

Supplementary file 1

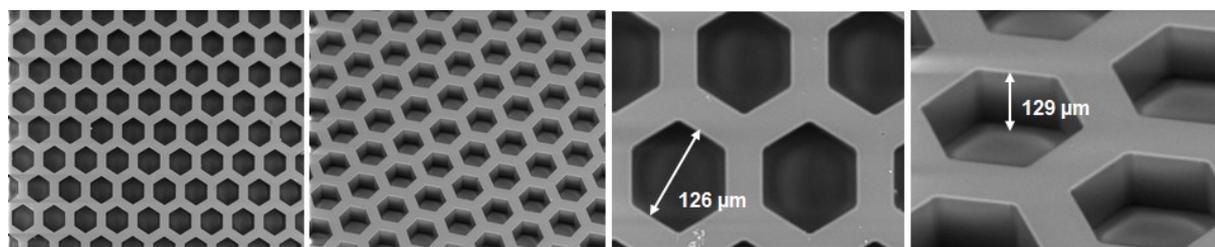


Fig.S1. Design and structure of honeycomb used for hiPSC derived β-cells spheroids formation and cultures. View from Scanning Electronic Microscope (SEM).

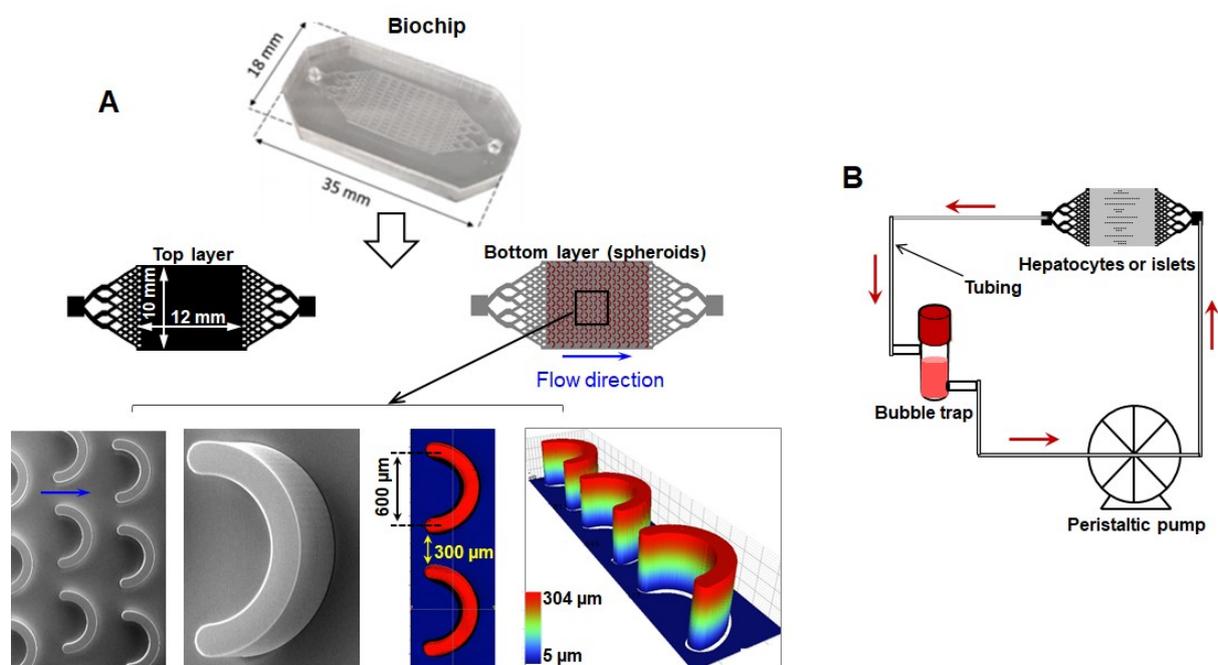


Fig.S2. (A) Design and dimensions of biochips used for hiPSC derived β-cells spheroids cultures and (B) setup used for dynamic culture in biochips.

