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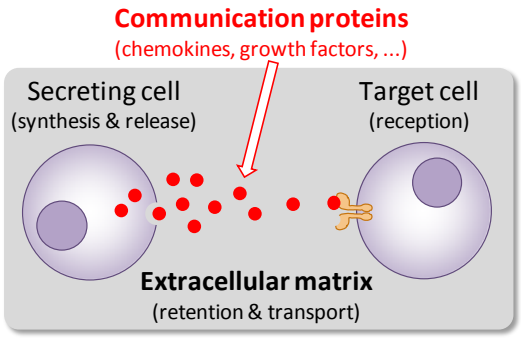
This proposal is representative of the projects on offer in our lab. For more details of active research projects, please visit our webpage at http://www.fbs.leeds.ac.uk/staff/profile.php?tag=Richter_R.

Chemokine gradient formation in extracellular matrix – defining physico-chemical mechanisms



Small signaling proteins in the extracellular space are essential to inter-cellular communication in higher organisms. Gradients of chemokines, for example, guide the migration of immune cells in inflammation and of stem cells in tissue repair. For these proteins to function, they need to be at the right time and concentration at the right place. Polysaccharides of the glycosaminoglycan (GAG) family are abundant in extracellular matrix. They bind many chemokines and other communication proteins, and thereby play a decisive role in their distribution and presentation, and thus, function. It is clear that the strength and dynamics of GAG-chemokine interactions are important but how these are tuned to enable effective chemokine diffusion and gradient formation is not well understood.

In this project, you will seek to reveal the physico-chemical mechanisms that define the redistribution of chemokines in the extracellular space. This topic is an example of physical chemistry at play in a biological system. More broadly, this question connects to physics, biology, chemistry and materials sciences. The insights gained will advance our fundamental understanding of how extracellular matrix works. They may also help to design novel strategies to interfere with diseases such as cancer metastasis or chronic inflammation, or advanced biomaterials with novel functions.

You will combine physico-chemical analysis methods with well-defined models of GAG-rich extracellular matrices to study the physical and biochemical mechanisms underlying the formation of chemokine gradients. Your work will cover several levels of complexity: from the interaction of individual molecules to the self-organization of biological materials to the complex cell-matrix interface. Methodological approaches include modern methods of surface functionalization, techniques for the nanoscale characterization of biomolecular interactions (such as quartz crystal microbalance, spectroscopic ellipsometry, atomic force microscopy and fluorescence microscopy) and cell assays.

Please contact Dr. Ralf Richter (r.richter@leeds.ac.uk) for further details about this and other opportunities in the group

References:

1. Migliorini, E.; Thakar, D.; Kuhnle, J.; Sadir, R.; Dyer, D. P.; Li, Y.; Sun, C.; Volkman, B. F.; Handel, T. M.; Coche-Guerente, L.; Fernig, D. G.; Lortat-Jacob, H.; Richter, R. P. 2015. Cytokines and growth factors cross-link heparan sulfate. *Open Biol* 5:150046.
2. Migliorini, E.; Thakar, D.; Sadir, R.; Pleiner, T.; Baleux, F.; Lortat-Jacob, H.; Coche-Guerente, L.; Richter, R. P. 2014. Well-defined biomimetic surfaces to characterize glycosaminoglycan-mediated interactions on the molecular, supramolecular and cellular levels. *Biomaterials* 35:8903-15.
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