Preface to Special Issue: “Glycomechanics: Sugar Coating Blood Cell–Endothelial Interactions in Shear Flow”

Genomic and proteomic based publications have increased exponentially over the last decade, while glycomics research focused on the complement of sugars produced by an organism, is in its relative infancy. In the human cell, for example, almost all secreted and cell-surface proteins are modified by sugars. Protein glycosylation provides for receptor mediated specificity and affinity modulation that is central to regulation of cellular interactions including adhesion, growth factor functions, and biomolecule/cell half-life in circulation. Further, by forming a glycocalyx layer on almost all cells the glycans are essential regulators of cell and molecular transport.

While the number of biological processes regulated by glycans is vast, this special issue is focused on selected aspects that are of current interest to the Biomedical Engineering community. A central theme is the link between specific glycosylation patterns on membrane proteins and how this regulates a diverse set of mechanically-based cell functions in leukocytes, stem cells, and endothelial cells. How receptor-ligand interactions confer specificity during immune cell recruitment, in particular under the shear stress of blood flow, have fascinated biomedical engineers for decades. It was a mutual interest in how leukocytes adhere in the linear shear field produced by blood flow that motivated our early research collaborations. Employing cone-plate viscometry, we observed that selectins are endowed with unique bond properties that regulate the efficiency of adhesion as a function of shear rate and stress.^{1–3} In the ensuing decade much has been discovered regarding how each selectin exploits subtle differences in sialylation and fucosylation patterns in guiding blood cell recruitment into tissues during the multistep process of emigration. A common theme that has emerged is that a specific pattern of glycosylation adapted by a particular cell lineage can endow it with well-defined biophysical properties that can dictate temporal and spatial regulation of cell phenotype. These include endothelial adhesiveness, permeability, and mechanotransduction that in turn influence recruitment of tumor, dendritic, leukocyte, and hematopoietic stem cells. A prime example of this is illustrated in Robert Sackstein’s review of HCELL. This glycoform of CD44 converts it to a potent E-selectin ligand that in turn effectively targets human mesenchymal stem cell homing to bone marrow.

In the case of dendritic cells and their regulation of the adaptive immune response, Paula Alexandra Videira in her review shows how glycosylation dictates their interaction with endothelium under shear and how it may be exploited to guide therapy. Particularly exciting is the promise that carbohydrate engineering can tailor receptor-ligand interactions under force to translate clinical solutions. Michael King reveals how a detailed understanding of fluid mechanical forces on glycoprotein mediated cancer cell rolling and adhesion can be used to guide the design of tumor cell capture and diagnostic lab-on-a-chip devices. Kevin Yarema’s review reveals how oligosaccharide engineering can dramatically alter leukocyte extravasation and cancer cell metastasis by targeting specific glycosylation patterns through feeding cells synthetic monosaccharide analogs. Sriram Neelamegham in his review describes a systems bioengineering *in silico* approach to model the process of N- and O-linked glycosylation and highlights strategies to alter glyco-metabolism to elicit desired structure and function. Finally, this special issue is anchored by the reviews of Fitz-Roy Curry and Herbert Lipowsky whose significant contributions elucidate how the dynamics of synthesis and degradation of the polysaccharide rich glycocalyx structures function to regulate transvascular exchange and vascular permeability.

In conclusion, the current issue highlights areas of current interest to biomedical engineers and maps out additional directions that may prove to be fruitful avenues for future research, exploration and discovery. We hope that you enjoy this special issue dedicated to the emerging field of Glycomechanics.

REFERENCES

- ¹Konstantopoulos, K., S. Neelamegham, A. R. Burns, G. S. Kansas, K. R. Snapp, E. L. Berg, J. D. Hellums, L. V. McIntire, and S. I. Simon. Venous levels of shear induce neutrophil-platelet and neutrophil aggregation in blood via P-selectin and $\beta 2$ -integrin. *Circulation* 98:873–882, 1998.
- ²Neelamegham, S., A. D. Taylor, A. R. Burns, C. W. Smith, and S. I. Simon. Hydrodynamic shear reveals distinct roles for LFA-1 and Mac-1 in Neutrophil Adhesion to ICAM-1. *Blood* 92(5):1626–1633, 1998.

³Taylor, A., S. Neelamegham, C. W. Smith, D. Hellums, and S. I. Simon. Molecular dynamics of the transition from L-selectin to β 2-integrin dependent neutrophil adhesion. *Biophys. J.* 71:3488–3500, 1996.

SCOTT I. SIMON
Department of Biomedical Engineering
University of California, Davis
Electronic mail: sisimon@ucdavis.edu

SRIRAM NEELAMEGHAM
Department of Chemical Engineering
State University of New York at Buffalo
Electronic mail: Neel@buffalo.edu

KONSTANTINOS KONSTANTOPOULOS
Department of Chemical and Biomolecular Engineering
The Johns Hopkins University
Electronic mail: konstant@jhu.edu