

Mucin self-interactions studied at the single-molecule level

K. E. Haugstad*, C. F. Brewer**, T. A. Gerken#, B. T. Stokke* and M. Sletmoen*

*Section of Biophysics and Medical Technology, Dept. of Physics, The Norwegian University of Science and Technology, NTNU, Norway

**Departments of Molecular Pharmacology, and Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461, USA,

W. A. Bernbaum Center for Cystic Fibrosis Research, Departments of Pediatrics and Biochemistry, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106-4948, USA.

Increased awareness of the important roles of carbohydrates in a variety of physiological and pathological processes has made 'glycomics' (the study of glycan decoration pattern of cells) emerge as a frontier research field. Complex oligosaccharides found in glycoconjugates are known to act as receptors for a number of carbohydrate binding proteins (lectins). Furthermore, the role of carbohydrate-carbohydrate interactions cell-cell and cell-extracellular matrix interactions are being increasingly explored. However, the understanding of the molecular basis of this association is still in its infancy, and the rich supply of potential low affinity binding sites offered by carbohydrates, arranged in a polyvalent array, makes such interactions challenging to study. The structural heterogeneity of many carbohydrate structures add to the complexity and experimental challenges.

We have previously used dynamic force spectroscopy to investigate pairs of SBA and Tn-PSM as a tool to understand the mechanisms of binding and cross-linking of lectins with multivalent glycoprotein receptors.¹ Recently, we have demonstrated that the sensitive force probes AFM and optical tweezers are also potent tool for determining mucin interactions and their dependence on specific carbohydrate decoration patterns. By quantifying the strength, lifetimes and free energy of self-associations occurring between mucin molecules with different carbohydrate decoration patterns, we have taken the first steps towards unravelling the mechanism governing such interactions. The interaction strengths varied in the range 37 to 55 pN at a force loading rate equal to 6 nN/s. The data allowed us to adress questions related to the importance of the sialic acid group for the self-interaction probability, and more generally relate carbohydrate decoration patterns to interaction strengths and probabilities.

(1) Sletmoen, M.; Dam, T. K.; Gerken, T. A.; Stokke, B. T.; Brewer, C. F. *Biopolymers* 2009, *91*, 719-728.