



Immune Cells as Architects of Function in Vascularized Organs-on-a-Chip



MILICA RADISIC

Professor, Tier 1 Canada Research Chair in
Organ-on-a-Chip Engineering
University of Toronto

Senior Scientist
Toronto General Research Institute

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Despite significant advances, the generation of stable, functional, and perfusable vascularized cardiac tissues remains a central challenge in the field. This presentation highlights how organ-on-a-chip technologies can be leveraged to reproduce higher-order organ functions, with a particular emphasis on innovations developed in the Radisic laboratory. These include the Biowire heart-on-a-chip platform for cardiac maturation and functional assessment; the AngioChip and inVADE platforms for engineering perfusable vasculature in cardiac and hepatic tissues; and bioengineered substrates that mimic the fractal geometry of the kidney glomerulus for kidney-on-a-chip applications. The integration of advanced 3D printing and biofabrication strategies is also discussed as a means to improve device scalability, throughput, and reproducibility, while enabling cell culture on substrates that are soft, permeable, and mechanically robust.

A major focus is placed on multicellular co-culture strategies that promote vascular stability and cardiac function. By combining four human cell types—endothelial cells, stromal cells, pluripotent stem cell-derived cardiomyocytes, and primitive macrophages—vascularized cardiac microtissues were generated within fibrin-based matrices. These studies demonstrate a critical role for primitive macrophages in supporting vascular morphogenesis and cardiac performance through direct cell-cell interactions and the secretion of matrix-remodeling, pro-angiogenic, and cardioprotective factors. Finally, the presentation addresses how automation and machine-learning-driven self-driving laboratory approaches can further enhance the throughput, robustness, and reproducibility of complex organ-on-a-chip systems.