Abstract (lay version) of project

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In vitro study of the involvement of cell-cell and cell-matrix and focal adhesion formation in desmoid-type fibromatosis myofibroblastic differentiation under pro-inflammatory stimuli

Desmoid-type fibromatosis (DF) is a rare benign tumor characterized by a fibroblastic features and a variable and often unpredictable clinical course. Despite lacking metastatic potential, DF is locally invasive and associated with a high local recurrence rate. Desmoid-type fibromatosis is often associated with local and repeated injuries; it shows differences in growth rate, spontaneous regression, and recurrences. The heterogeneity and the variable clinical course of this tumor suggest the involvement of altered signaling or aberrant response of DF cells to external microenvironmental stimuli. A small portion of desmoid tumors is associated with Familial Adenomatous Polyposis (FAP), a genetically inherited tumor disease linked to mutations in the APC gene, while most of the desmoid tumors are sporadic. Of the later, 50-80% have somatic mutations (mutations that are only present in the area of the tumor and therefore not inheritable) in the gene encoding β-catenin, CTNNB1. However the wide variability of the growth rate, localization and aggressiveness of the tumour indicate that the desmoid tumor requires a favorable microenvironment to develop and grow. We recently demonstrated that the inflammatory cytokine, TGF-β, play a key role in the proliferation and myofibroblasts differentiation of DF cells providing evidences of the formation of a fibrotic tissue derived from interactions between external factors and Wnt pathway alterations.

We observed a formation of stress-fiber pattern in DF cells with a higher cell spreading and a higher cell-cell contacts in presence of this cytokine suggesting the involvement of cell-adhesion and cellcell contact in DF myofibroblast differentiation.

In this project we aim to investigate the type and the role of cellular communications with ECM in desmoid tumours cells. In particular we will study the role of cell adhesion receptors, and of focaladhesion formation in the induction of stress-fiber assembly and myofibroblastic differentiation after TGF-β stimulus.