THE DANISH SOCIETY FOR MATRIX BIOLOGY

Newsletter

No. 10, December, 2022

From the Chairwoman

Welcome to the Christmas edition of our 10th Newsletter! It has been a tough year for everyone.

And therefore, we are excited to announce an in-person **Danish Society for Matrix Biology Symposium on Thursday 19th January 2023. Attendance will be free of charge.**

The **symposium theme is the Role of Extracellular Matrix in Inflammation and Immunology,** with an invited **keynote lecture** from **Douglas Dyer** from the University of Manchester (UK) on **Proteoglycan and chemokine collaboration in immune cell recruitment**, and two invited speakers, **Grith Lykke Sørensen** (University of Southern Denmark) and **Rikke Louise Meyer** (Aarhus University).

The symposium is sponsored by **Tebu-bio** and there will be prizes for the two best elevator pitches.

My appreciation also extends to our current board and members as well, especially for your support and patience throughout these stressful times. We are always open to taking on new board members joining, which is great for the CV and career grants.

Finally, we would like to wish you all a Merry Christmas and Happy New Year and we look forward to another year of exciting seminars and new matrix research in 2023. Take care and stay safe!

Sincerely,

Christine Chuang

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Danish Society for Matrix Biology 2023 Symposium

Role of Extracellular Matrix in Inflammation and Immunology

Thursday 19 January 2023, 1 PM – 6 PM, Mærsk Tower, Level 15

Keynote lecture

Proteoglycan and chemokine collaboration in immune cell recruitment

Douglas Dyer
Wellcome Centre for Cell-Matrix Research, Lydia Becker Institute of Immunology and Inflammation, Manchester, UK

Confirmed invited speakers:
Grith Lykke Sørensen, University of Southern Denmark
Rikke Louise Meyer, Aarhus University

Call for abstracts for 3 short talks and 8 elevator pitches. Prizes sponsored by DSMB and tebubio for the 2 best elevator pitches!

Registration and abstract submission deadline is 16/12/22.

To register:
This meeting is **free**. However, please register attendance by sending your name and affiliation to dsmb.dk@gmail.com

To submit an abstract:
Send a word document with the title, author list, affiliations and abstract with the sections Introduction, Hypothesis, Methods, Results and Conclusion (max 250 words) to dsmb.dk@gmail.com

Abstract

Chemokine mediated leukocyte recruitment is a key facet of the immune response, classically explained by interaction with receptors on leukocytes. Chemokines are central to inflammatory pathology but have yet to be targeted during inflammation. Therefore, we must revisit the field with fresh approaches to inform therapeutic development.

Chemokine interactions with glycosaminoglycan (GAG) extracellular matrix components are important for their function, however, we do not understand why. CXCL4 mediates recruitment of a range of immune cells during diseases such as sepsis, atherosclerosis and cancer; however, there have been conflicting reports on its' functional receptor. We hypothesise that CXCL4, and possibly other chemokines, function principally via interactions with the extracellular matrix components, glycosaminoglycans, instead of via classical chemokine receptors; a new understanding of the basic biology of chemokine function.

Furthermore, we propose that the extracellular matrix, specifically proteoglycans within the cellular glycocalyx, play a much wider role in the immune cell recruitment and the immune response than is currently understood. Our lab is focused on uncovering novel pathways to inform development of future therapeutics to target the immune system.

Biography

Doug graduated in Medical Microbiology and Immunology from the University of Newcastle and then undertook his PhD at the University of Manchester. His early research investigated how an anti-inflammatory protein functions by disrupting the interactions between chemokines and their extracellular matrix glycosaminoglycan binding partners. Supervised by Prof. Anthony Day, Dr Caroline Milner and Dr Amanda Proudfoot (MerckSerono).

