Supplementary Material

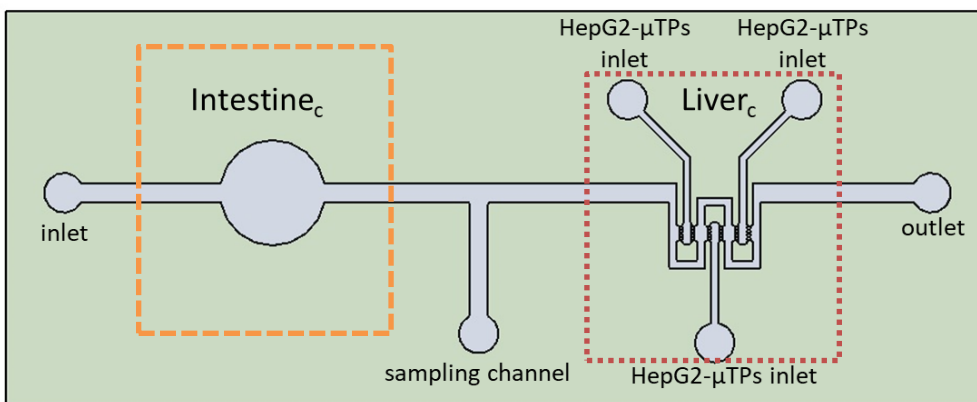**Materials and methods:**

Figure. S1

InLiver-OC

Figure. S1 Schematic representation of the InLiver-OC

Top view of the InLiver biochip with Intestine compartment (Intestine$_c$, orange dotted line) and Liver compartment (Liver$_c$, red dotted line); culture medium inlet was indicated as inlet; the HepG2-µTPs inlet showed the HepG2-µTPs loading points; sampling channel and outlet were showed as the collection site between the Intestine$_c$ and Liver$_c$ and downstream to the outlet Liver$_c$, respectively.

Figure. S2 Circuit for TEER measurement
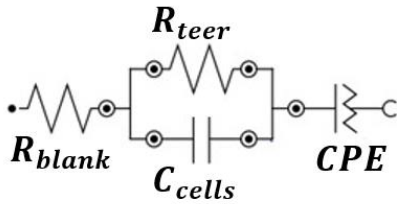

Figure. S2 Simplified equivalent circuit used to fit and analyze the impedance spectrum of cellular systems. R_teer includes resistive contribution of both the cell membrane (R_cells) and tight junction (R_tight). However, since these equivalents elements are in parallel, and since R_cells >> R_(tight), R_teer= R_tight // R_cells ≈ R_tight.

Results

Figure. S3 Growth curve
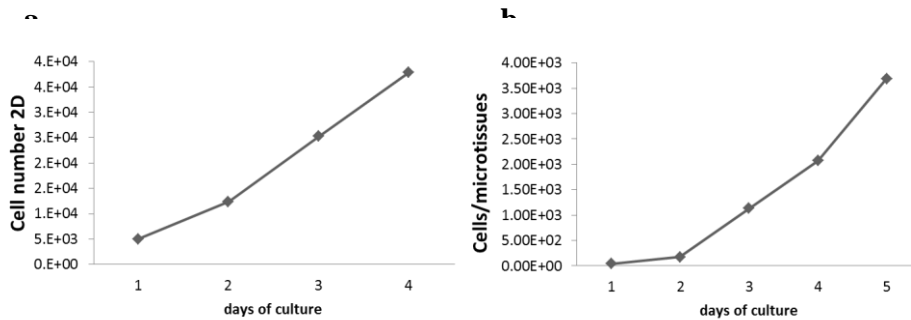
Figure. S3 The graphs indicated the cell number growth during the culture time in 2D (a) and 3D configurations (b).

