Figure EV1. Molecular characterization of embryonal and fetal-like HB cells.

A Schematic representation of the primers used to amplify the genomic region spanning exon 3 to exon 4 of the CTNNB1 gene (left panel). Genomic DNA was isolated from the indicated cells lines and amplified by PCR. A PCR product of 640 bp was obtained from the full-length CTNNB1 gene. The appearance of a 124-bp band in HepG2 and Hep293TT indicated a heterozygous deletion of CTNNB1 gene (right panel).

B Real-time PCR analysis for the expression of LIN28A in the indicated cell lines. Data show means ± s.d. (n = 3). P-values were determined by Mann–Whitney test.

C Immunocytochemistry of Lin28A on the indicated cell lines. Dashed squares highlight a zoom on a cell. Scale bar: 20 μm.

D Expression analysis (RPKM) of the fetal marker claudin-1 (CLDN1) in the HB cell lines.
**Figure EV2.** Representative histological and immunohistochemistry findings.

A–F GLUT3 reactivity was observed in the embryonal and squamous components only. Standard HPS stain shows squamous differentiation foci (A), confirmed by a CK5/6 immunostain (B and E). In the two tumors shown (C and F), focal mild 1+ cytoplasmic, and moderate 2+ membranous GLUT3 reactivity is seen. The embryonal component of the second tumor (D–F) shows a serpiginous architecture, with foci of tumor necrosis (star). Scale bars = 100 μm, except for (A) (scale bar = 50 μm).

G Relative expression of GLUT3, LDHB, and HK1 in Huh-6 cells treated or not for 24 h with cisplatin (cis). Data show means ± s.d. (n = 4). P-values were determined by Mann–Whitney test.

**Figure EV3.** α-Catenin interacts with short but not long deletion HB mutant β-catenin.

A Ribbon representation of the modeled 3D structure of human β-catenin in complex with human α-catenin. Residues that are absent in HepG2 and Hep293TT are in dark blue, and are responsible for binding to α-catenin. The experimental binding position of BCL9 on β-catenin is shown in pink for information. However, this model does not presume that BCL9 and α-catenin are able to bind concomitantly to β-catenin.

B Co-immunoprecipitation using protein extracts from 293T cells transfected with the indicated mutant forms of VSV-β-catenin and FLAG-α-catenin constructs or empty-FLAG as negative control. Proteins were immunoprecipitated using anti-FLAG antibody.

C Protein extracts from the indicated cell lines were used for endogenous α-catenin or control IgG immunoprecipitation, followed by Western blot using the indicated antibodies. The arrowheads indicate the position of the full-length or deleted (Δex3-4) forms of β-catenin. TI, total input; IP, immunoprecipitation.

Source data are available online for this figure.
Figure EV3.