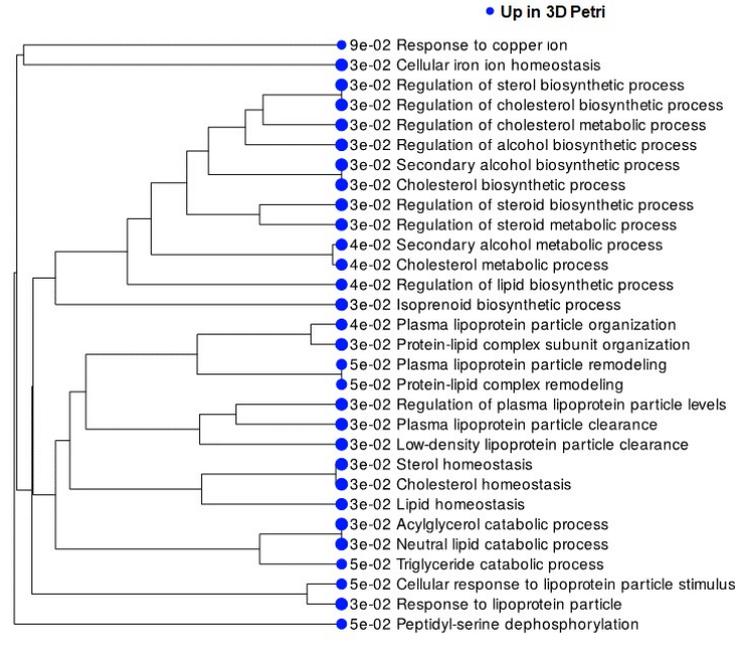


Fig.S3. GO_biological_process pathways identified by Gene Set Enrichment Analysis (GSEA) method (3D petri vs. iPSCs stage 1 comparison).

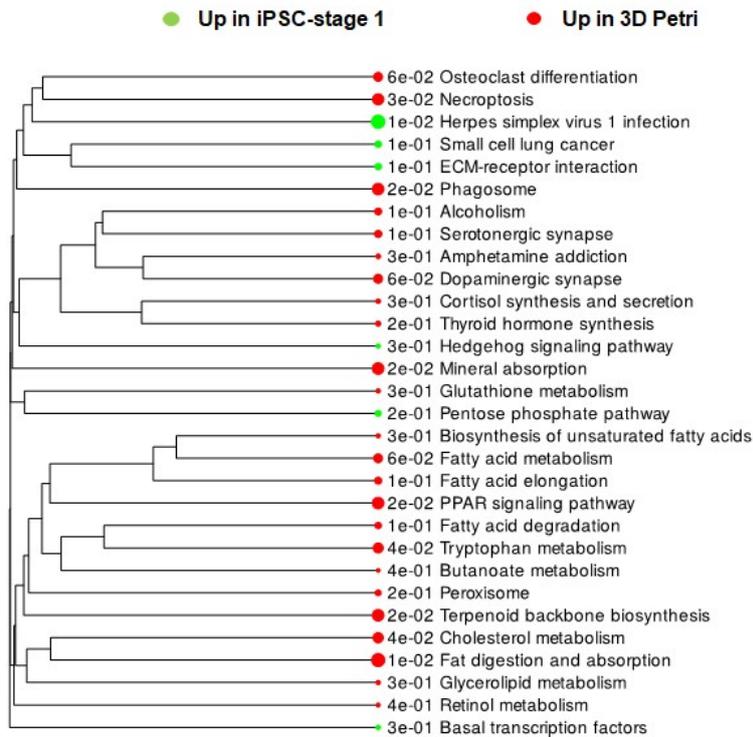


Fig.S4. GO_KEGG pathways identified by Gene Set Enrichment Analysis (GSEA) method (3D petri vs. iPSCs stage 1 comparison).

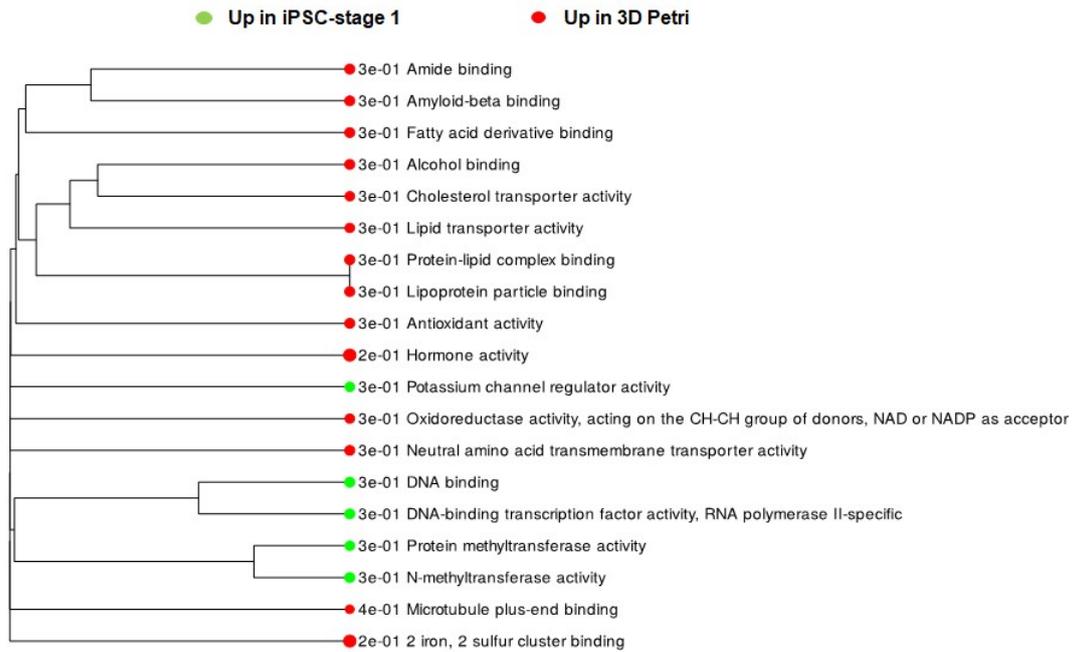


Fig.S5. GO_molecular_functions identified by Gene Set Enrichment Analysis (GSEA) method (3D petri vs. iPSCs stage 1 comparison).