Doug then went on to focus on the biological importance of chemokine:GAG interactions in leukocyte migration during his postdoc in the lab of Prof. Tracy Handel (UCSD). During this time, he and his colleagues demonstrated that chemokines have strikingly different interactions with GAGs according to their oligomerisation potential. A collaboration with Dr Ralf Richter's group (San Sebastian, Spain) then described how chemokines can re-structure these GAG chains, proposing a new mechanism underlying chemokine function.

During his second postdoc, with Prof. Gerry Graham (Glasgow), Doug learned *in vivo* analytical skills focused on the biological role of the chemokine receptors CXCR2, CCR1, CCR2, CCR3 and CCR5, and was part of the team that demonstrated their specificity of function during leukocyte recruitment.

Doug moved to the Wellcome centre for cell-matrix research at the University of Manchester in 2018 to start his lab as a University of Manchester Presidential Fellow before becoming a Wellcome Trust and Royal Society funded Sir Henry Dale fellow. The glyco/chemokine immunology group that he leads is now focused on using multi-disciplinary approaches from biophysics to *in vivo* real-time imaging to dissect the role of the extracellular matrix in regulating chemokine biology and increasingly immunology more widely. His group has now published two papers on BioRxiv, and a number of reviews, beginning to shed light on these topics and paving the way for future research in this area.

https://www.research.manchester.ac.uk/portal/en/researchers/douglas-dyer(556fc70c-17d0-45a0-ac02-6aff92ca9760).html

https://twitter.com/tripledougdyer

Research of Board member Rebecca Miller

Rebecca Louise Miller, PhD – Associate Professor at the Copenhagen Center for Glycomics, Department of Molecular and Cellular Medicine.

Scientific career

2011-12: Postdoctoral Researcher, Dept. of Molecular and Cellular Biology, University of California, UC Davis, CA.

2012-14: Postdoctoral Researcher, Institute of Integrative Biology, University of Liverpool, UK.

2015-16: Postdoctoral Researcher, Department of Oncology, University of Oxford, UK.

2016-17: Postdoctoral Researcher, Argonaut Therapeutics Limited, Oxford, UK.

2017-18: Postdoctoral Researcher, Department of Oncology, University of Oxford, UK.

2018-21: Assistant Professor, Copenhagen Center for Glycomics, University of Copenhagen, DK.

2021- : Associate Professor, Copenhagen Center for Glycomics, University of Copenhagen, DK.

Research

Glycosylation is one of the most common post-translational modifications (PTMs) of proteins essential to all eukaryotic systems, where glycans (ie. carbohydrates) are covalently attached to the protein (Fig. 1). The biological role of glycosylation in the extracellular matrix is vast, including; trafficking cells in the immune system, cell adhesion, recognizing foreign materials, controlling cell metabolism, to providing cartilage and tendon flexibility. Research and development to harness these extracellular glycomes, even when limited to the simplest forms of glycosylation, have led to the approvals of over 200 biologicals to treat diverse diseases with a global market value of €250 billion and a 10% annual growth. Glycosaminoglycan (GAG) polysaccharides is one example of these carbohydrates, they have relatively simple repeating disaccharide backbones, however, their complexity and structural diversity arise through extensive sulfation of these disaccharides (Fig. 1) and my group focuses predominately on this complex molecule.

Mammalian glycosaminoglycans (GAGs) are sulfated polysaccharides commonly exemplified by their most abundant forms: heparin, heparan sulfate (HS), chondroitin/dermatan sulfate (CS/DS), keratan sulfate (KS) and hyaluronic acid (HA). GAGs are major components of the extracellular matrix that regulate many diverse functions, such as cell migration, injury, anticoagulation, angiogenesis, inflammation, as well as normal growth and development. GAGs are primarily defined by their disaccharide repeats that are extensively sulfated in distinct patterns along the chain. These sulfation codes are the source of the structural complexity and heterogeneity of GAGs, which dictate

