



S2 Fig. Tyr metabolism in CD13⁺ cancer stem cells (CSCs) feeds mitochondrial acetyl-CoA into the TCA cycle. (A) FAH expression in HepG2 and HuH7-derived CD13⁺ cells transfected with control siRNA or FAH siRNA. (B) Relative metabolite abundance in HepG2 and HuH7-derived CD13⁺ cells grown in ¹³C-tyrosine upon FAH knockdown. Data are presented as the total metabolite pool (encompassing both metabolite derived from tyrosine and that not tyrosine-derived) and the ¹³C-labeled and tyrosine-derived metabolite pool. (C) Oxygen consumption of HepG2 and HuH7-derived CD13⁺ cells cultured in complete medium or medium deprived of essential nutrients (glucose, amino acids, and fatty acids) for 24 hours. (D) Homogenisate production in HepG2 and HuH7-derived CD13⁺ fraction treated with or without nitisinone (100 nM) for

6 hours. (E) Extracellular acidification rate (ECAR, glycolytic rate) is plotted as a parameter of time in HepG2-derived CD13⁺ cells in the absence and presence of 100 nM nitisinone. (F) ATP levels in HepG2 and HuH7-derived CD13⁻ cells treated with or without 100 nM nitisinone for 6 hours. Values shown are mean± standard deviation. p-values were calculated by two-tailed t test unless otherwise indicated. **p < 0.05.