GLYCOMICS AND CANCER

Aberrant glycosylation has been implicated in many diseases due to changes associated with biological function and protein folding. Several studies have now clearly established the glycosylation changes associated in cancer. Alteration of the cell surface glycosylation can lead to enhanced tumour progression and invasion. Identification of relevant glycosylation changes in proteins could facilitate novel glycan based biomarkers for diagnostic and prognostic indicators of cancer.

DIFFERENTIATING TISSUE TYPES BY IMAGING MASS SPECTROMETRY OF GLYCANS

Recent developments in targeting protein distribution in tissue sections by spatial proteomics imaging have paved the way for retrospective in situ mass spectrometry (MS) analyses of formalin-fixed clinical tissue samples. We are using enzymatic mediated release and measurement of N-linked glycans from sections of formalin-fixed tissue to allow analyses of tissue-specific N-glycosylation profiles that can differentiate a tumour from other tissue types.
DEVELOPMENT OF ADVANCED MASS SPECTROMETRY TECHNIQUES TO CHARACTERISE GLYCOCONJUGATES

There currently are three main mass spectrometric analytical approaches to the analysis of protein glycosylation which are at various levels of technological development: Glycomics (the global structural analysis of N- and O-glycans attached to proteins); glycoprotein (glycan structure and site analysis of a single protein); and glycoproteomics (glycan structure and site analysis of complex mixtures of glycoproteins).

GLYCOINFORMATICS

As has been the case in proteomics and genomics, an essential requirement for glycomics and glycoproteomics to progress out of our relatively small community into the greater scientific sphere is the development of informatics tools to interpret and store diverse experimental glycan data and enable public accessibility. Ultimately the analytical data must relate to the function of these glycans and their glycoconjugates. UniCarbKB (www.unicarbKB.org) is an initiative that is providing an online information storage and search platform for glycoproteomics research.

INNATE PROTECTION AGAINST PATHOGENS BY GLYCANS IN BODILY FLUIDS

One of the key initial processes involved in pathogen infection is the attachment to host cell receptors, typically glycans (sugars) conjugated to proteins or lipids on epithelial cell surfaces. We have shown that the host provides an ingenious innate defence mechanism that uses the glycoproteins in their secreted fluids to competitively bind to the bacterial pathogens to prevent infection. Our research shows that bacteria bind differentially to glycan moieties on secreted glycoproteins from human tears, milk, saliva and sweat, potentially providing decoys for selective adhesion and clearance of pathogens as the secretory fluids wash the epithelial cell surface.

NANOPARTICLE LABELLING FOR BIOMEDICAL IMAGING

Despite significant advancement in the methodology used to conjugate, incorporate and visualize fluorescent molecules at the cellular and tissue levels, biomedical imaging predominantly relies on the limitations of established fluorescent molecules. These fluorescent dyes and conjugates are highly susceptible to photobleaching and compete with cellular autofluorescence, making biomedical imaging unreliable, difficult and time consuming in many cases. In addition, some proteins have low copy numbers and/or poor antibody recognition, further making detection and imaging difficult. We are developing better methods for imaging with labelled with fluorescent nanodiamonds or lanthanide chelates. These tags have increased signal and photostability and can also discriminate against tissue/cell autofluorescence.

Selected Publications
