

Supplementary Material

- **1** Supplementary Figures and Tables
- 1.1 Supplementary Figures

Supplementary Figure 1. Distribution of spontaneous and PhIP-induced mutations in the coding region of the *gpt* gene in hepatic organoids.

Hot Spot Mapping

- 1 ATGAGCGAAA AATACATCGT CACCTGGGAC ATGTTGCAGA TCCATGCACG TAAACTCGCA AGCCGACTGA 70
- 71 TGCCTTCTGA ACAATGGAAA GGCATTATTG CCGTAAGCCG TGGCGGTCTG GTACCGGGTG CGTTACTGGC 140
- 141 GCGTGAACTG GGTATTCGTC ATGTCGATAC CGTTTGTATT TCCAGCTACG ATCACGACAA CCAGCGCGAG 210
- 211 CTTAAAGTGC TGAAACGCGC AGAAGGCGAT GGCGAAGGCT TCATCGTTAT TGATGACCTG GTGGATACCG 280
- 281 GTGGTACTGC GGTTGCGATT CGTGAAATGT ATCCAAAAGC GCACTTTGTC ACCATCTTCG CAAAACCGGC 350
- 351 TGGTCGTCCG CTGGTTGATG ACTATGTTGT TGATATCCCG CAAGATACCT GGATTGAACA GCCGTGGGAT 420
- 421 ATGGGCGTCG TATTCGTCCC GCCAATCTCC GGTCGCTAA

 \triangle Control \bigcirc PhIP pprox deletion

ΔX1 ΔX5 •X1 OX5 •• A •• T •• C •• G * Control *PhIP



Supplementary Figure 2. Relative expression levels of *CYP2E1* in the lung-derived organoids in the absence of the S9 mix. Real-time PCR analysis is used to determine the mRNA expression levels of *CYP2E1*. In untreated controls, values are set at 1.0, and relative levels are expressed as mean \pm SE (n = 6). *GAPDH* mRNA levels are used to normalize data. Data significantly different from the AA(-)/S9(+) group is indicated as *p < 0.05, **p < 0.01.