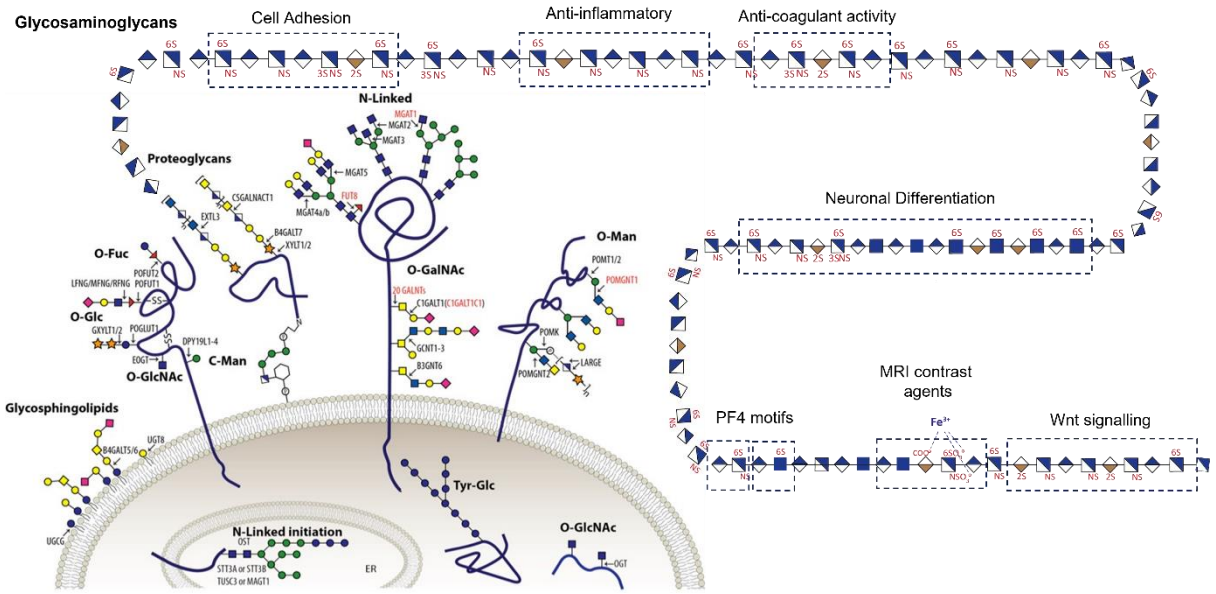


Figure 1. All cells are covered in a husk of carbohydrates including glycolipids, O- and N-linked glycans and glycosaminoglycans which is essential for all life.

the functional properties. Despite the biological importance of GAGs, analysis continues to be challenging. Illustrating this conundrum is the widely used anti-coagulant drug heparin, a highly sulfated heparan sulfate (HS) isolated from animals, which is a heterogenous mixture lacking complete structural characterization.

Whilst heparin is successful in preventing and treating thromboembolic events, a great variety of other biological effects are attributed to the heterogeneous heparin, including anti-inflammatory, anti-metastatic, and anti-viral properties. Given that the effects are expected to arise from distinct sulfation codes in GAGs, our knowledge of which codes lead to therapeutic effects is very limited due to the lack of tools to read the sulfation codes in GAGs, where my group works on the development of tools and technologies to define these sulfation codes and to develop homogenous GAG chains as therapeutics.

The biosynthesis of GAGs involves a large number of glycosyltransferases and over 40 sulfotransferases. Using the KO/KI of genes orchestrating the biosynthesis of GAGs in CHO cells, we have been able to produce cell-derived libraries that display distinct heparin, HS, CS, and DS on the cell surface (Fig 2). Therefore, the GAG program aims to investigate how the sulfation codes lead to specific biochemical properties. The availability of this GAG library (i) advances the dissection of these sulfation codes into structure-function relationships, (ii) enables the ability to tailor the design of homogenous GAG molecules with the desired biological effects, such as anti-coagulant, anti-inflammatory or anti-viral properties, and (iii) enables the development of analytical tools and

technology development, including a variety of mass spectrometry instruments and single molecule imaging modalities of GAG:protein complexes, and (iv) sparks new strategies for molecular dissection of GAG specific roles such as proliferation, adhesion, angiogenesis, and protein gradients (such as TGF-beta, Wnt) involved in growth and development.

