Fig. S1

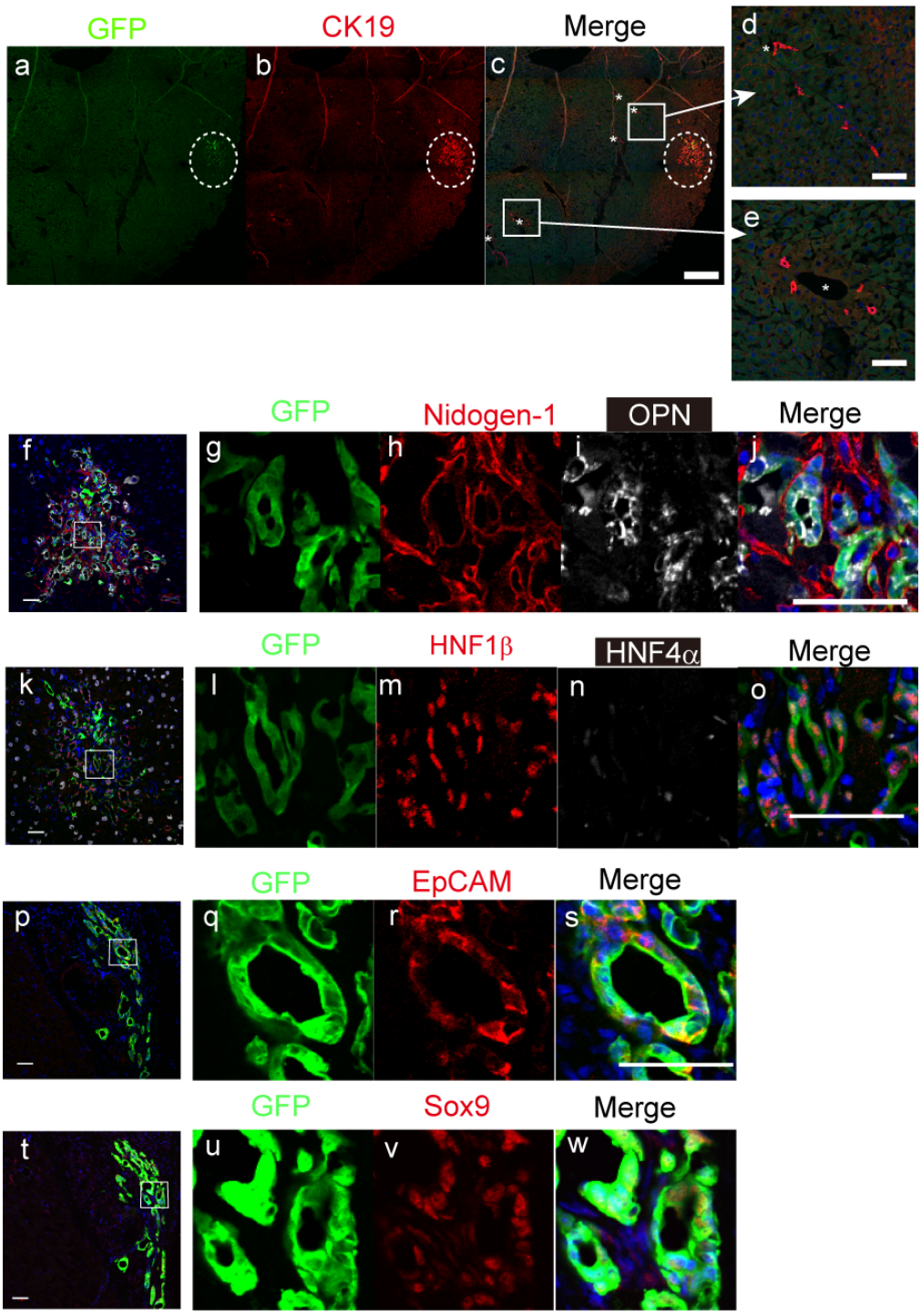


**Fig. S1. Adult clone 1 differentiates to cholangiocyte-like cells and forms ductular structures in the recipient liver.** GFP$^+$ donor cells form ductular structures, surrounded by dotted circles, apart from portal veins (asterisks). Boxes in panel c are enlarged in panels d and e. Bars in panel c and d&e represent 500 and 100 μm, respectively. GFP$^+$ donor cells express cholangiocyte markers including OPN, HNF1β, EpCAM and Sox9 but not a hepatocyte marker HNF4α. GFP$^+$ ductular structures are associated with the ECM layer recognized with Nidogen-1. Bars in panels a, f, p, and t represent 100 μm. Bars in panels e, j, o, and s represent 50 μm.

