Combined influence of topography and co-culture on cellular behavior

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In their native context, cells exist not in isolation but within a dynamic environment composed of a complex heterogeneity of cell types, extra-cellular matrix (ECM) structure, and biomolecules. The cell probes and responds to its environment through a collection of inputs guided by cell-cell and cell-ECM communication. Communication among cells can be varied, with cells of both the same type (homotypic) and different types (heterotypic) participating in these interactions. Cell communication in various biosystems (blood and lymph vasculature, renal glomeruli, intestinal villi, pulmonary alveoli) is also heavily influenced by the complex 3D interfacial cellular arrangements found in native tissues.

Current studies have explored the dual aspects of topography and co-culture, but only in isolation. Several techniques have been used to pattern cells in variety of biomaterials, however these approaches cannot be translated to a 3D biomimetic context and do not provide a complex multi-cell interface found in native tissues. Since functional output of native tissues is influenced by the heterogeneity of cell types as well as interfacial-topography, there is a need to develop a monolithic construct to concurrently investigate (a) spatially arranged 3D co-culture systems along with (b) complex topographical variations as found in native biology.

The successful execution of this project necessitates the synergetic application of methods from Materials Science, Biology, and 3D printing technologies. A Digital Projection Printer (DPP) needs to be optimized for multi-cell encapsulation. DPP will use dynamic masks adapted from user-defined computer aided design (CAD) images to fabricate virtually any micron-scale geometries with embedded cells. Naturally-derived gelatin-based biomaterial will be used to encapsulate vascular endothelial and smooth muscle cells in bioinspired vascular-like geometries. Since this approach provides orthogonal control to allow probing of independent and synergistic effects of 3D topography and multi-cell populations, we anticipate finding novel differences in cell morphology, collective organization, and cell function. The development of this system provides an important approach to explore the mechanisms of angiogenesis as well as vascular pathophysiologies.

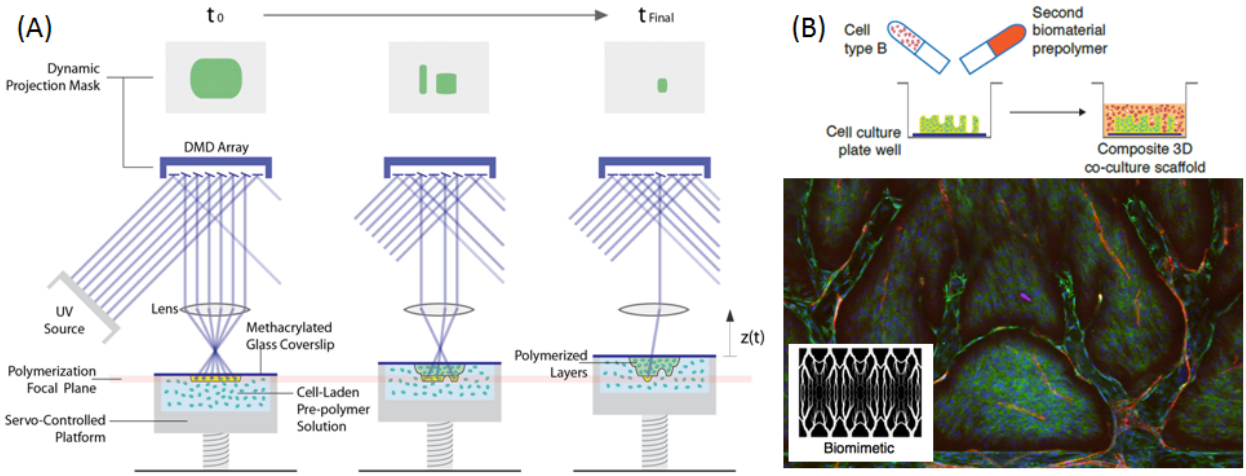

Figure: (A) Schematic of the Dynamic Projection Printing process. (B) A complex co-culture model with biomimetic vascular topography manufactured using Gelatin biomaterial. Confocal image demonstrate co-localization of endothelial (red) and smooth-muscle cells (green). Inset shows the digital mask used .