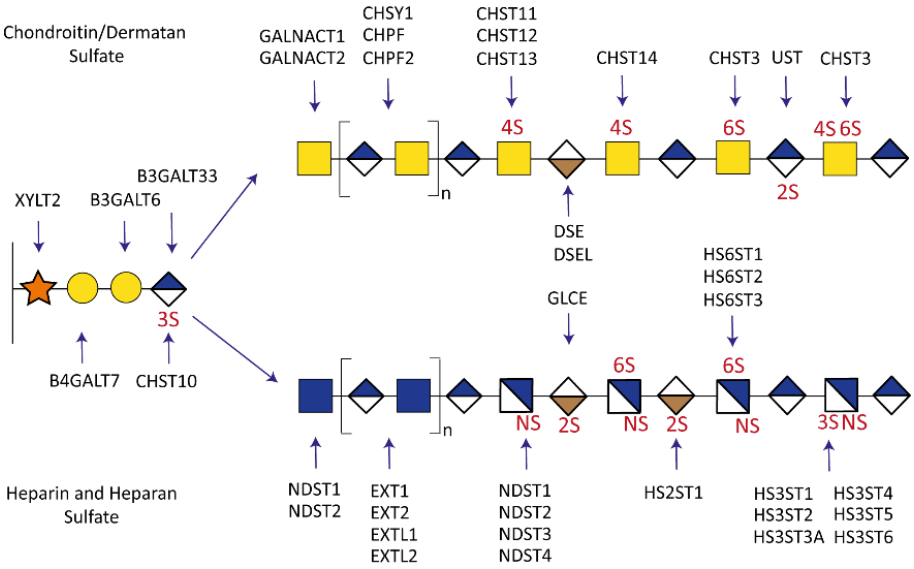


Figure 2. Genetic dissection of the GAG biosynthetic pathway.

Recent stories

We have recently made strides in a cell-based anticoagulant heparin with comprehensive disaccharide characterisation.
https://healthsciences.ku.dk/newsfaculty-news/2022/02/blood-thinning-medications-typically-come-from-pig-intestines.-but-maybe-not-very-much-anymore/#:~:text=The%20blood%2Dthinning%20drug%20heparin,and%20the%20result%20is%20promising.

Karlsson R, Chopra P, Joshi A, Yang Z Vakhrushev SY, Clausen TM, Painter CD, Szekeres G, Chen YH, Sandoval DR, Hansen L, Esko JD, Pagel K, Dyer DP, Turnbull JE, Clausen H, Boons GJ, **Miller RL**. Dissecting structure-function of 3-O-sulfated heparin and engineered heparan sulfates. **Sci Adv** (2021), 7; 52, eabl6026. https://www.science.org/doi/10.1126/sciadv.abl6026

The development of an ion mobility mass spectrometry method to analyse biologically relevant glycosaminoglycan motifs
https://healthsciences.ku.dk/newsfaculty-news/2020/03/researchers-invent-method-to-unlock-potential-of-widely-used-drug/

Miller RL, Guimond SE, Schwörer R, Zubkova OV, Tyler PC, Xu Y, Liu J, Boons GJ, Grabarics M, Manz C, Hofmann J, Karlsson N, Turnbull JE, Struwe WB, Pagel K (2020) SIMMS^2: Shotgun Ion Mobility Mass Spectrometry of Heparan Sulfate Saccharides. **Nat Commun** 11:1481-1493. https://www.nature.com/articles/s41467-020-15284-y

