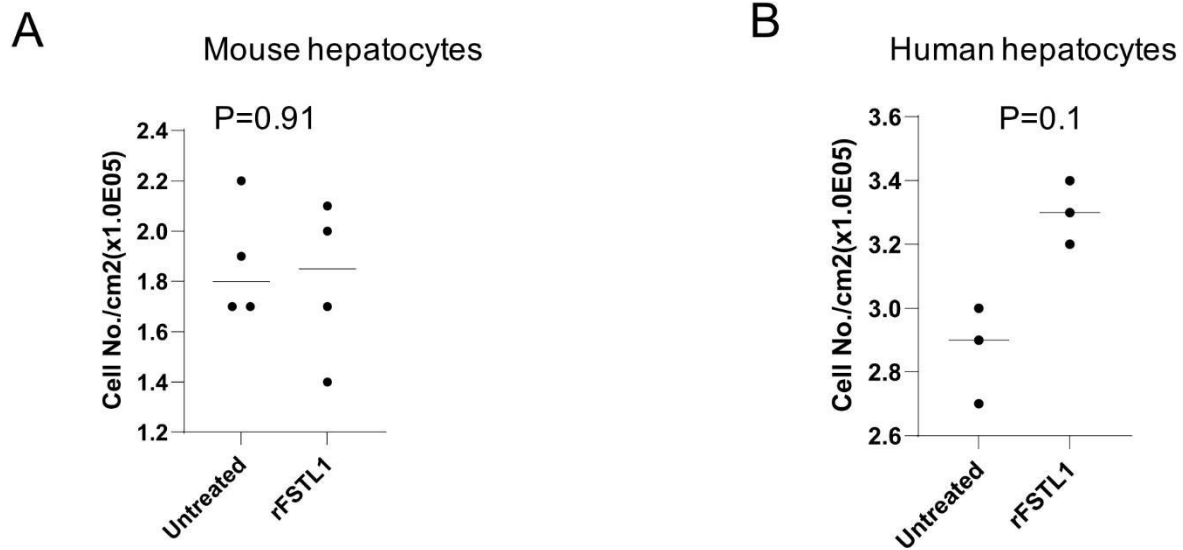
Figure S2 Ligand-receptor analysis by CCl₄



(A-B) Pdgf β ligand in LSEC and its receptor in hepatocyte in normal (A) and liver regeneration (B), respectively.

(C-D) Tgfa ligand in LSEC and its receptor in hepatocyte in normal (C) and liver regeneration (D), respectively. Log2FC: log2fold change.

Figure S3 Effects of rFstl1 on mouse and human hepatocytes



Recombinant FSTL1(rFSTL1) was added into the cell culture supernatant.

(A) Cell densities for mouse hepatocytes culture treated with rFSTL1 and untreated (n = 4 for each treatment). Statistical analyses: Student's t test, p = 0.91.

(B) Cell densities for human hepatocytes cultured with rFSTL1 and untreated (n= 3). Statistical analyses: Student's t test, p = 0.1.

Table S1 OnOn interactions

This table summarizes the numbers of receptor/ligand interactions. Each sheet reports numbers for all interactions and numbers for interactions involving selected genes. The first sheet reports counts for interactions between all cell types. The additional sheets report interactions involving each cell type and involving each cell type specifically as a ligand or as a receptor. The columns for each sheet are: Gene - either all genes or one of a list of selected genes of interest, ValidInteractionPairs - number of possible interactions, OnOnInGroundState - number of active interactions in the pre partial hepatectomy state (pre PHx), OnOnInPHxState - number of active interactions in the post partial hepatectomy state (post PHx), OnOnInBothStates - number of active interactions shared in both states, OnOnInGroundStateOnly - number of active interactions specific to the pre PHx state, and OnOnInPHxStateOnly - number of active interactions specific to the post PHx state. To determine OnOn interactions we first estimated an on state expression level threshold for each gene based on the distribution of expression levels in our data (this was done independently in the pre and post PHx states, see methods). We then required that all replicates of respective cell types exceed this threshold for a receptor/ligand pair in the database. Only these cases are considered valid OnOn interactions.

Table S2 All of the interactions

This table shows all active interactions between all cell types. Active interactions are reported for pre and post partial hepatectomy states separately. The columns are: Name - the format is gene1_cell type1~gene2_cell type2 where the cell type 1 is interacting with cell type 2 via gene 1 and gene 2 respectively (the receptor/ligand order is not defined), GeneStateLog2FCnodeA - the log2 Fold Change (FC) for node A (gene 1, cell type 1), GeneStateLog2FCnodeB - the log2 FC for node B (gene 2, cell type 2), Rank - the rank order of these interactions based on the maximum of the two log2 FC values. Note that the log2 FC is calculated based on expression in the given cell type compared to the off state expression level estimated based on all cell types (see methods).

