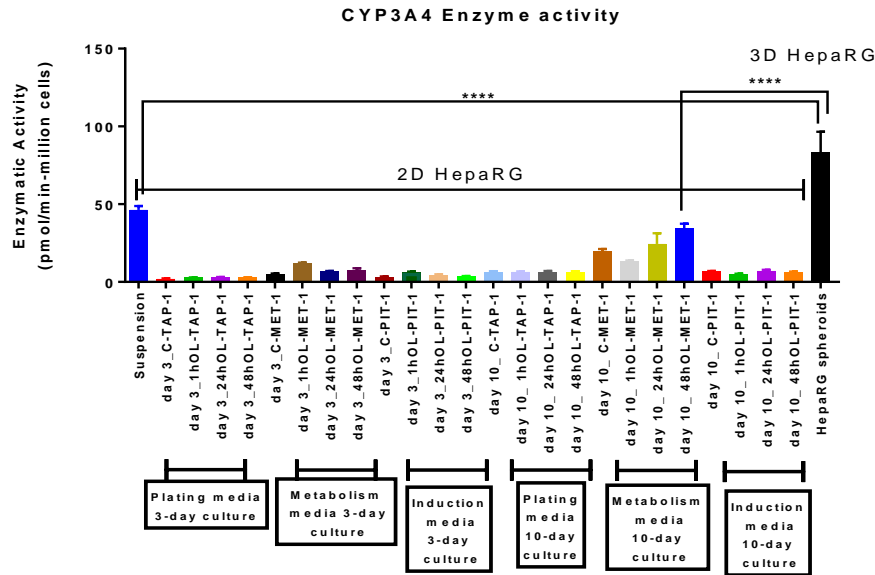
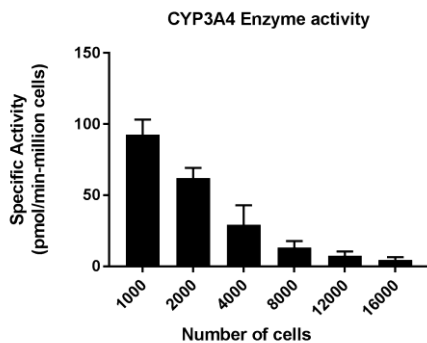


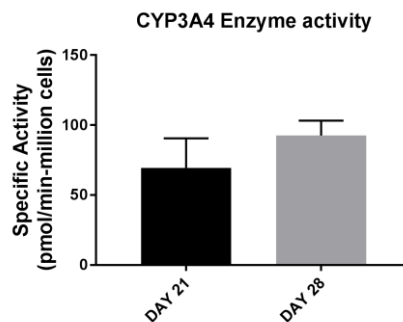
A



B



C



Supplementary S2: Liquid chromatography-mass spectrometry analysis of major CYP450 enzyme CYP3A4 (Formation of 1-hydromidazolam from midazolam) in 2D and 3D HepaRG cells (A). HepaRG cells in 2D (100,000 cells/ well) cultured in different media types – DMSO containing (M1, M2) and non-DMSO (M3) with matrigel overlay conditions (OL) at different time points. HepaRG spheroids (1,000 cells per well). Data is representative of 3 independent experiments. Rate of formation of 1-hydroxymidazolam (CYP3A4) from midazolam in 3D spheroid culture (B), data mean of two independent experiments (\pm SD) from 14-day cultured HepaRG spheroids with various seeding densities. CYP450 enzyme CYP3A4 (Formation of 1-hydromidazolam from midazolam) of HepaRG spheroids cultures at day 21 and day 28 (C), data mean of two independent experiments \pm SD.