Title: Magneto-mechanical study of cell growth and proliferation in micro-pores

PI: John Dunlop

In Collaboration with: Damien Faivre and Stefan Klumpp

Project description:

Understanding tissue growth in biomaterial micro-pores can help design scaffolds to optimally support the healing process of tissue defects. One model that predicts tissue growth in confined geometries suggests that growth is positively linked to surface curvature of the substrate-cell interface; cells are hypothesized to proliferate preferentially at the interface between surfaces, including both scaffolding and extant cells [1]. This model suggests that where curvatures are highest, cells grow most quickly and fill largest volumes; thus, pores with high degrees of curvature should be filled by a relatively small number of cells. Forecasts based on this model that predict the number of cells as a function of pore size and geometry, and tissue growth rates in confined geometries have been found to closely match experimental results [1,2]. Preliminary results suggest that curvature driven growth behaviour is mediated by mechanical signalling in cells. In addition to global geometrical constraints, it is also known that cells generate forces that influence growth and differentiation of other cells. In terms of "tissues" mechanically guided cell growth has been studied in two-dimensions using force traction studies of cell sheets. This demonstrates a link between proliferation and differentiation and mechanical stress [3]. By probing three-dimensional physical properties of growing tissues in confined geometries at high spatial resolutions and generating forces within them, we hope to gain insight into the mechano-regulation of tissue formation.

Growing tissues in Hydroxyapatite scaffolds while imaging their growth pattern using phase contrast microscopy has been established as a technique in John Dunlop's lab. We would like to measure physical properties of the growing tissues using two techniques: The first will involve growing tissues in the presence of micro magnetic particles that are dispersed throughout the tissue, and then actuating the particles using magnetic forces while observing their movement using a setup available in Damien Faivre's lab [4]. This setup allows for applying a spatially homogenous magnetic gradient for controlled durations at various angles relative to the measured sample. Analyzing the particles' trajectories will provide insight into the material's viscoelasticity, cohesion and adhesive strength at high spatial resolution [5] and how these vary as a function of the direction of the applied magnetic tension relative to the tissue-substrate interface. The second technique will involve adding diluted surface-functionalized polystyrene microbeads to tissue cultures, and then imaging and analyzing their motion. This can give us insight into how tissues' mechanical properties, charge interactions and spatial density change over time [6]. Additionally, manipulating tissue properties using chemical treatments that can either inhibit contractility, alter surface roughness, or break peptide bonds in the extra-cellular matrix's collagens while using microrheological techniques to observe the tissues' mechanical properties may provide insight on the effect of contractility, roughness, and ECM on how the spatial mechanics of the tissues change over time. Finally, imaging the tissue's growth patterns using phase contrast microscopy while tracking the particles' motion will enable us to study the link between the tissue's mechanical properties and its growth and will provide additional tools to study tissue growth.

Relation to previous projects

I received my M.Sc. in physics in the field of magnetism and magnetic materials and am trained in physical interpretation of magnetic forces and various microscopy techniques. For the past year I have been studying magneto-aerotaxis in magnetotactic bacteria and have applied magnetics to

biological systems, imaging magnetic bacteria under various magnetic fields and analyzing their motion. Similar experimental and analytical techniques will be applied to magnetic particles in tissues.

References

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