Supplementary Figure Legends:

- Sup Fig. 1: Lineage tracing demonstrates that HCA originates from AAV-Cre-marked hepatocytes when carcinogenesis is induced by DEN and CCI₄ treatment. Serial sections of a representative HCA stained for H&E, Opn, AFP, Sox9, YFP/EpCAM, Yap1, and CK19. Dotted lines indicate tumor margins. Box indicates the area of shown in the high-magnification images.
- Sup Fig. 2: Lineage tracing demonstrates that HCA originates from AAV-Cre-marked hepatocytes when carcinogenesis is induced by DEN and TCPOBOP treatment. Serial sections of a representative HCA stained for H&E, Opn, AFP, YFP/Sox9, YFP/EpCAM, Yap1, and CK19 are shown. Dotted lines indicate the tumor margins. Box indicates the area of shown in the high-magnification images.
- Sup Fig. 3: *Foxl1-Cre*-marked HPCs are not tumor-initiating cells in the **DEN/TCPOBOP** hepatotoxin–induced HCA. Serial sections of a representative HCA stained for H&E, Opn, AFP, YFP/Sox9, YFP/EpCAM, Yap1, and CK19. Dotted lines indicate tumor margins. Box indicates the area of shown in the high-magnification images.





