Utilizing 3D bioprinting and microfluidics technologies to establish reliable models of cardiovascular disease for drug and toxicity testing

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Cardiovascular disease is the leading cause of death in the world. In women, preeclampsia is a type of cardiovascular disease that occurs during pregnancy and predisposes both mothers and the offspring to future cardio-metabolic diseases. Yet, this disease is still without a cure. Inappropriate placentation is the root cause of preeclampsia. Similar to many other types of cardiovascular diseases including peripheral artery disease (PAD) and heart failure, aberrant angiogenesis is a hallmark feature of preeclampsia. However, the mechanisms regulating these processes are poorly understood, impeding the development of effective treatments for these conditions. *In vitro* tissue models of cardiovascular disease that closely recapitulate human early placenta, vasculature or fibrosis are lacking. To address this gap, we have developed robust, low-cost and reproducible 3D *in vitro* models of placental, vascular and fibrotic tissues. 3D bioprinted placental organoids, placenta-on-a-chip[1], vasculature-on-a-chip and 3D bioprinted cardiac fibrosis models, were utilized to identify key pathogenic mechanisms and test new therapies for cardiovascular disease in pregnancy and beyond. This talk will present new results on the development, validation and characterization of the first trimester trophoblast 3D bioprinted organoid model of placental tissue (Figure 1), and 3D bioprinted cardiac fibrosis model, both using RASTRUM matrices and 3D cell culture platform. Furthermore, 3D microfluidics models of placenta-on-a-chip[1] and vasculature-on-a-chip will also be described that model preeclampsia or PAD, respectively. Finally, results related to novel molecular insights and therapeutic and toxicity evaluation of potential treatments and biologicals for cardiovascular diseases, will be presented.

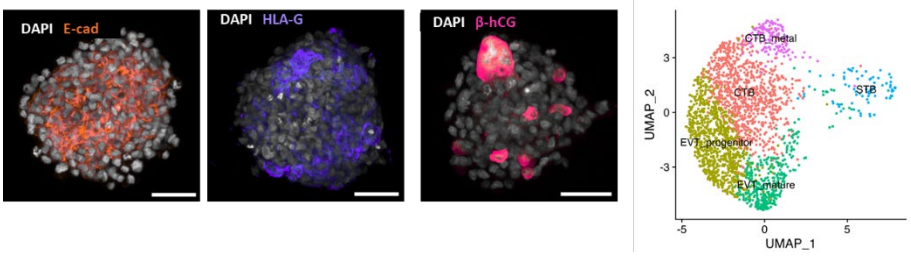

Figure 1. Novel 3D bioprinted organoids of first trimester placental tissue. First trimester trophoblast (ACH-3P) organoids grown by 3D bioprinting were harvested and labelled for whole organoid immunofluorescence confocal imaging. Organoids were fixed and immunolabelled for DAPI (grey), cytokeratin 7 (Cyk7, cyan hot), human leukocyte antigen G (HLG-A, purple) and beta human chorionic gonadotropin (β-hCG, bright pink). Images were acquired using a Nikon A1R inverted confocal microscope at 20x magnification. Uniform manifold approximation and projection (UMAP) following single cell RNA sequencing of 3D bioprinted ACH-3P trophoblast organoids.

(1) Ghorbanpour, S. M.; Richards, C.; Pienaar, D.; Sesperez, K.; Aboulkheyr Es., H.; Nikolic, V. N.; Karadzov Orlic, N.; Mikovic, Z.; Stefanovic, M.; Cakic, Z.; Alqudah, A.; Cole, L.; Gorrie, C.; McGrath, K.; Kavurma, M. M.; Ebrahimi Warkiani, M.; McClements, L. A Placenta-on-a-Chip Model to Determine the Regulation of FKBPL and Galectin-3 in Preeclampsia. Cell. Mol. Life Sci. 2023, 80 (2), 44. https://doi.org/10.1007/s00018-022-04648-w.