Supplement Figures and Tables

Fig S1. CAD Schematics and Measurements of the 6-Unit Bioreactor Manifold. (A) Design of the bottom part of the manifold. Manifold measures 128.5 × 87 mm fitting standard multi-well plate holders, allowing simple integration to standard microscope stages and systems. Manifold is designed to support up to 6 individual bioreactors in standard 6-well plate configuration (B) CAD of the top part of bioreactor manifold, each unit is designed to fit a slot on the bottom plate while being individually perfused. Both CNC machined (***methods***) parts are designed to be fitted with a 0.13-0.16 mm thick cover glass and a 20G blunt end needle, bonded with transparent 2-part biocompatible epoxy glue. The needle connects to disposable low-adhesion 0.03" Tygon tubing. (C) CAD image of needle placements into the top unit. (D) Photo of the assembled unit.

Fig S2. CAD Schematic and Specification of Microfluidic Biosensor Array. (A) CAD of the cover and housing unit for the microfluidic biosensor array. (B) Technical data and measurements of the microfluidic biosensor array and housing. (C) Photo of the array and its connections. (D) Photo and technical specification of the complete proceeding unit including the on-chip potentiostat and sensors.

Fig S3. The Metabolic Flux Balance Analysis Model. (A) Representative curves of oxygen, glucose, and lactate fluxes during continuous perfusion with untreated medium. Oxygen uptake (black), Glucose uptake (red), and lactate production (green). (B) Representative changes in lactate over glucose ratio following exposure to untreated medium (blue line). (C) Representative relative glucose utilization, shown as pie chart. (D) Numbered metabolic flux map correlating to **Table S1**. Pathways are color coded for visual effect. Model is described in detail in Levy et al. Nature Chemical Biology 2016 [46].

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Table S1. Metabolic Flux Balance Analysis for Primary Human Hepatocytes (PHH) and HepG2/C3A Cells. Primary human hepatocytes were cultured as previously described [46]. Briefly, fluxes were calculated following metabolic stabilization of both cultures (*i.e. steady state*) and measured over 48 hours. Values are shown as μM/day/10^6cells. Flux balance analysis shows that glucose utilization fluxes are 1 to 3 orders of magnitude higher the amino acid and lipid metabolism. Glutamine uptake and other complementary processes play only a minor role in establishing central carbon metabolism behavior in our *in vitro* system. Similar trends are seen regarding glucose utilization in primary human hepatocytes.

Table S2. List of Primers used for mRNA Quantification.