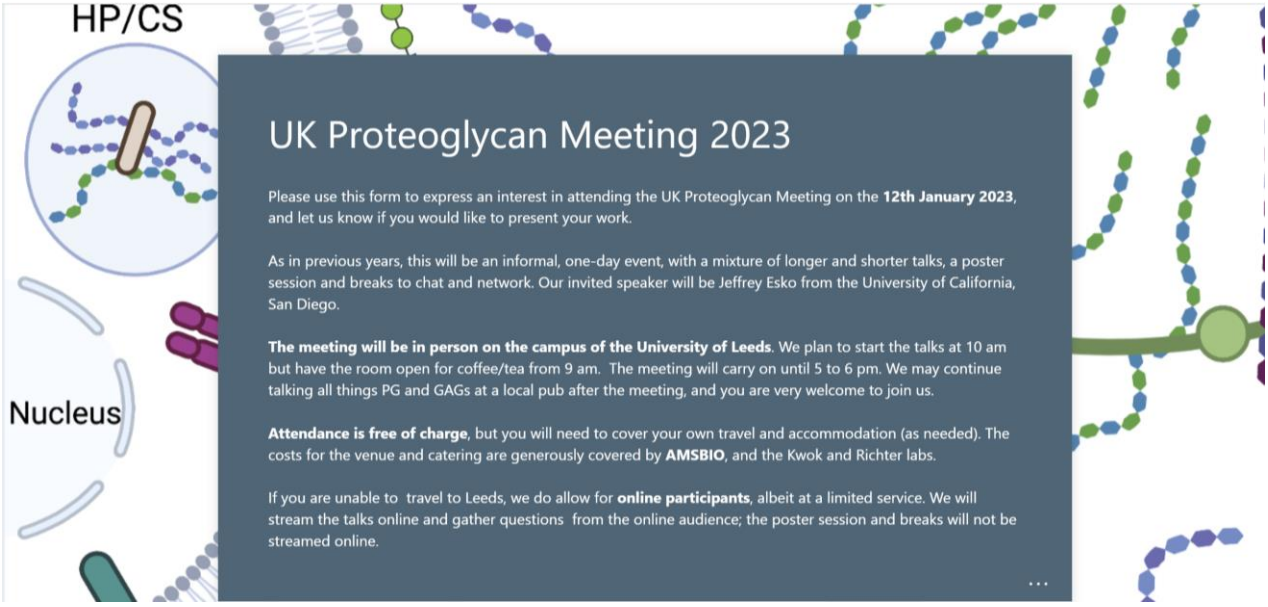
Matrix Biology PhD course 2023

The matrix biology PhD course will take place Wednesday 8th – Friday 10th November next year. We will be announcing the program and registration in 2023.

UK Proteoglycans 2023

The UK PG Meeting 2023 will take place at the University of Leeds, on 12 January. The meeting is open to anyone interested in proteoglycans and glycosaminoglycans, in the UK and further afield. If there are people you know who would like to come along, please pass this email on.

If you would like to join, please register and let us know if you would like to present through this link: https://forms.office.com/r/wEQ4XdWq7H



Membership

Our membership (100 DKK) includes free registration to our annual meeting, 3-4 newsletters a year, updates on position openings and conferences as well as eligibility for travel grants to local and international matrix meetings. We also appreciate any extra donations and will acknowledge your contribution in our next newsletter. Please remember to EMAIL with “Membership” as the subject your name and receipt of your payment to **dsmb.dk@gmail.com**.

You can pay by any of these options:

1) Transferring via MobilePay to **46151** (Danish Society for Matrix Biology). Please indicate “DSMB membership and the name” on the payment ***OR***

2) Transferring to the DSMB bank account: Reg: 1551 Account: 1227130 (Danske bank). Please indicate "DSMB membership and the name" on the bank transfer ***OR***

3) Email our treasurer Chloé Yeung (chloe.yeung@gmail.com) if you need to transfer from an international account or use an alternative method.