Figure. S4 Regression line of Et-OH Dose-response

Figure caption legend: —●— 3D HepG2-mTPs

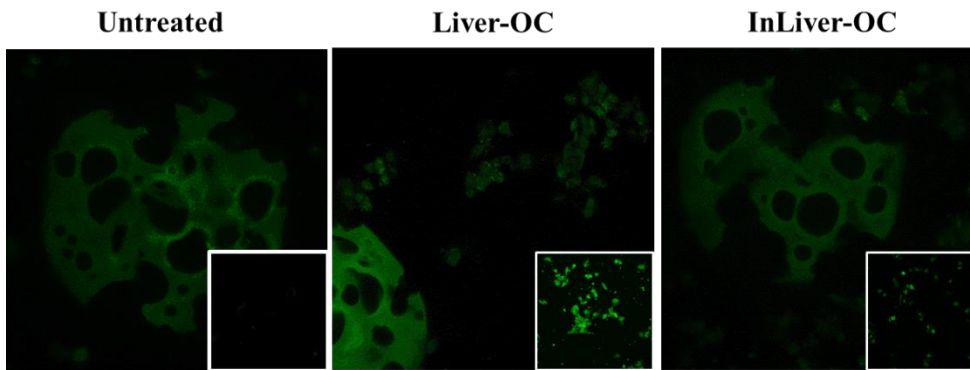$$y = -10.433x + 114.58$$
$$R^2 = 0.9694$$
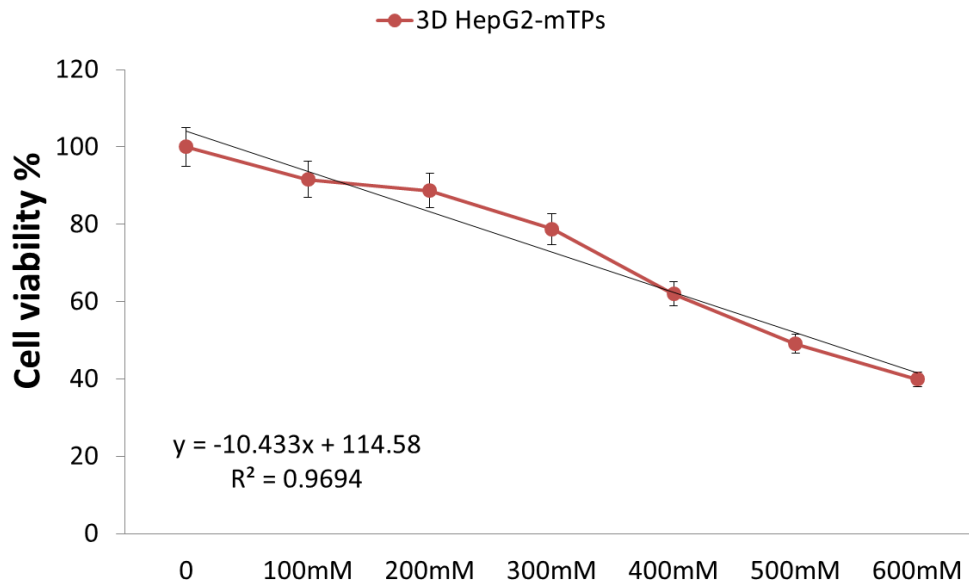
Figure. S4 The graph indicates the linear regression line of the Et-OH dose-response curve

Figure. S5 Oil red staining on chip
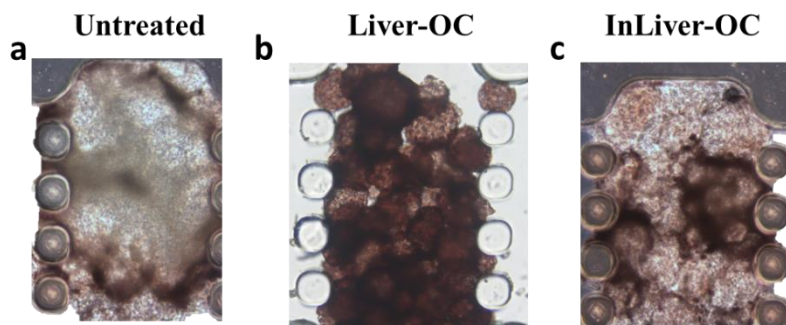
Figure. S5 Oil red staining was performed directly into the microfluidic device in order to evaluate the lipid accumulation in different configurations: untreated (a), Liver-OC (b), InLiver-OC (c).

Figure. S6 ROS expression

Figure. S6 Representative immunofluorescence images and high magnification insets of the HepG2-µTPs highlight a high production of ROS stained in green in Liver-OC (b) compared to InLiver-OC (c). Untreated samples revealed no signal for ROS (a). Scale bar 75 µm.

Figure. S7 Biomass quantification
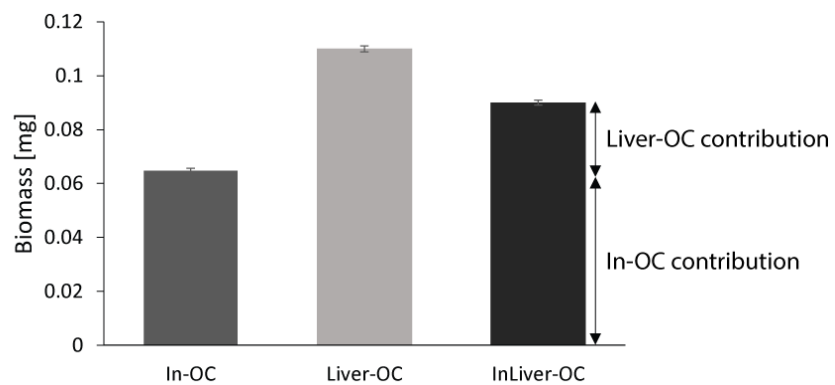
Figure. S7 The graph indicated the biomass quantification of In-OC, Liver-OC and InLiver-OC_supernatants after Et-Oh treatment.