Visualising N-glycosylation patterns in cancer and non-cancer cells

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Glycomics is the study of the structure and function of complex biological carbohydrates (or glycans) that have been estimated to be attached to at least 50% of the proteins encoded by the mammalian genome. Our work is analysing and defining the function of these molecules in the living system. Glycans are found in all eukaryotes and prokaryotes, where they are expressed on the surfaces of cells and therefore serve as the first molecules involved in cell-cell contact. Their capacity for heterogeneity confers an ability to "fine-tune" the functions of proteins, which is integral in crucial processes such as development, blood coagulation, immune recognition, fertility, and more. Analysis of these post-translational modifications requires specialized sample preparation, mass spectrometric and bioinformatic techniques which our lab is applying to a range of glycobiological questions. 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 formalinfixed paraffin-embedded clinical tissue samples. Aberrant glycosylation on these proteins has been implicated in many diseases due to changes associated with biological function and protein folding. 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 in the same section. Alteration of the cell surface glycosylation can lead to enhanced tumour progression and invasion and identification of relevant glycosylation changes on proteins could facilitate novel glycan based biomarkers for diagnostic and prognostic indicators of cancer.