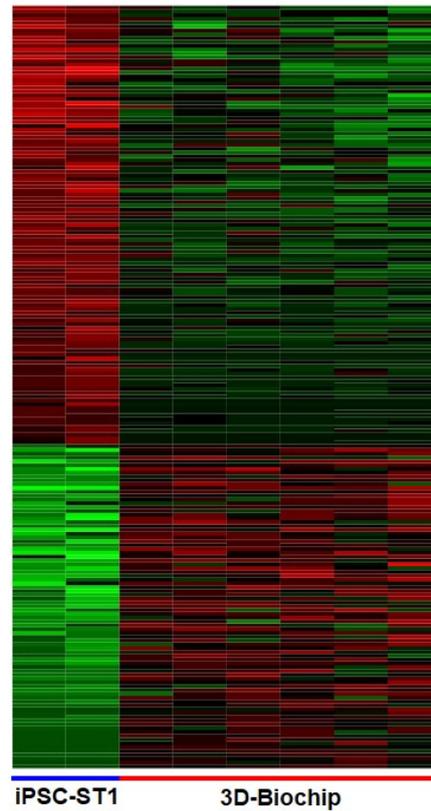


Fig.S6. Heatmap illustrating the transcriptomic separation (418 genes, 185 upregulated in biochip; 233 upregulated in stage 1 iPSC) of the 3D Biochip (spheroids at the end of the cultures) and stage 1 iPSC conditions (red upregulated, green downregulated). The list of genes is given in Supplementary file 5. Among them TTR, GCG, IAPP, CGA, CHGB, HIF3A, ACAT2, HMGCS1, PLIN2, APOB, SQLE were upregulated in 3D biochips.

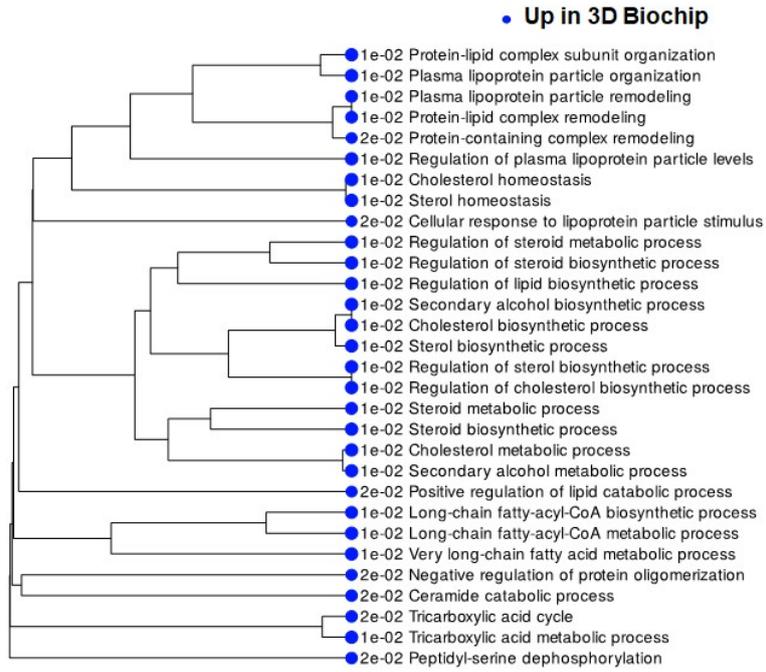


Fig.S7. GO_biological_process pathways identified by Gene Set Enrichment Analysis (GSEA) method (3D Biochip vs. iPSCs stage 1 comparison).

