ABSTRACT

The proposed program of research will establish the foundational science required to create programmable human tissues across multiple scales replete with native organ function. This advancement will enable the rapid design and fabrication of complex, multicellular human tissues spanning from stem cell-based organ building blocks to whole organs. While our research will lead to foundational advances relevant for bioengineering multiple organ-specific tissues, we will focus on creating functional cardiac tissues for repair and replacement. Driven by this overarching goal, we will pursue a *blue-sky* technical approach that focuses on: (1) generating renewable supplies of cardiomyocyte and non-myocyte cells from wildtype and orthogonally differentiated human induced pluripotent stem cells (hiPSCs), (2) assembling these cell populations on massively parallel micropillar arrays to create chamber-specific, organ building blocks (OBBs) that exhibit the desired cellular density, alignment, and function, (3) manufacturing aligned, vascularized cardiac tissues via embedded bioprinting of atrial OBB, ventricular OBB, and sacrificial (vascular) inks, and (4) embedded electroporative printing of a conduction system composed of specialized cardiomyocytes that are genetically programmed "on-the-fly" during their patterning within functional cardiac tissues. Expected outcomes from this transformative program of research include the scalable assembly of genetically programmed cardiac cells, multicellular building blocks, and functional tissues of critical interest to the DoD mission for target applications ranging from drug discovery and chem/bio agent screening to repair, replacement, and regeneration of human organs.