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IMFT - Amphithéâtre Nougaro
Allée du Professeur Camille Soula 31400 Toulouse

Growth and function of microvascular structure *in vitro* and *in vivo*

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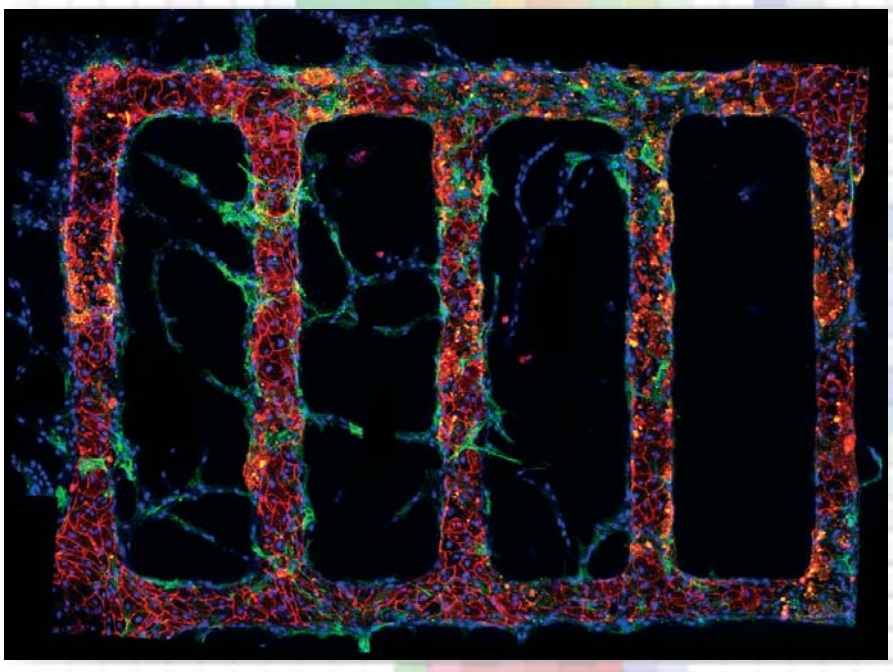

Caption: Endothelized capillaries grown in vitro in co-culture with perivascular cells. Fixed and stained sample after two weeks of culture. Stains: blue = DAPI (nuclei), red = CD31 (endothelial cells), and green = alpha smooth muscle actin (perivascular cells). Credit Dr. Ying Zheng, Stroock Laboratory.

To begin, I will present an overview of the biological understanding of vascular morphogenesis in development, in healthy response in wounds, and in pathological contexts such as in tumors. I will point out biophysical hypotheses about the guidance of these processes. I will then turn to three examples of our efforts to dissect these mechanisms using microfabricated, three-dimensional (3-D) environments:

1) ***Cellular dynamics and interactions during vasculogenesis***. The initial vascular system emerges as a uniform capillary bed formed via local self-organization of endothelial cells (ECs). Studies of this process (vasculogenesis) in 2-D suggest that the individual cells search their environment via migration under the influence of gradients of chemical factors or of mechanical deformations in their substrate. In 3-D, less is known due to the lack of live tracking data and the challenge of separating chemical and mechanical interactions. I will present experiments in which we track the dynamics of individual cells and pairs of cells in 3-D cultures with well-defined conditions on diffusive flux and deformation at the boundaries. I will show that the dynamics is dominated by biased random motion of protrusions, rather than by migration. Further, I will describe how we have used the concept of “image” cells in permeable and impermeable rigid boundaries to deduce that the bias in the search is dictated by chemical not mechanical signals.

2) ***Invasion of porous matrices in vivo***. Biomaterials with random porous structure are used successfully in the clinic to encourage the regrowth of the dermis in deep wounds. Yet roles of the pores have not been elucidated and these scaffolds fail to provide fast enough invasion of the host vasculature for many applications. I will present the development of implantable scaffolds with pores and networks of conduits of well-defined size and shape formed by microfabrication. Based on multi-week implantation of these scaffolds in a murine (mouse) wound model, I will show that the geometry and dimension of the pores have a dramatic impact on the invasion of tissue and blood vessels. I will discuss our insights into the cellular, chemical, and mechanical processes that dictate this process. Finally, I will show that appropriate deterministic paths guide rapid invasion over macroscopic distances, leading to significantly higher densities of tissue and vascular structure than in random matrices.

3) ***Model microvessels in vitro.*** The recapitulation of microvascular structure in vitro would provide a basis for dissecting angiogenic processes in development and in clinical contexts such as wound healing and tumor vascularization. I will present a summary of our effort to grow physiologically appropriate microvessels in the lab. In particular, I will show that we can use microfluidic structure formed in cell-remodelable matrices to initiate the growth of vessels with appropriate physiology, permeability, and response to biochemical and mechanical stimuli.

I will conclude with a discussion of outstanding challenges and future opportunities for these approaches to studying and engineering microvascular structure and function.

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