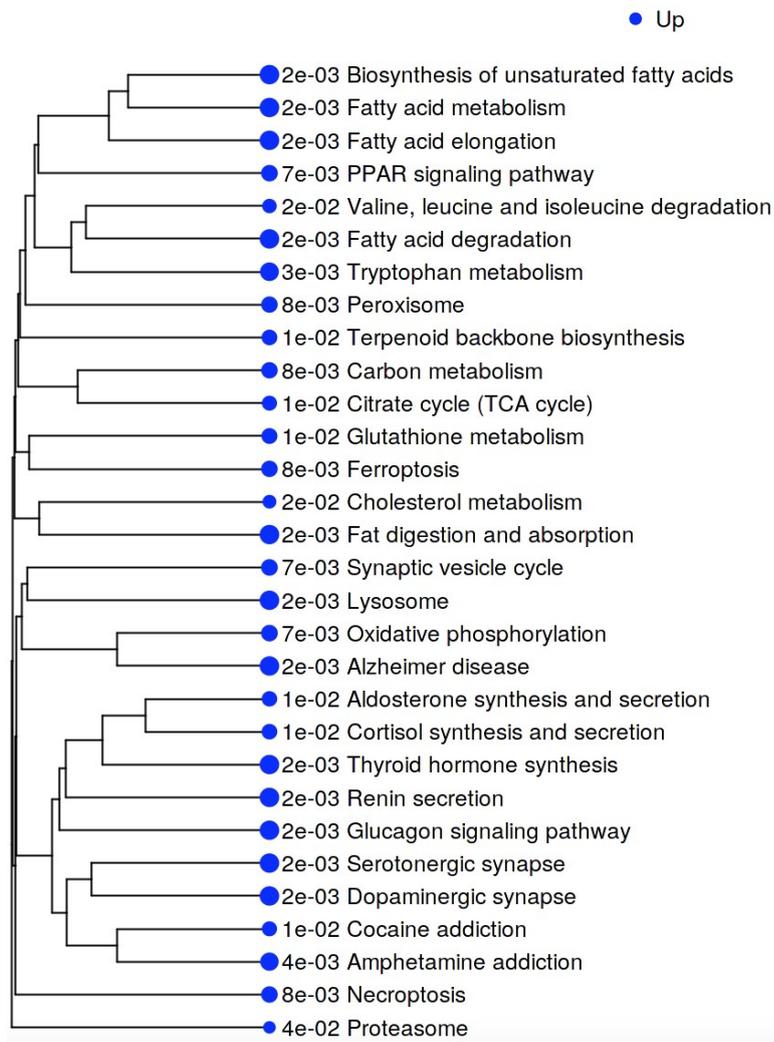


Fig.S8. GO_KEGG pathways identified by Gene Set Enrichment Analysis (GSEA) method (3D Biochip vs. iPSCs stage 1 comparison).

