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BIOPHYSICS OF ANGIOGENIC SPROUTING: A NEMATIC PERSPECTIVE

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There is mounting evidence that blood flow-derived biophysical forces contribute to angiogenesis; however, the precise mechanical cues involved and the underlying mechanisms remain poorly understood. Vascular endothelial growth factor (VEGF) has been shown to stimulate endothelial cell (EC) migration and to promote angiogenic sprouting. Besides being a potent pro-angiogenic factor, however, VEGF also has a dramatic impact on EC elongation and alignment, leading to zones of elongated and aligned cells and other zones of more cuboidal cells within the same monolayer. If one considers the EC monolayer within the framework of active liquid crystals, then regions of abrupt changes in EC shape and alignment would correspond to singularities in nematic order and would be expected to generate elevated mechanical stresses. In this talk, I will focus on experiments in which we cultured ECs to confluence on the surfaces of flat collagen hydrogels and monitored angiogenic sprouting into the hydrogel following VEGF treatment. The results demonstrate that VEGF changes EC morphology, with cells organizing into elongated cell "streams" that coexist with more polygonal regions. Angiogenic sprouting preferentially initiates at the tips of these streams, regions we term "wedges". Traction force microscopy measurements reveal that traction forces are particularly elevated at wedges. Wedge areas are also associated with wrinkling of the underlying collagen hydrogel. Cell streams arise from a balance between microtubule polymerization and actomyosin contractility, and disrupting this balance drives the appearance of topological defects and significant changes in substrate deformation. The occurrence of wedges can be actively abolished through surface patterning of the collagen hydrogel, leading to a dramatic decrease in sprout formation. Finally, similar processes occur in 3D as angiogenic sprouting in a microvessel-on-chip can be significantly attenuated when the vessel is subjected to a mechanical environment that leads to uniform EC alignment. These findings underscore the crucial role of mechanics in angiogenic sprouting and suggest new strategies for active control of angiogenesis.

Invited by : Eva Faurobert

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Allée des Alpes, 38700 La Tronche (tram line B, stop : Grand Sablon)
The seminar is followed by discussions and exchanges with the speaker and a sandwich buffet is offered

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