Multi-scale mechanics of soft fibrous tissues : application to pancreatic cancer stroma

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Sujet de stage :
Tumor mechanical environment is a key parameter driving cancer progression. For instance, stiffening of the tissue surrounding tumors, called the stroma, promotes tumor growth and metastasis. This tissue is made of a dense extra-cellular matrix (ECM) secreted and modeled by deregulated fibroblasts called CAFs. Since CAFs mechanical activity is controlled by tumor cells via soluble factors, complex feedbacks exist between CAFs, tumor cells and their mechanical environment. In addition, fibrous networks such as stromal matrix exhibit visco-elastic, strain-stiffening and plastic properties, while CAFs actively rearrange the matrix by pulling on it.
Our goal is to establish the mechanical and biological parameters that sets the complex mechanical properties of the tumor stroma. For that, we developed a setup based on uni-axial mechanical testing of suspended *in vitro* reconstitued stroma micro-tissues (Fig 1A). This allows us to characterize the linear and non-linear rheological response of the tissue and to identify the cellular and moleculars actors that control it.
Various molecular actors of the ECM have been shown to influence stroma mechanical properties. Nevertheless, there impact is often very limited. In parallel, the role of traction forces exerted by CAFs have been neglected until now. The objective of this internship will thus be to couple our tissue-scale mechanical testing apparatus to the measurement of active forces generated locally by CAFs. For that, local strains of collagen matrix and displacements of fluorescent markers will be characterized using confocal microscopy (Fig 1B). This will open the way to a mechanical model of the stroma integrating fiber
The intern will profit of strong interactions with the group of R. Tomasini (CRCM, Marseille, expert in pancreatic cancer), with the group Mécanique des Cellules en Milieu Complexe (LiPhy, Grenoble) for mechanical modeling and with the group of D. Duprez at the LBD (specialized in connective tissue biology).

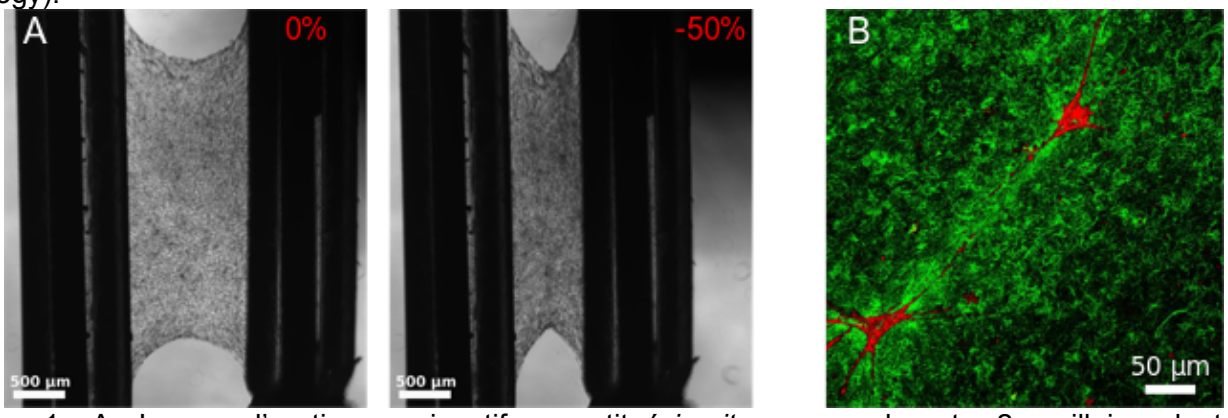

Figure 1 - A : Images d'un tissu conjonctif reconstitué *in vitro*, suspendu entre 2 capillaires dont l'un (droite) est déplacé par une plateforme motorisée afin de contrôler la déformation et l'autre (gauche) est connecté à un senseur de force. L'image de droite montre le tissu après une compression correspondant à 50 % de sa longueur initiale. B : Image du tissu en microscopie confocale. En rouge, des cellules de type C3H/10T1/2 (fibroblastes embryonnaires de souris). En vert, la matrice de collagène.