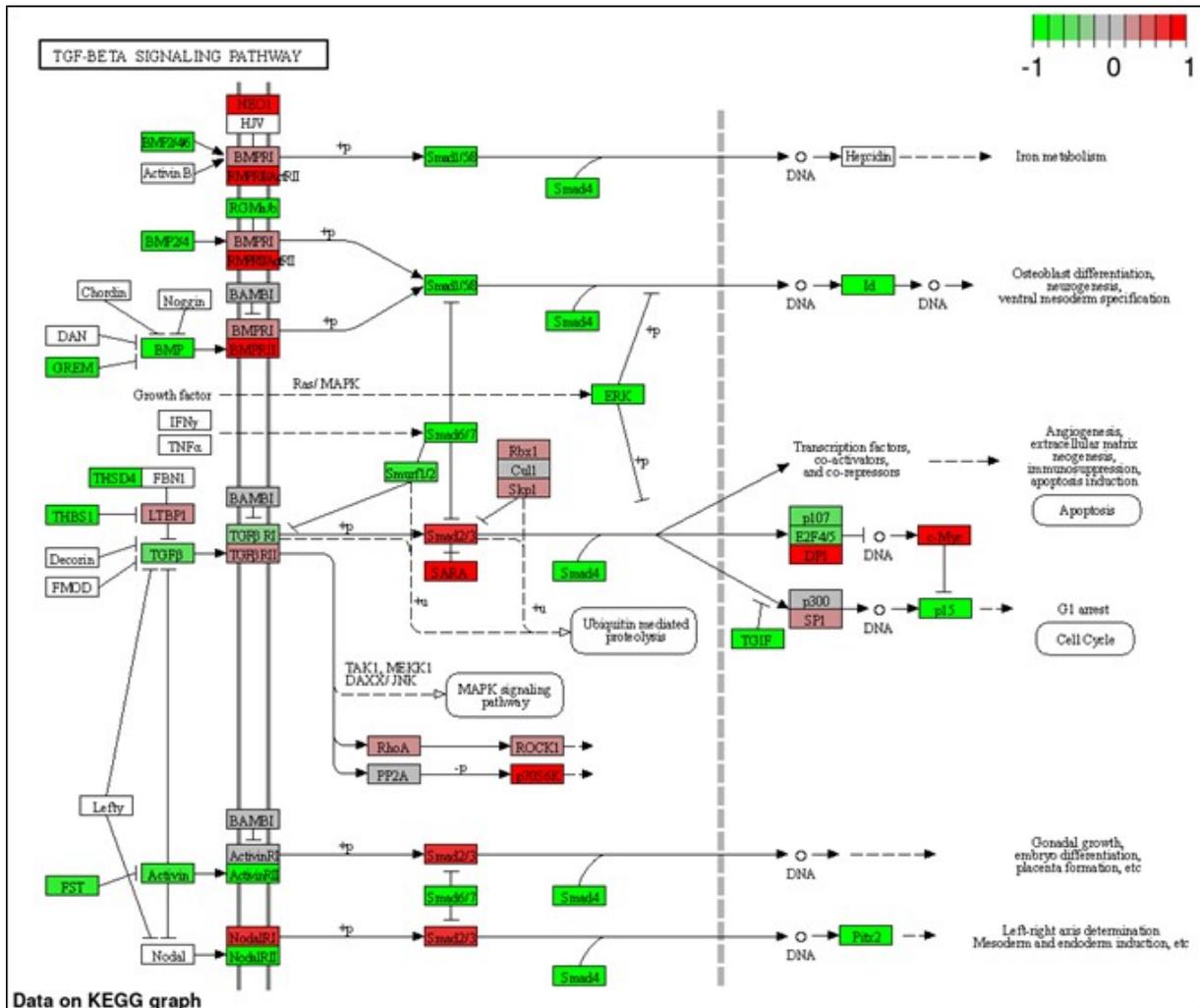


Fig.S9. Comparison of the transcriptomes of 3D biochips and 3D Petri cultures: genes significantly modulated in TGFβ signaling pathway highlighted by KEGG pathways analysis. Genes upregulated in biochips are highlighted in red, while those upregulated in 3D Petri are highlighted in green.

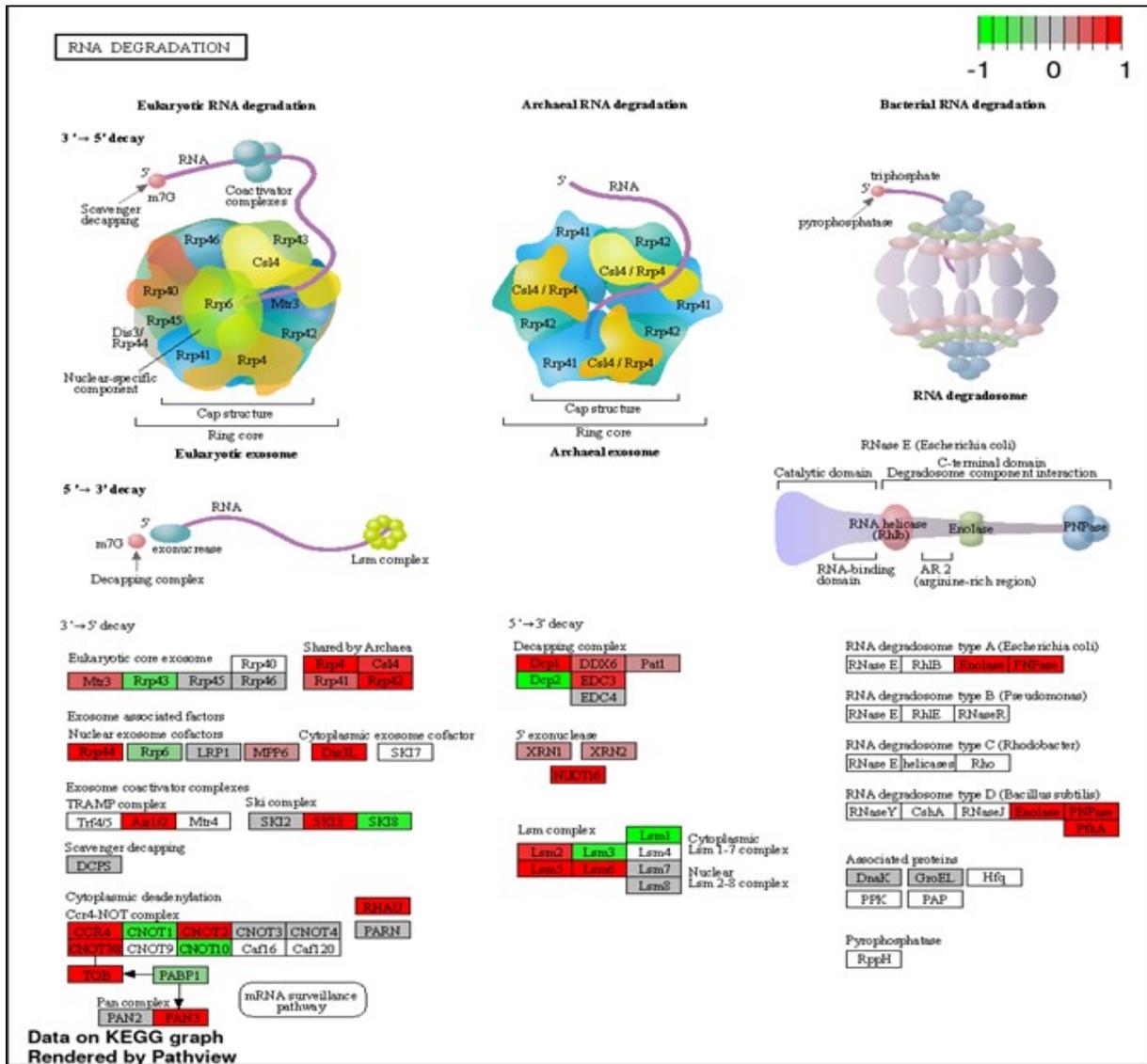


Fig.S11. Comparison of the transcriptomes of 3D biochips and 3D Petri cultures: genes significantly modulated in RNA degradation pathway highlighted by KEGG pathways analysis. Genes upregulated in biochips are highlighted in red, while those upregulated in 3D Petri are highlighted in green.

