

Mini-Symposium: The Glycocalyx and its Role in Immunomodulatory Therapeutic Strategies

March 8, 2024 | 12:00 - 2:30 p.m.

121 Building | 1111 Classroom

Zoom: <https://kgi.zoom.us/j/94707393644>

SCHEDULE

Time	Speaker
12:00 - 12:10	Dr. Jim Sterling, PhD Program Director, Keck Graduate Institute <ul style="list-style-type: none">• Symposium Overview and Introductions
12:10 - 1:00	Dr. Tracy M. Handel, Distinguished Professor, Skaggs School of Pharmacy, UCSD <ul style="list-style-type: none">• Keynote Speaker
1:00 - 1:20	Dr. Shenda Baker, PhD President and CEO, Synedgen, Inc.
1:20 - 1:40	Megan Lord, Professor, University of New South Wales
1:40 - 2:00	Megan Priestly, PhD Student, University of Manchester
2:00 - 2:20	William Ceely, PhD Candidate in Mathematics, Claremont Graduate University
2:20 - 2:30	Dr. Jim Sterling, PhD Program Director, Keck Graduate Institute <ul style="list-style-type: none">• Closing Remarks/Adjourn.

We are excited to present this hybrid online/in-person Mini-Symposium of presenters and attendees from around the globe! The presenters each contribute a unique perspective on multivalent - binding of immunomodulatory proteins to cell-surface macromolecular glycans. Speakers will be delighted to answer your questions. Join us!



Dr. Tracy M. Handel

Choosing a Partner: Chemokine Interactions with Receptors vs Glycosaminoglycans

Chemokines are master regulators of cell migration in the context of immune system function. They are also implicated in many diseases particularly inflammatory diseases and cancer. Chemokines have two types of receptors that are both important for regulating cell migration: (i) G protein-coupled (chemokine) receptors, which are expressed on migrating cells and coordinate cell movement and (ii) glycosaminoglycans (GAGs), which are ubiquitously expressed and contribute to chemokine localization. In this presentation, our current understanding of how chemokines bind and activate GPCRs and GAGs will be described as well as implications for how chemokines may be presented on GAGs to receptors.

Dr. Shenda Baker

Targeting the glycocalyx with modified glycopolymers to treat infection and inflammation



Innate immune receptors and their activity is modulated by the presence of a highly negatively charged glycocalyx. Further, the glycocalyx plays a key role in regulating transport into and out of cells, as well as along cell surfaces. The use of a highly cationic, safe glycopolymer to modulate interactions at mucous and dermal cell surfaces through targeting the glycocalyx will be discussed.

Professor Megan Lord

Toward improved drug delivery across the endothelium: Affinity interactions between glycopolymers and the endothelial glycocalyx



Delivery systems are widely designed to transport therapeutics to target tissues via the bloodstream. Endothelial cells lining blood vessels are coated in an extracellular matrix called the glycocalyx. While the role of the glycocalyx in regulating transport to the cell membrane is undisputable, it has been largely overlooked in both the design of delivery systems and their biological evaluation. Here, we will discuss the role of biomaterial affinity for the glycocalyx in mediating interactions with the glycocalyx. We use chitosan-based glycopolymers leveraging their molecular recognition moieties for glycans to yield insights into biomaterial properties which enable interactions with the glycocalyx.

Megan Priestley, PhD Student

Heparan sulfate on the immune cell surface regulates their migration into skin



The glycocalyx has been shown to regulate immune cell recruitment during inflammation, most often in an endothelial context. My work shows that heparan sulfate on the surface of immune cells themselves may regulate their migration into skin in a mouse model of psoriasis, whilst we observed little change of HS on the endothelium. These findings emphasise the importance of HS proteoglycans to leukocyte recruitment in inflammatory disease but challenge the model that these proteoglycans are primarily endothelial. We also demonstrated that heparan sulfate mimetics enhance skin inflammation rather than reduce it, urging caution on their use to treat inflammatory diseases.



William Ceely, PhD Candidate

Mathematical Modeling Applications of Glycosaminoglycan Brushes in Microscale Biology

Glycosaminoglycans are typically anionic and can span domains of up to hundreds of nanometers and even micron length scales. The structures exist in crowded environments that are dominated by multivalent electrostatic interactions that can be modeled using mean-field continuum approaches that represent underlying molecular biophysics. Both steady state modified Poisson-Boltzmann models and transient modified Poisson-Nernst-Planck models that incorporate important ion-specific effects can be used. The results quantify how electroneutrality is attained through ion electrophoresis, spatially-varying permittivity hydration forces, and ion-specific pairing.