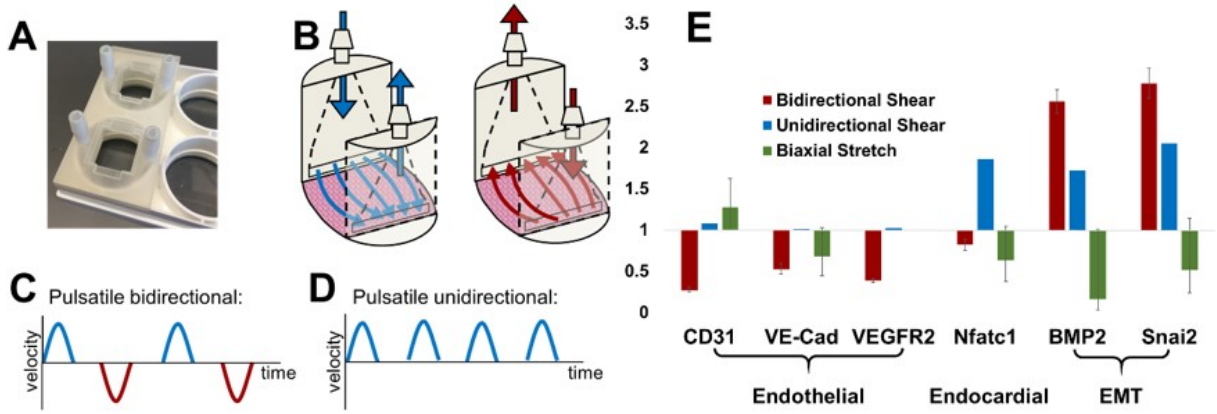
**Shear Stress Maintains Endocardial Phenotype in Ipsc Derived Endocardial Cells**

**Mark Vander Roest**, Camryn Johnson, H. Scott Baldwin, W. David Merryman, Vanderbilt Univ, Nasvhille, TN

**Objectives:** Specialized endocardial cells are responsible for the development of heart valves *in utero*. During a highly regulated morphogenetic process, these endocardial cells undergo endothelial-to-mesenchymal transformation (EMT) to become valve interstitial cells (VICs) and reorganize the extracellular matrix to form the structure of the valves. Potentially, induced pluripotent stem cells (iPSCs) may be coaxed into endocardial cells, then to VICs, to yield a suitable cell source for tissue engineered heart valves. Unfortunately, no method to generate iPSC derived endocardial cells exists. Current biochemical strategies utilize static culture, which does not represent the dynamic mechanical environment of the developing heart, which is known to affect differentiation and function of endocardial cells. **Methods and Results:** Human iPSCs were differentiated and purified to endothelial progenitors (CD34+), seeded onto collagen IV coated plates, and grown to confluency. Using a FlexCell system and a custom-built fluid shear device **(A,B)**, mechanical strain and shear stress were administered to the maturing cells independently, which were then assayed via qPCR for changes to endocardial and EMT markers. Bidirectional shear stress **(C)** was found to downregulate endothelial markers CD31, VE-cadherin and VEGFR2, as well as endocardial specific gene Nfatc1, yet increased expression of EMT markers BMP2 and Snai2. Conversely, unidirectional shear **(D)** increased Nfatc1 while causing lower expression of BMP2 and Snai2 than bidirectional shear. Cyclic strain decreased both endocardial and EMT markers **(E)**. **Conclusions:** These data suggest that unidirectional shear stress maintains an endocardial phenotype, while bidirectional shear stress induces EMT, promoting an interstitial cell phenotype. These stimuli may be utilized to maintain and expand patient-specific endocardial and valve interstitial cells for the creation of tissue engineered heart valves.

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