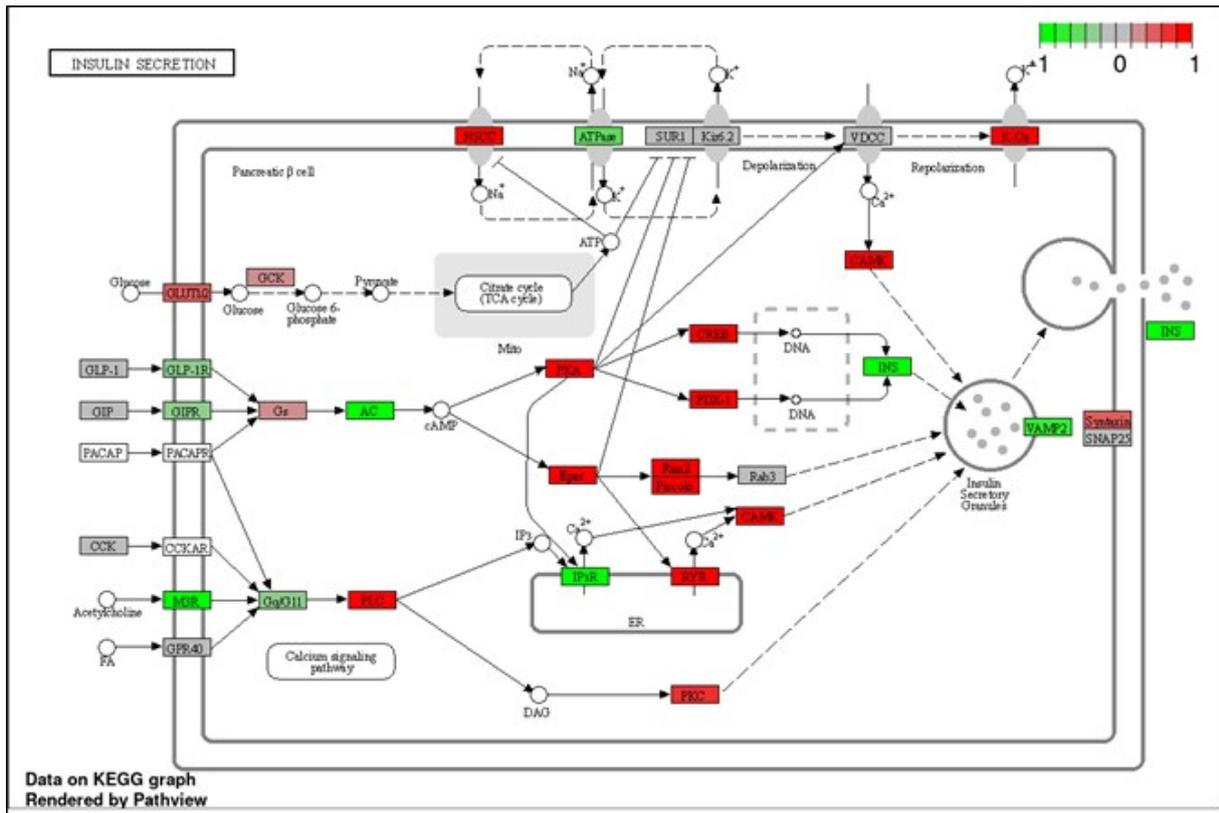


Fig.S12. Comparison of the transcriptomes of 3D biochips and 3D Petri cultures: genes significantly modulated in insulin pathway highlighted by KEGG pathways analysis. Genes upregulated in biochips are highlighted in red, while those upregulated in 3D Petri are highlighted in green.