Fig. S2

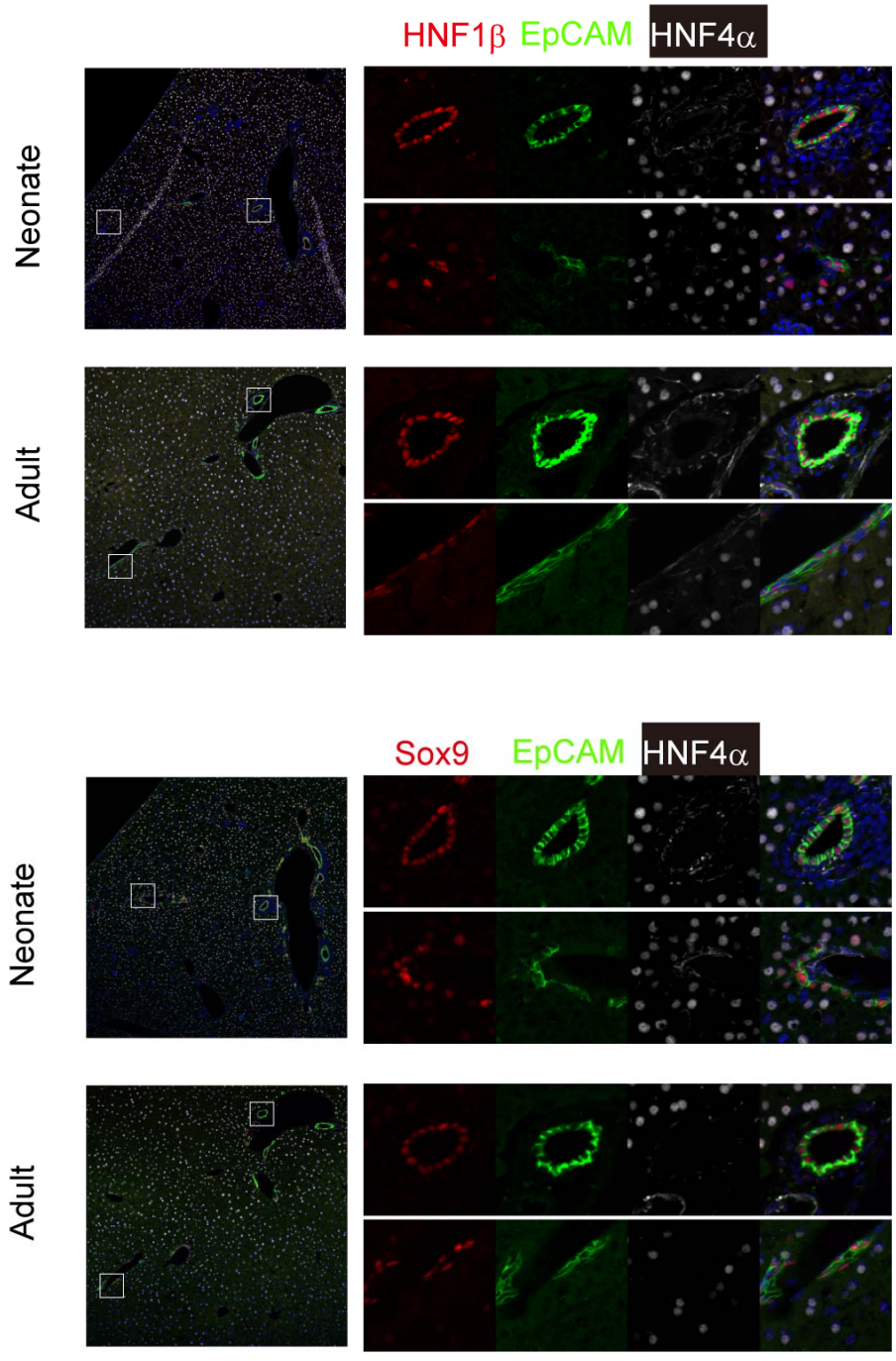


**Fig. S2. Neonatal and adult EpCAM$^{+}$ cells are positive for HNF1β and Sox9.**

Fig. S3

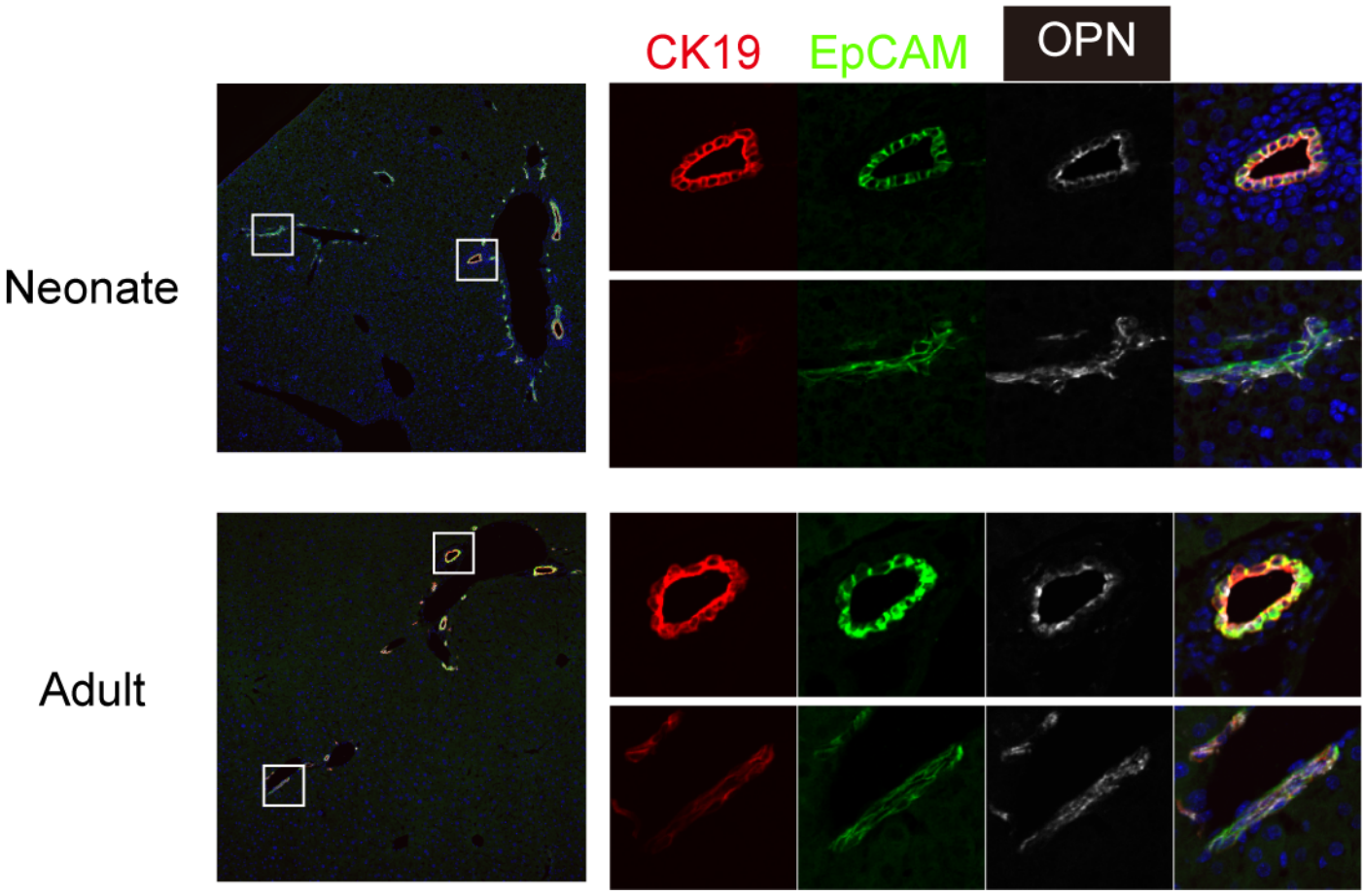


**Fig. S3. Neonatal small ductules in the periphery are negative for CK19.