Cluster of Excellence
- “From Regenerative Biology to Reconstructive Therapy”

REBIRTH Special Lecture:

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Sugar-coated webs to drive stem cell differentiation

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Lecture Hall Q (I6-S0-4100)

5 p.m. (c.t.)

Host: Dr. Robert Zweigerdt, Phone 0511 / 532-9802

Sugar-coated webs to drive stem cell differentiation

Catherine Merry, Stem Cell Glycobiology, Materials Science, University of Manchester, UK

Glycosaminoglycans (GAGs) are essential cofactors for many signalling molecules regulating stem cell expansion and differentiation. Whereas many groups are investigating the protein components of these signalling complexes, the carbohydrate fraction is less well understood and remains an under-appreciated factor in strategies for stem cell expansion or directed differentiation. Several key issues need to be addressed before pluripotent human stem cells can fulfil their potential for therapy and improved understanding of disease. Foremost amongst these is the development of defined cell culture systems for the high-efficiency differentiation of stem cells to the target cell type. These systems must be scalable, fully-defined and xeno-free.

Our work[1, 2], and that of others, has defined specific GAG epitopes in mouse ES cells and has demonstrated that selected GAG saccharides can be used to influence specific signalling pathways during neural[3] and mesodermal[4] differentiation. Importantly we were also able to show lineage-specific requirement for sulphation pattern and size of saccharides. This suggests that GAG saccharides could be used in addition to, or possibly in place of, protein additives in differentiation protocols.

Improvements in the chemoenzymatic production of xeno-free structurally-defined GAG oligosaccharides now allow exploitation of these compounds in the determination of specific sulphation pattern requirements for the control of cell signalling. We are combining this work with the design of artificial 3D cell environments, generated by electrospinning or by the formation of hydrogels[5]. By permeating these scaffolds with defined GAG oligosaccharides, we control the mechanical environment of the cells (via the scaffold architecture) as well as their biological signalling environment (using the oligosaccharides). This enables control of ES cell pluripotency and differentiation in a 3D setting, allowing the generation of differentiated cell types for use in drug discovery/testing or in therapeutics.

1. Johnson, Merry et al. *Stem Cells*. 2007 25(8):1913-23.
2. Baldwin, Merry et al. *Stem Cells*. 2008 26(12):3108-18.
3. Holley, Merry et al. *Journal of Biological Chemistry*. 2011 286(8):6241-52
4. Pickford, Merry et al. *Stem Cells.* 2011 29(4):629-40
5. Meade, Merry et al. *Journal of Biological Chemistry*. 2013 288(8):5530-5538