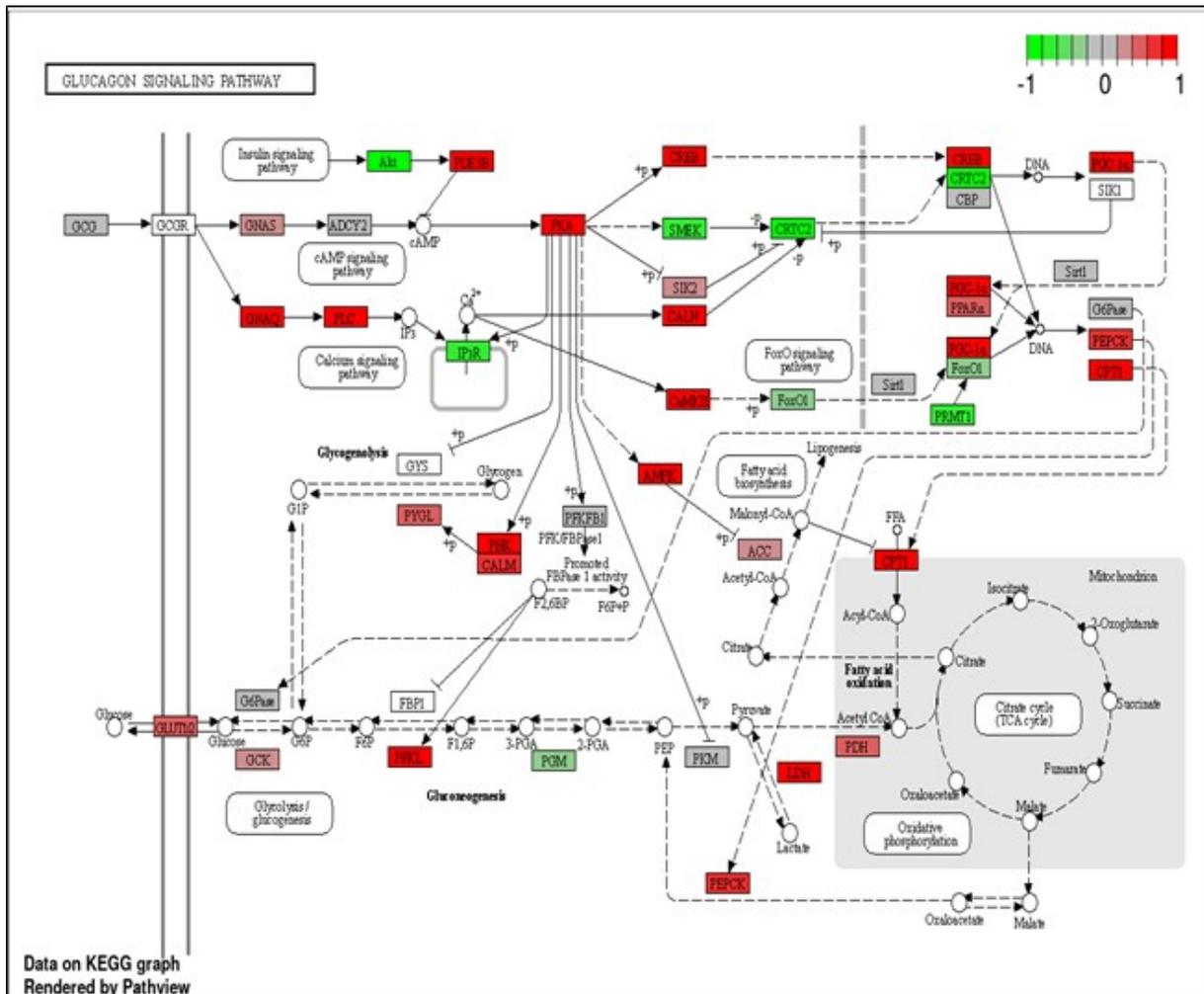


Fig.S13. Comparison of the transcriptomes of 3D biochips and 3D Petri cultures: genes significantly modulated in glucagon signaling pathway highlighted by KEGG pathways analysis. Genes upregulated in biochips are highlighted in red, while those upregulated in 3D Petri are highlighted in green.

