Regulating Capillary Morphogenesis in a Microfluidic System

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Angiogenesis is a complex process involving numerous cell-cell and cell-matrix interactions, mediated by a variety of biochemical and biophysical factors. *In vivo* experiments suffer from the lack of tight control, and most *in vitro* experiments allow for regulation of only a few variables. Using a new microfluidic platform, we have been able to control a number of factors, introduce controlled gradients in growth factors, vary scaffold stiffness and fluid shear effects, co-culture with multiple cell types, and observe microvascular growth in real time. Experimental results will be presented to demonstrate system design and capabilities, and its use in controlling the sprouting of capillary networks from an endothelial monolayer. Sprouting from a human microvascular cell line occurs in the presence of a gradient in either Sphingosine-1-Phosphate (S1P) or Vascular Endothelial Growth Factor (VEGF) into a collagen gel. The nature of the network formed can be switched from sheet-like invasion along a surface to 3D capillary network formation either by changing the stiffness of the collagen gel (by forming at different values of pH) or by coating the surface of the device with Poly-D-Lysine rather than collagen. Interstitial flow direction, either apical-to-basal or basal-to-apical can also influence the tendency for sprouting. When grown in co-culture with two different cancer cell lines, sprouting from an endothelial monolayer can be either stimulated or inhibited. These effects will be demonstrated both with time-lapse phase contrast imaging and end-point fixation and immunostaining. [Supported by Draper Laboratories and the NIBIB.]

Short bio:

Roger Kamm is the Germeshausen Professor of Mechanical and Biological Engineering and Associate Head of the Department of Mechanical Engineering at MIT. A primary objective of Kamm's research group has been the application of fundamental concepts in fluid and solid mechanics to better understand essential biological and physiological phenomena. Studies over the past thirty years have addressed issues in the respiratory, ocular and cardiovascular systems. More recently, his attention has focused on two new areas, the molecular mechanisms of cellular force sensation, and the development of new scaffold materials and microfluidic technologies for vascularized engineered tissues. Kamm is a Fellow of the American Institute for Biomedical Engineering and the American Society for Mechanical Engineering. He is the current chair of the US National Committee on Biomechanics and the World Council on Biomechanics, and Director of the Global Enterprise for Micro Mechanics and Molecular Medicine.