**

Fig. S4

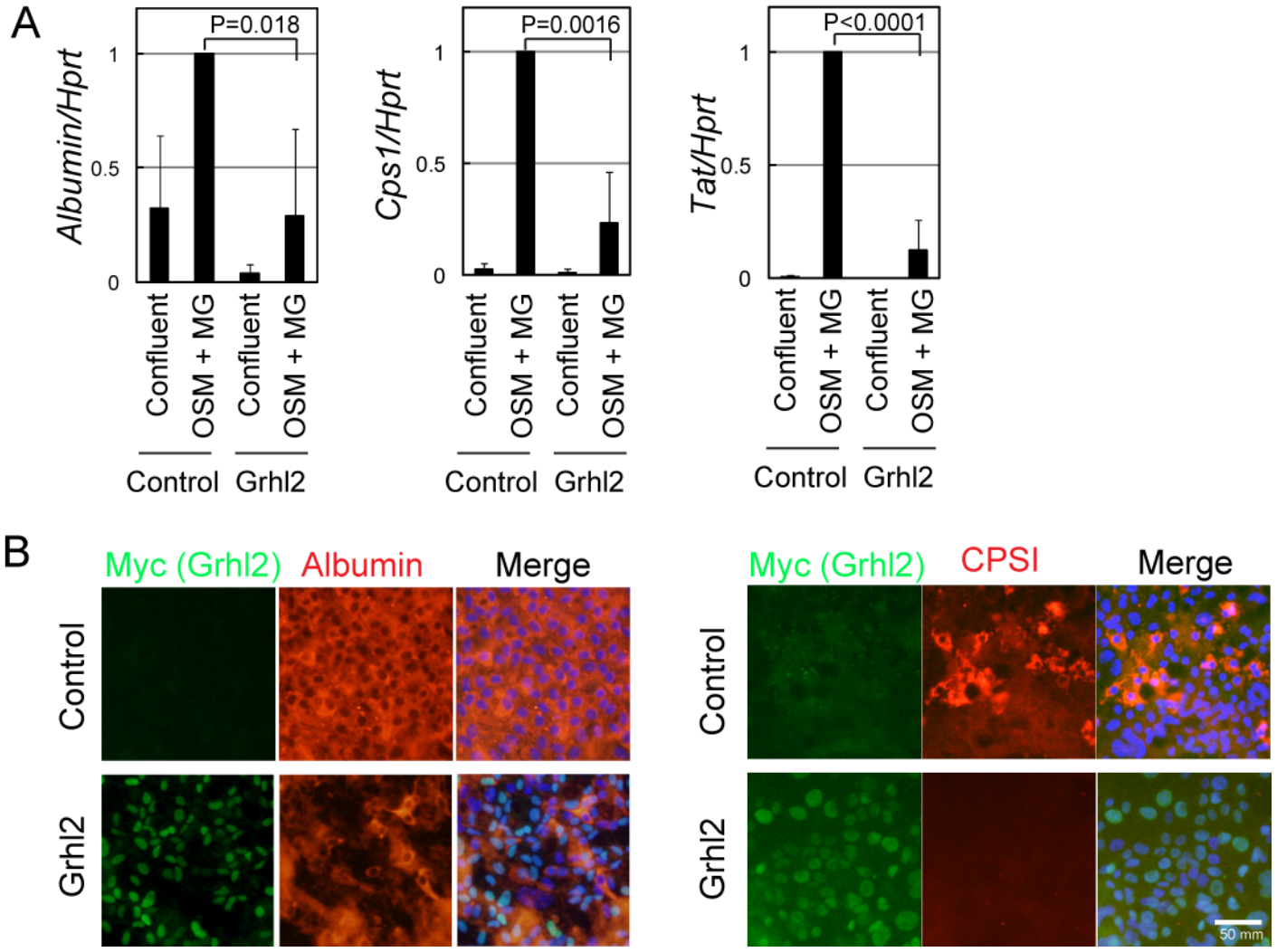


**Fig. S4. Grhl2 inhibits hepatocytic differentiation of liver progenitors.** HPPL, bipotential liver progenitor cell line, was introduced with Grhl2 by using a retrovirus vector. Hepatocytic differentiation was induced by oncostatin M (OSM) and Matrigel (MG). Grhl2 inhibits induction of *Albumin*, *Cps1*, and *Tat* (A) as well as ALBUMIN and CPSI (B). A bar represents 50 μm.

Fig. S5.