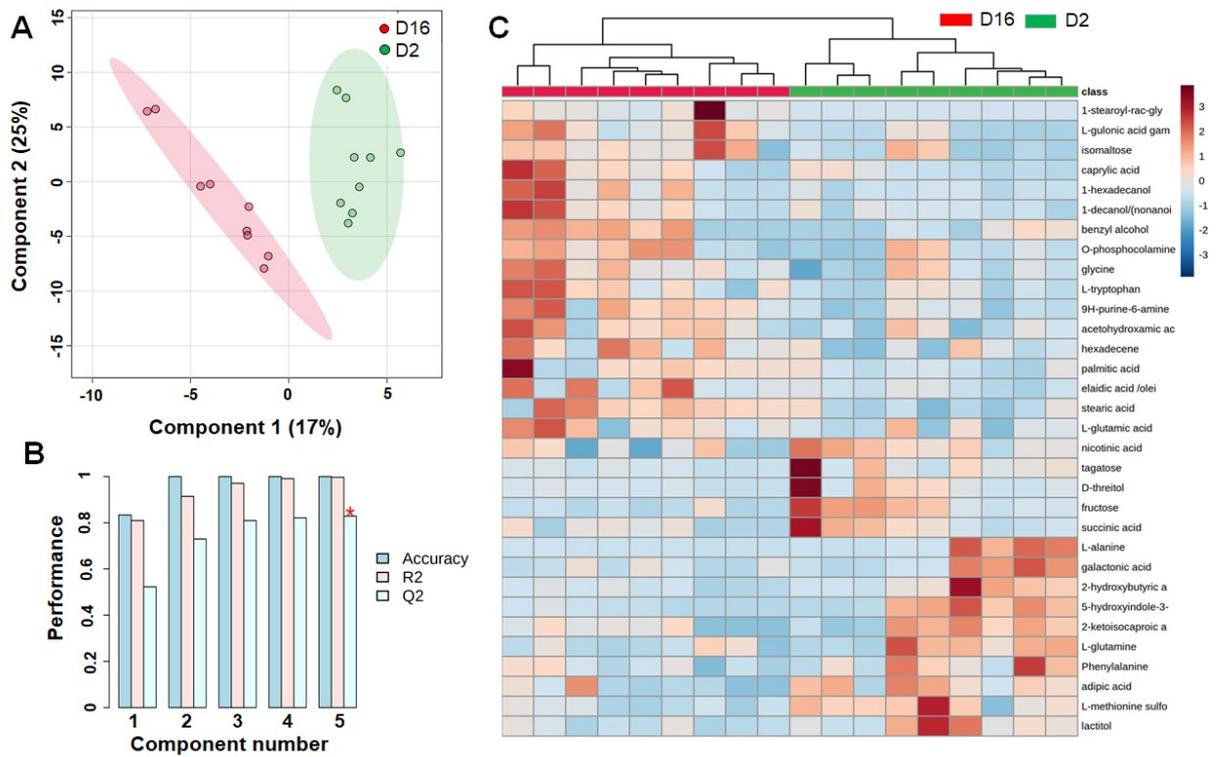


Fig.S14. Comparison of metabolomic profiles of 3D Petri cultures at day 2 and day 16. (A) PLS-DA score plot separating the two conditions; (B) PLS-DA model validation (R^2 and $Q^2 > 0.5$ confirming the good predictability of the model); (C) heatmap of metabolites significantly modulated between the two conditions.

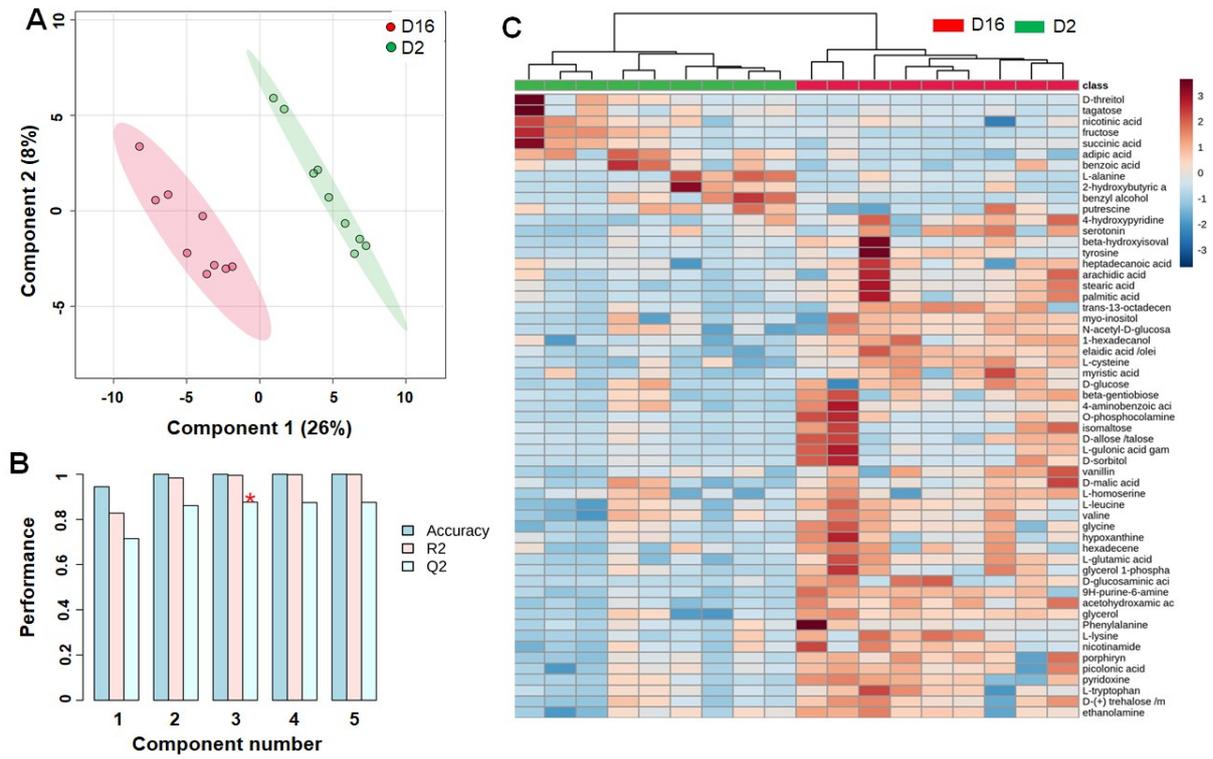


Fig.S15. Comparison of metabolomic profiles of 3D Biochip cultures at day 2 and day 16. (A) PLS-DA score plot separating the two conditions; (B) PLS-DA model validation (R^2 and $Q^2 > 0.5$ confirming the good predictability of the model); (C) heatmap of metabolites significantly modulated between the two conditions.