Fluid Shear Stress Promotes Embryonic Stem Cell Differentiation towards a Hematopoietic Phenotype

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The mechanical forces to which cells are exposed during early embryonic development may provide a key to understanding and directing stem cell fate. Fluid shear stress, a force present in the AGM region of a developing embryo due to the inception of a primitive heartbeat, plays a critical role in the development of the circulatory system. Embryos which lack a heartbeat fail to develop hematopoietic cells. It is thought that hematopoietic cells are generated from precursors which are present in the AGM which can differentiate into endothelial or hematopoietic cells.

Previously we have shown that the application of fluid shear stress to embryonic stem cells during early differentiation promotes an endothelial type. Studies by Daley et al using an embryoid body rotational culture have shown that the application of shear during later stages of differentiation can promote a hematopoietic phenotype. It has yet to be determined if fluid shear stress applied during early embryonic stem cell differentiation can promote a hematopoietic phenotype.

We applied fluid shear stress to embryonic stem cells in vitro using a parallel plate flow chamber apparatus. We used this system to vary the parameters of shear stress including magnitude, duration, and point of application. Changes in cell state resulting from shear were characterized by assessing protein and genomic changes in a host of hematopoietic (RUNX1, SCL, CD41, and CD34) and endothelial (FLK1, TIE2, PECAM, and VECAD) markers.

Application of fluid shear stress promoted both endothelial and hematopoietic phenotypes as we observed an increased expression of markers. Duration and point of application, but not magnitude, were critical for this phenotypic promotion. Further studies will examine the impact of shear on the formation of hematopoietic and endothelial cells and their precursors.