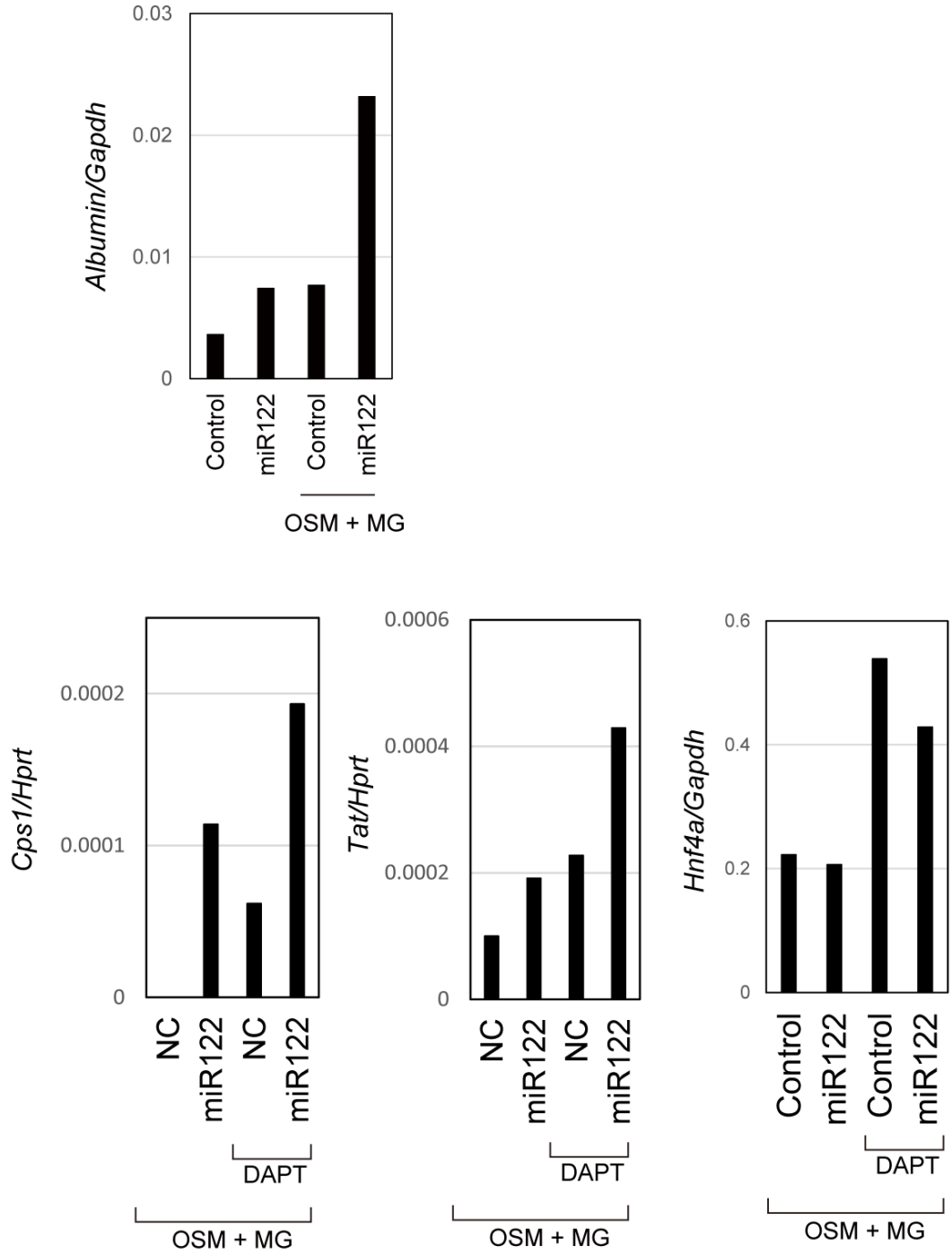


**Fig. S5. miR122 promotes hepatocytic differentiation of adult EpCAM$^+$ cells.** miR122 slightly upregulates hepatocyte markers. EpCAM$^+$ cells isolated from adult livers were cultured on gelatin coated dishes. They were transfected with miR122 and then treated with OSM and MG. For inducing *Cps1* and *Tat*, EpCAM$^+$ cells were also treated with DAPT, a γ-secretase inhibitor, and potential inhibitor of the Notch signaling pathway.

