Targeting Mechanobiological Mediators of Fibrosis

Abstract: Tissue fibrosis contributes to progressive functional decline and end stage disease in the lungs, heart, kidneys and liver. Fibrotic tissue remodeling is accompanied by stiffening of the extracellular matrix, and recent work indicates that fibroblasts respond to matrix stiffening in a positive-feedback loop of cellular activation and matrix deposition. Identifying the cellular and molecular pathways that drive fibroblast mechanoresponses may thus open new opportunities for treating fibrosis across multiple organs. Furthermore, delineating the homeostatic interactions that normally keep fibroblast activation in check during normal tissue function and healthy wound healing may open new perspectives on how fibrosis arises, and how tissue homeostasis might be restored. In this seminar I will focus on YAP and TAZ as mechanobiological mediators that promote fibroblast activation and fibrosis in the lung, and a novel GPCR-based approach for targeting fibroblasts to reverse cellular activation and arrest fibrosis progression.