Research Interests

In the area of cardiovascular tissue engineering, we have developed the use of the “tissue-equivalent” as a replacement for a diseased or damaged small diameter artery, heart valve, and myocardium. Tissue-equivalents are fabricated from entrapping the relevant tissue cell into a biopolymer (fibrin) gel and constraining the cell-mediated gel compaction to engineer the alignment of the gel fibrils, so as to mimic the alignment of the target tissue. In prior work we have extensively researched the process by which cell traction exerted on gel fibrils by cells causes fibril reorganization on the microscale and contraction of the fibril network on the macroscale, inducing fibril alignment and thereby cell contact guidance in a complicated but fascinating biomechanical feedback loop. This understanding guides the design of molds presenting appropriate mechanical constraints for fabrication of tissue-equivalents with prescribed alignment. Bioreactors are used to create tissue-equivalent tubes by simulating the cells to replace the aligned fibrin with an aligned collagenous matrix. Upon decellularization, they are sufficiently strong to be implanted as vascular grafts and tubular hearts valves and are conducive to recellularization by the host, leading to growth capacity. Engineered human cardiac tissue that beats via entrapped iPSC-cardiomyocytes and contains a self-assembled microvascular network has been created using the same tissue-equivalent approach.

Our current research in cardiovascular tissue engineering focuses creating transcatheter heart valves and vein valves, combining our unique tubes of cell-produced matrix with stent technology, and conferring immediate or rapid hemocompatibility of the matrix using autologous stem cell and small molecule strategies.

Contact guidance -- the ability of cells to sense and aligned with aligned fibers -- is crucial to our ability to create tissues with prescribed alignment, such as the circumferentially-aligned tubes. The underlying mechanism of contact guidance is also being investigated using methods, including magnetic alignment and photo-crosslinking of fibrin, to systematically vary the chemical/physical cues contained in aligned fibers that cells might be sensing.

Awards

Distinguished McKnight University Professor
Selected Publications