Table S3 Top10 weighted interactions in normal liver by CCl₄

This table shows the top active interactions in normal liver for all cell types. The top 10 CCl₄ weighted interactions from each cell type are combined (duplicates are removed). The columns

are: Ligand_Cell_Type - Cell type expressing ligand, Receptor_Cell_Type - Cell type expressing receptor, Interaction_Type - Paracrine or Autocrine, Name - Formatted name of interaction, Interaction_Weight - Relative strength of interaction from CCInx tool, Ligand_log2FC - Log 2 Fold Change (FC) of ligand relative to calculated off state in respective cell type, Ligand_Symbol - Gene symbol of ligand, Ligand_Weight - Relative degree of ligand expression from CCInx tool, Receptor_log2FC - Log 2 FC of receptor relative to calculated off state in respective cell type, Receptor_Symbol - Gene symbol of receptor, Receptor_Weight - Relative degree of receptor expression from CCInx tool.

Table S4 Top10 weighted interactions in PHx liver by CCInx

This table shows the top active interactions in PHx liver for all cell types. The top 10 CCInx weighted interactions from each cell type are combined (duplicates are removed). The columns are: Ligand_Cell_Type - Cell type expressing ligand, Receptor_Cell_Type - Cell type expressing receptor, Interaction_Type - Paracrine or Autocrine, Name - Formatted name of interaction, Interaction_Weight - Relative strength of interaction from CCInx tool, Ligand_log2FC - Log 2 Fold Change (FC) of ligand relative to calculated off state in respective cell type, Ligand_Symbol - Gene symbol of ligand, Ligand_Weight - Relative degree of ligand expression from CCInx tool, Receptor_log2FC - Log 2 FC of receptor relative to calculated off state in respective cell type, Receptor_Symbol - Gene symbol of receptor, Receptor_Weight - Relative degree of receptor expression from CCInx tool.

Table S5 List of Antibodies

Primary Antibodies

Name	IgG type	Use	Dilution	Company	Lot
CD11b	Rat mAB	FACS	1/100	BD biosciences	552850
CD144	Rat mAB	FACS	1/100	eBioscience	12-1441-82
CD146	Rat mAB	FACS	1/100	BD biosciences	562230
CD26	Rat mAB	FACS	1/100	BD biosciences	4278805
CD309	Biotin	FACS	1/100	eBioscience	13-5821-82
CD31	Rat mAB	FACS	1/100	BD biosciences	561410
CD34	Rat mAB	FACS	1/20	eBioscience	50-0341-80
CD45	Rat mAB	FACS	1/100	BD biosciences	552848

CD90(Thy1)	Rat mAB	FACS	1/100	BD biosciences	553007
F4/80	Rat mAB	FACS	1/100	eBioscience	17-4801-80
Lyve1	Rat mAB	FACS	1/100	eBioscience	53-0443-80
MIC1-1C3	Rat mAB	FACS	1/20	Grompe lab	
OC2-2F8	Rat mAB	FACS	1/20	Grompe lab	
ST14	Rabbit pAB	FACS	1/100	Abcam	ab28266
BrdU	Rat mAB	IHC	1/100	Abcam	Ab6326

Secondary Antibodies

Name	IgG type	Use	Dilution	Company	Lot
Anti rabbit APC	Donkey	FACS	1/200	JacksonImmuno	711-056-152
Anti Rat PE	Goat	FACS	1/200	JacksonImmuno	112-116-143
APC/Cy7	Streptavidin	FACS	1/250	Biolegend	405208
Goat Anti-Rat	HRP	IHC	1/500	JacksonImmuno	112-035-003

