

Supplementary Video 1 | HpBD connecting to a preexisting hBD. 3D projection and surface rendering of a confocal z-stack from a hepatocyte-fate-traced P120 *Alb-Cre*^{+/-}; *Rbpj*^{ff}; *Hnf6*^{ff}; *R26ZG*^{+/+} mouse liver (n=2) showing hepatocyte fate tracing (GFP, green) and labeling of both peripheral and hilar cholangiocytes (wsCK, red) and specifically hilar cholangiocytes (DBA, blue).

Supplementary Video 2 | Clones of hepatocyte-derived peripheral cholangiocytes. 3D projection of a confocal z-stack from a P150 *Alb-Cre*^{+/-}; *Rbpj*^{ff}; *Hnf6*^{ff}; *R26R-Confetti*^{+/-} mouse liver (n=4) showing clonally labeled (yellow, cyan and red) peripheral cholangiocytes (wsCK, purple) and hepatocytes.

Supplementary Table 1 | RNA-seq analysis. Excel file showing differentially expressed genes, including analysis of pathway and biological process enrichment, between normal peripheral cholangiocytes (pC, n=3 mice), hepatocytes (H, n=3 mice) and hepatocyte-derived peripheral cholangiocytes (HpC, n=4 mice) as defined by fold-change > 3 for at least 1 of the 3 pairwise comparisons and FDR-corrected $P < 0.05$ (1-way ANOVA).

Supplementary Table 2 | Primary antibodies

Supplementary Table 3 | Secondary antibodies

Supplementary Table 4 | qPCR primers

Supplementary Figure 1 | Western blot source data

Supplementary Figure 2 | Hepatocyte sorting scheme

Supplementary Table 2 | Primary antibodies

Antigen	Dilution	Host	Supplier	Catalog #	Clone/Lot #
ACTIN	1:500	Mouse	Seven Hill Bioreagents	LMAB-C4	Clone C4
acTUB	1:100	Mouse	Abcam	ab24610	Clone 6-11B-1
CD11b-PE-Cy7	1:100	Rat	Tonbo Bio	60-0112	C0112012616602, C0112012616603
CD31-PE-Cy7	1:100	Rat	BioLegend	102417	B212261, B212262
CD45-PE-Cy7	1:100	Rat	Tonbo Bio	60-0451	C0451080615602, C0451080615603
CK7	1:25	Rabbit	Ventana	790-4462	Clone SP52
CK19	1:100	Rabbit	Abdomax	602-670	1101-766
CK19	1:50	Rat	DSHB	Troma-III-s	8G4, 48
DBA-biotin	1:100-300		Vector Labs	B-1035	ZA0417
DBA-FITC	1:80		Vector Labs	FL-1031-2	ZA0722
DESMIN	1:100	Rabbit	Thermo Fisher Scientific	RB9014P0	9014P1604F, 9014P1604G
EPCAM	1:100-500	Rat	BD Biosciences	552370	7089730
EPCAM-BV421	1:100	Rat	BioLegend	118225	B204922
F4/80	1:100	Rat	BioRad	MCA497GA	Clone A3-1, Batch 1014, 1610
GFP	1:200-500	Chicken	Abcam	ab13970	GR236651-10, GR236651-21
GFP	1:500	Rabbit	Abcam	ab6556	GR277888-1
HNF1	1:50	Rabbit	Santa Cruz	SC-8986	G3112
KI67	1:200	Rabbit	Thermo Fisher Scientific	RM-9106-S0	Clone SP6, Lot 9106S1607G
LYVE1	1:200	Rabbit	ReliaTech	103-PA50AG	1208R1, 1210R03
MUP	1:250	Goat	Cedarlane	GAM/MUP	5023
OC2-2F8	1:20	Rat	Craig Dorrell	⁵⁵	⁵⁵
OPN	1:250	Goat	R&D Systems	AF808	BDO0613101, BDO0617041
pSMAD3	1:400-500 (IF), 1:1,000 (WB)	Rabbit	Abcam	ab52903	GR128879-61
pSMAD3	1:400	Rabbit	Cell Signaling	9520	Clone C25A9
SOX9	1:500	Rabbit	MilliporeSigma	AB5535	2847051, 2975230
SSTR2	1:500	Rabbit	Bioss	bs-1138R	9A25V1
wsCK	1:200	Rabbit	Dako	Z0622	10088577

⁵⁵ Huch, M. *et al.* In vitro expansion of single Lgr5⁺ liver stem cells induced by Wnt-driven regeneration. *Nature* **494**, 247-250 (2013).

