



## **Screening of Protein Glycosylation to Distinguish between Health and Disease State**

Kristina Thomsson

Home Department: Department of Medical Biochemistry, Göteborg University  
External Lab: Proteome Systems Ltd, Locked Bag 2073, North Ryde, Sydney, NSW 1670, Australia  
Doctor's Degree: 2000-05-19, Department of Medical Biochemistry, Göteborg University

Project Description: The aim of the current project is to develop strategies for performing high throughput screening of glycosylation of proteins, to enable comparative studies between large numbers of individuals and to distinguish between health and disease states. Using liquid chromatography-mass spectrometry we can perform semi-quantitative studies allowing partial characterization of saccharides in short time, consuming small amounts of starting material such as from western blots.

Mucins are large (0.1-10 Mda) and heavily O-glycosylated proteins. Mucins make up the major protein component in the mucus that covers the epithelial surfaces of the respiratory, gastrointestinal and genitourinary tracts. The mucus layer lubricates the underlying surface and acts as a protective barrier. The glycosylation epitopes serve as interaction sites for bacteria. At the same time, the mucus layer permits an exchange of nutrients, salt, and water. We are currently screening the glycosylation of the two major mucins MUC7 and MUC5B in saliva from thirty individuals, using gel electrophoresis of 50 ul saliva on agarose gels followed by western blots, release of oligosaccharides from the proteins and analysis with liquid chromatography-mass spectrometry. Preliminary data show that MUC7 appears to carry a consistent glycosylation, whereas MUC5B varies extensively between individuals, with regard to terminal epitopes and the relative distribution of glycoforms. To a large extent, these variations can be explained by the individual's inherited repertoire of glycosyltransferases that define the ABO-, the secretor- and Lewis blood group status. Our experiments show that there is a considerable natural variation as to mucin glycosylation among healthy individuals, and more so than we had expected.

Many clinical studies suggest a link between blood group/secretor status and susceptibility to mucus-related diseases. Considering that if the glycosylation of MUC5B is so dependent on the presence of these transferases, it could be hypothesized that MUC5B would be a key player, carrying the epitopes that either promote or enhance bacterial binding and/or interfere with immune response reactions, leading to a decreased or increased susceptibility.