Fig. S6

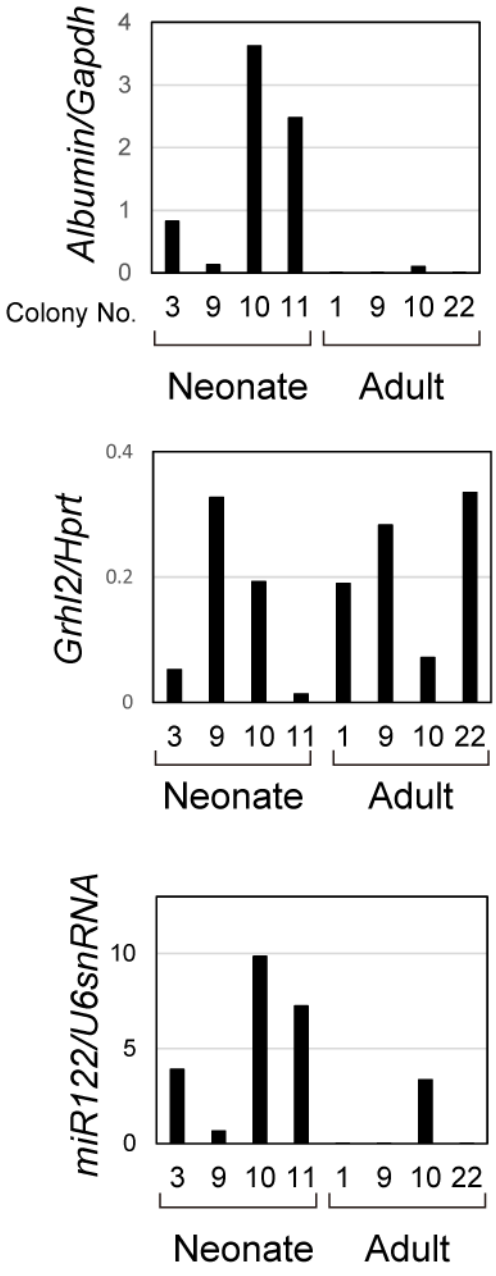


**Fig. S6. Expression of Albumin, Grhl2, and miR122 in colonies derived from neonatal and adult EpCAM$^+$ cells.**

**Table S1. Primary Antibodies**

| Antibody | Company | Cat. Number | Host animal | Method | Dilution |
|---|---|---|---|---|---|
| ALB | Bethyl laboratory | A90-234A | goat | IF | 1:1000 |
| CD16/32 | BD Pharmingen | 553141 | rat | FACS | 1:1000 |
| CD31 | Biolegend | 102501 | rat | IF | 1:1000 |
| CD31 (APC-conjugated) | BD Pharmingen | 551262 | rat | FACS | 1:1000 |
| CD45 (APC-conjugated) | BD Pharmingen | 559864 | rat | FACS | 1:1000 |
| C/EBPα | SantaCruz Biotechnology Inc. | sc-61 | rabbit | IF | 1:200 |
| CPSI | Santa Cruz Biotechnology Inc. | sc-10516 | goat | IF | 1:200 |
| Cytokeratin 19 | Tanimizu et al. 2003 | | rabbit | IF | 1:2000 |
| EpCAM | BD Pharmingen | 552370 | rat | IF | 1:500 |
| EpCAM (FITC or APC-conjugated) | Biolegend | 118208 118213 | rat | FACS | 1:1000 |
| GFP | MBL | 598 | rabbit | IF | 1:1000 |
| GFP | Nakarai Tesk | GF090R | rat | IF | 1:1000 |
| GRHL2 | Sigma-Aldrich | HPA004820 | rabbit | IF | 1:1000 |
| HNF1β | SantaCruz Biotechnology Inc. | sc-22840 | rabbit | IF | 1:200 |
| HNF4α | SantaCruz Biotechnology Inc. | sc-8987 | rabbit | IF | 1:200 |
| HNF4α | SantaCruz Biotechnology Inc. | sc-6557 | goat | IF | 1:200 |
| Myc-tag | Millipore | 05-074 | mouse | IF | 1:1000 |