Table S6 Plasmid Sequence

FstI1	ATGTGAAACGATGGCTGGCGCTCTCGCTGGTGACCATCGCCCTGGTCCACGG CGAGGAGGAACCTAGAAGCAAATCCAAGATCTGCGCCAATGTGTTTTGTGGAGC TGGCAGGGAATGTGCCGTACAGAGAAGGGGGAGCCCACGTGCCTCTGCATTG AGCAATGCAAACCTCACAAGAGGCCTGTGTGTGGCAGTAATGGCAAGACCTACC TCAACCACTGTGAACTTCATAGAGATGCCTGCCTCACTGGATCCAAGATCCAGGT TGATTATGATGGGCACTGCAAAGAAAAGAAGTCTGCGAGTCCATCTGCCAGCCC AGTTGTCTGCTATCAAGCTAACC GCGATGAGCTCCGACGGCGCCTCATCCAGTG GCTGGAAGCTGAGATCATTCCAGATGGCTGGTTCTCTAAAGGCAGTAACTACAGT GAGATCCTAGACAAGTACTTTAAGAGCTTTGATAATGGCGACTCTCACCTGGACT CCAGTGAATTCCTGAAATTCGTGGAGCAGAATGAAACAGCCATCAACATCACCAC TTATGCAGATCAGGAGAACAACAACTGCTCAGAAGCCTCTGTGTTGACGCCCTC ATTGAACTGTCTGATGAGAACGCTGACTGGAACTCAGCTTCCAAGAGTTCCTCA AGTGCCTCAACCCATCCTTCAACCCTCCTGAGAAGAAGTGTGCCCTGGAGGACG AAACCTATGCAGATGGAGCTGAGACTGAGGTGGACTGCAATCGCTGTGTCTGTT CCTGTGGCCACTGGGTCTGCACAGCAATGACCTGTGATGGAAAGAATCAGAAGG GGGTCCAGACCCACACAGAGGAGGAGAAGACAGGATATGTCCAGGAACTCCAG AAGCACCAGGGCACAGCAGAAAAGACCAAGAAGGTGAACACCAAGAGATCTAA
TBG	TGCATGTATAATTTCTACAGAACCTATTAGAAAGGATCACCCAGCCTCTGCTTTTG TACAACTTTCCCTTAAAAAACTGCCAATTCCACTGCTGTTTGGCCCAATAGTGAGA ACTTTTTCTGCTGCCTCTTGGTGCTTTTGCCTATGGCCCCTATTCTGCCTGCTG AAGACACTCTTGCCAGCATGGACTTAAACCCTCCAGCTCTGACAATCCTCTTTC TCTTTTGTTTTACATGAAGGGTCTGGCAGCCAAAGCAATCACTCAAAGTTCAAAC CTTATCATTTTTTGCTTTGTTCTCTTGGCCTTGGTTTTGTACATCAGCTTTGAAA TACCATCCCAGGGTTAATGCTGGGGTTAATTTATAACTAAGAGTGCTCTAGTTTTG CAATACAGGACATGCTATAA
Sfrp1	ATGGGCGTCGGGCGCAGCGCGCGGGGTCGCGGGCGGGGCCGCTCGGGAGTG CTGCTGGCGTTGGCCGCCGCTCTGCTGGCCGCGGGTTCGGCCAGCGAGTACGA CTACGTGAGCTTCCAGTCCGACATCGGCTCGTATCAGAGCGGGCGCTTCTACAC CAAGCCCCCGCAGTGCGTGGACATCCCGGTGGACCTGAGGCTGTGCCACAACG TGGGCTACAAGAAGATGGTGCTGCCAACCTGCTGGAGCACGAGACCATGGCA GAGGTGAAGCAGCAGGCCAGCAGCTGGGTGCCGCTGCTCAACAAGAACTGCCA CATGGGCACCCAGGTCTTCTCTGTTCTGCTCTTCCGCGCCCGTCTGTCTGGACCG GCCATCTACCCGTGTCGCTGGCTCTGCGAGGCCGTGCGGACTCGTGCGAGC CGGTCATGCAGTTCTTCGGCTTCTACTGGCCCGAGATGCTCAAATGTGACAAGTT CCCCGAGGGCGACGTCTGCATCGCCATGACCCCGCCCAATACCACGGAAGCCT CTAAGCCCCAAGGTACAACCGTGTGTCCTCCATGCGACAACGAGTTGAAGTCAG AGGCCATCATTGAACATCTCTGTGCAAGCGAGTTTGCCTGAGGATGAAAATCAA AGAAGTGAAGAAGGAAAACGGTGACAAGAAGATTGTCCCAAGAAGAAGAAACC CTTGAAGCTGGGGCCCATCAAGAAGAAGGAGCTGAAGCGGCTTGTGCTGTTCT GAAGAACGGTGCCGACTGTCCCTGCCACCAGCTGGACAACCTCAGCCACAACCT TCTCATCATGGGCCGCAAGGTGAAGAGCCAGTACCTGCTGACAGCCATTCACAA GTGGGACAAGAAAACAAGGAGTTCAAAAACCTCATGAAGAGAATGAAAACCCAC GAGTGTCCACCTTCCAGTCTGTTTTTAAGTGAAGCTTGTACAAGTAA