The project will mainly be performed at CQM, University of Madeira, the Island of Madeira, Portugal. Madeira is a tourist attraction, water and air temp. appr. 20°C, low/no criminality, subtropical Africa, living costs appr. 40% of Stockholm, direct flights to Arlanda; http://www.madeiratourist.com
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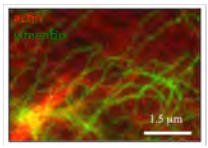

The Molecular Control of Extracellular Fibre Mechanics on Human Cells

Introduction

Although it is evident that all tissues and cells in the body are subjected to mechanical cues, such as the force and stiffness of their environment, the possibility that these cues can regulate the functions of cells has been greatly overlooked in the past. Recent findings show, however, that the stiffness of the surrounding environment can govern fundamental cell functions, such as cell proliferation, differentiation and migration, functions which, when defective, can result in various diseases, including cancer. Cancer development is marked by massive increase of matrix fibres around tumor cells, which changes the mechanical properties of the tissue and is used to diagnose tumours by manual palpation. It is possible that defective mechanical properties of the fibres in the cell microenvironment promote the initiation and progression of tumours.

Aim

To determine the molecular mechanisms that control cellular mechanorespons to fibres, cell invasion and cancer growth, for future drug development against cancer. For this, we will use an multidisciplinary strategy combining tumour cell and molecular biology, nanomaterial sciences, fibre and polymer technology and biomedicine.

What and How

We will create a fibrillar microenvironment, that allows a separate tuning of the material´s chemical and mechanical properties. We will then separately alter these parameters in the presence of cells, and detect the effect on cell size, growth, movement, mechanorespons, fibre recruitment, fibre alignment, and identify the underlying molecular cytoskeletal mechanisms.

Significance

The importance of mechanosensation for the behaviour of cells has been greatly overlooked in the past. Hence, the identification of the molecular mechanisms that control this cell property will significantly increase our understanding of all basic cell functions that depend upon mechanics, e.g. cell deformation, motility, cytokinesis and, thus, of all physiological processes that depend upon these functions, e.g. embryogenesis, tissue homeostasis and cancer. Identification of the molecular mechanisms that control cell invasion via cell mechanics can provide target molecules for future development of anti-metastasis drugs. As these drugs would be based only on mechanics, they can form a previously unknown, mechano-based, class of drugs. As tumor cell invasion and metastasis is the number one cause of cancer deaths, this can improve prevention of human death in cancer.

Conditions

The Student and I will discuss and mutually decide the aims of the project work, in particular the skills that s/he should gain. One overall aim will be to get knowledge in the different steps towards publishing of scientific data/findings. We then identify the activities to be performed to achieve the goals. We clearly define and document the mutual expectation that we have of each other and of the period we will work together. I regard that my role as a supervisor is to provide a clear structure, a frame-work with a clear focus on the initially decided aims and actions to be taken, ensuring that the constructive alignment of the project is kept. I perform these activities by regular, constructive, supporting feed back. The student can use the ERASMUS program to stay with us for one/two-semester(s), doing a master project.