COMPREHENSIVE CHARACTERIZATION OF CELL-SURFACE GLYCOPROTEINS AND THEIR DYNAMICS USING MASS SPECTROMETRY-BASED PROTEOMICS

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The cell surface contains many important proteins, such as receptors and transporters, and almost all of them are glycosylated. These surface glycoproteins regulate nearly every extracellular activity, including cell-cell communication and cell immune response. Systematic characterization of surface glycoproteins and their dynamics will advance our understanding of glycoprotein functions, cellular activities, and disease mechanisms. In our lab, we have worked on developing novel and effective methods to globally analyze surface glycoproteins. Integrating metabolic labeling and bioorthogonal chemistry, we can selectively separate and enrich glycoproteins only from the cell surface, enabling us to comprehensively and site-specifically analyze surface glycoproteins [1-2]. The method was applied to systematically analyze surface glycoproteins in different types of human cells. The results revealed that besides cell-specific glycoproteins, the uniqueness of each cell type further arises from differential expression of surface glycoproteins [3].
One big advantage of this method is that the experimental conditions are very mild, which allows for studying the dynamics of surface glycoproteins. In combination with multiplex proteomics, we systematically quantified the degradation of surface glycoproteins in human cells and the dynamics of surface glycoproteins during cell immune response [4-5]. For the dynamics of surface proteins in monocytes and macrophages with the infection, it was found that the surface glycoproteomes were remodeled in cells during the bacterial infection, including the expression of new glycoproteins to the surface and the removal/internalization of existing surface glycoproteins [5]. A comparison of the immune responses between monocytes and macrophages showed the similarities and differences between their surface glycoproteomes, and the priming of monocytes for the response during the differentiation process. Besides reported markers, the results revealed dramatic changes of other surface glycoproteins that have never been reported to play a role in the immune system. Furthermore, we systematically investigated the trafficking of glycoproteins on the cell surface [6]. The results demonstrated that protein folding, N-glycosylation, and N-glycan maturity have distinct impacts on the trafficking of surface glycoproteins. Considering the importance of cell-surface glycoproteins, systematic and quantitative analysis of these glycoproteins will allow us to discover novel biomarkers for disease detection and identify drug targets for disease treatment.

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