Supplementary Table 3 | Secondary antibodies

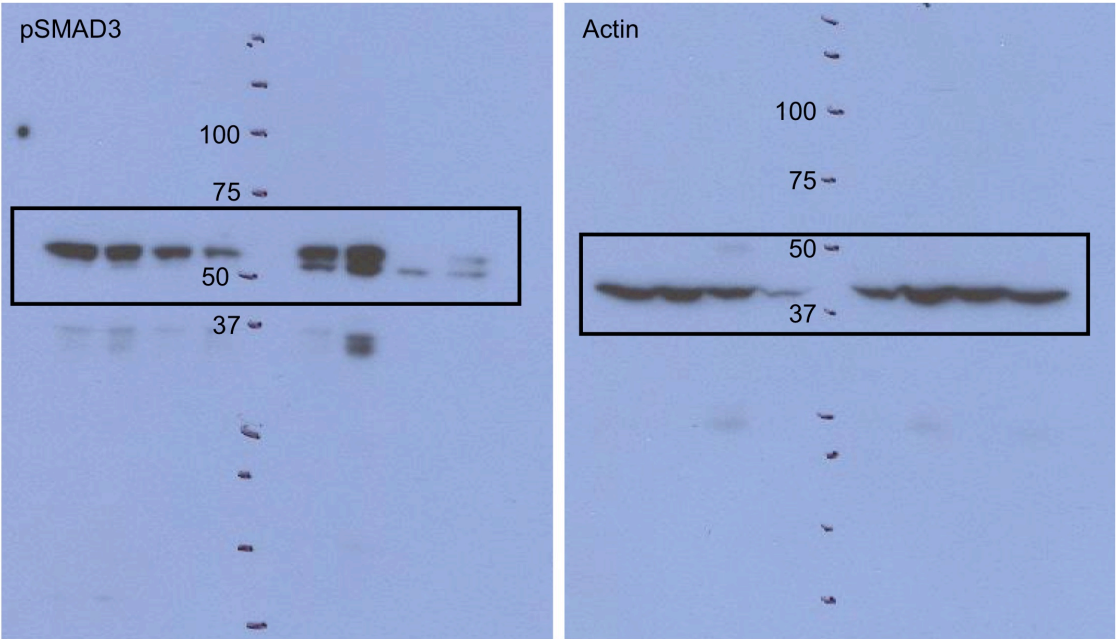
Reactivity	Species	Fluorochrome	Dilution	Supplier	Catalog #	Lot #
Chicken	Donkey	Alexa Fluor 488	1:500	Jackson Immuno	703-545-155	116967, 113085
Goat	Donkey	Alexa Fluor 488	1:500	Thermo Fisher Scientific	A11055	1869589
Goat	Donkey	Alexa Fluor 594	1:500	Jackson Immuno	705-585-147	106994
Goat	Donkey	Alexa Fluor 594	1:500	Thermo Fisher Scientific	A11058	1445994
Goat	Donkey	Alexa Fluor 647	1:200	Thermo Fisher Scientific	A21447	1841382, 1661244
Goat	Donkey	Biotin	1:1,000	Jackson Immuno	705-065-003	77098
Goat	Donkey	Cy3	1:500	Jackson Immuno	705-165-147	114067
Mouse	Horse	HRP	1:1,000	Cell Signaling	7076	27
Rabbit	Goat	Alexa Fluor 488	1:300	Jackson Immuno	111-545-144	105878
Rabbit	Donkey	Alexa Fluor 555	1:200-500	Thermo Fisher Scientific	A31572	1917920
Rabbit	Donkey	Alexa Fluor 647	1:200	Jackson Immuno	711-605-152	118217
Rabbit	Donkey	Biotin	1:1,000	Jackson Immuno	711-065-152	128874
Rabbit	Donkey	Cy3	1:500	Jackson Immuno	711-165-152	117211, 105494
Rabbit	Goat	HRP	1:1,000	Cell Signaling	7074	26
Rabbit	Goat	HRP	1:500	Jackson Immuno	111-035-144	91036
Rat	Donkey	Alexa Fluor 488	1:500	Thermo Fisher Scientific	A21208	1789917
Rat	Donkey	Alexa Fluor 647	1:200	Jackson Immuno	712-605-153	123845, 110001, 127806
Rat	Donkey	Cy2	1:300	Jackson Immuno	712-225-150	102982
Rat	Goat	PE	1:200	BD Biosciences	550767	5107876
Streptavidin		Alexa Fluor 594	1:300	Thermo Fisher Scientific	S-11227	1704463
Streptavidin		Cy2	1:250	Jackson Immuno	016-220-084	84799
Streptavidin		Cy3	1:300	Jackson Immuno	016-160-084	125000
Streptavidin		Dylight 649	1:300	Vector Labs	SA-5649	Y0718,

						Z0320
TSA Biotin Kit Streptavidin	HRP	1:100	Perkin Elmer	NEL700 A001KT	2075089	
Tyramide Plus	Cy3	1:300	Perkin Elmer	NEL7440 01KT	2310803	
Vectastain Elite ABC Reagent			Vector Labs	PK-7100	ZD0404	

Supplementary Table 4 | qPCR primers

Target	Forward primer (5'-3')	Reverse primer (5'-3')
<i>Alb</i>	gcagatgacagggcggaacttg	aaaatcagcagcaatggcagge
<i>Epcam</i>	gcggctcagagagactgt	ccaagcatttagaccagttt
<i>Fah</i>	accataggagactacacggact	accacaatggaggaagctcg
<i>Gapdh</i>	catggccttccgtgttct	gcggcacgtcagatcca
<i>Hnf4a</i>	catcaacgaccggcagtac	gcagcaggtgtcaatcttg
<i>Krt19</i>	agagacggaggcccgttat	ctggttctggcgctctatgtc
<i>Rbpj</i> (floxed)	gagatagacctggttgttg	ccactgttgtaactggcgt
<i>Rbpj</i> (reference)	gccactccatgtccaaaaga	gcaagttatagctcagaacagcaa
<i>Sox9</i>	agaccagtaccgcactctgcac	tcttctcgcctctcgttcagca
<i>Spp</i>	actgccaatctcatggctgt	actgccaatctcatggctgt
<i>Tr</i>	tggacaccaatcgtactgg	aattctgggggttctgac

Supplementary Figure 1 | Western blot source data



Supplementary Figure 2 | Hepatocyte sorting scheme