| Nidogen-1 | Millipore | MAB1946 | rat | IF | 1:1000 |
| Osteopontin | R&D systems | AF808 | goat | IF | 1:600 |
| SOX9 | Millipore | AB5535 | rabbit | IF | 1:3000 |
| TER119 (APC/Cy7-conjugated) | Biolegend | 116223 | rat | FACS | 1:1000 |

**Table S2. Primers used for PCR**

| Gene name | | Sequence |
|---|---|---|
| Albumin | Sense | 5′-GAA AGC CCA CTG TCT TAG TG-3′ |
| | Antisense | 5′-GGG TGT AGC GAA CTA GAA TG-3′ |
| Cyp1a2 | Sense | 5′-CCCTGCCCTTCAGTGGTACA-3′ |
| | Antisense | 5′-AAGCTGTAGAGGTCTGGTCG-3′ |
| Cyp2b10 | Sense | 5′-GTTGAGCCAACCTTCAAGGAA-3′ |
| | Antisense | 5′-AAGAGCTCAAACATCTGGCTG-3′ |
| Cyp2d10 | Sense | 5′-GATCCCAAGGTGTGGTCCTT-3′ |
| | Antisense | 5′-GCAGGAGTATGGGGAACATA-3′ |
| CPSI | Sense | 5′-ACT GAG AGA TGC TGA CCC TA-3′ |
| | Antisense | 5′-CCT GGA AAT TGG TGA GGA GA-3′ |
| GAPDH | Sense | 5′-ACC ACA GTC CAT GCC ATC AC-3′ |
| | Antisense | 5′-TCC ACC ACC CTG TTG CTG TA-3′ |
| G6pc | Sense | 5’-CCA ACG TAT GGA TTC CGG TG-3’ |
| | Antisense | 5’-TCC CAG GTT TTT GAA GAG GC-3’ |
| GFP | Sense | 5′-CTGAAGTTCATCTGCACCAC-3′ |
| | Antisense | 5′-TTGAAGTTCACCTTGATGCC-3′ |
| Pepck | Sense | TTGATGCCCAAGGCAACTTA |
| | Antisense | ACGGCCACCAAAGATGATAC |
| TAT | Sense | 5′-GAG GAG TGT GAC AAA TAG GC-3′ |
| | Antisense | 5′-AGA GGA CAC TCC TGT GTC AG-3′ |
| Tdo2 | Sense | 5′-TGAGTAAAGGTGAACGACGAC-3′ |
| | Antisense | 5′-AGCCGACTGAGAATCCTGTA-3′ |

**Table S3.**

Click here to Download Table S3