ProMoSCOPE™: Study the Role of Glycosylation in Infectious Diseases at Single Cell Level

Binding of pathogens such as viruses or bacteria to the host cell surface is the key step in pathogen infection. The molecules that are most commonly used for attachment and subsequent entry can be proteins, glycoproteins, lipids or glycolipids. Glycans, the sugar residues connected to proteins or lipids, have been known to play major metabolic, structural and physical role in biological systems (Figure 1A). In the research field of infectious diseases, glycans on host cells have been implicated in influencing pathogen infection, determining the host range and tissue tropism (2, 3) (Figure 1B).

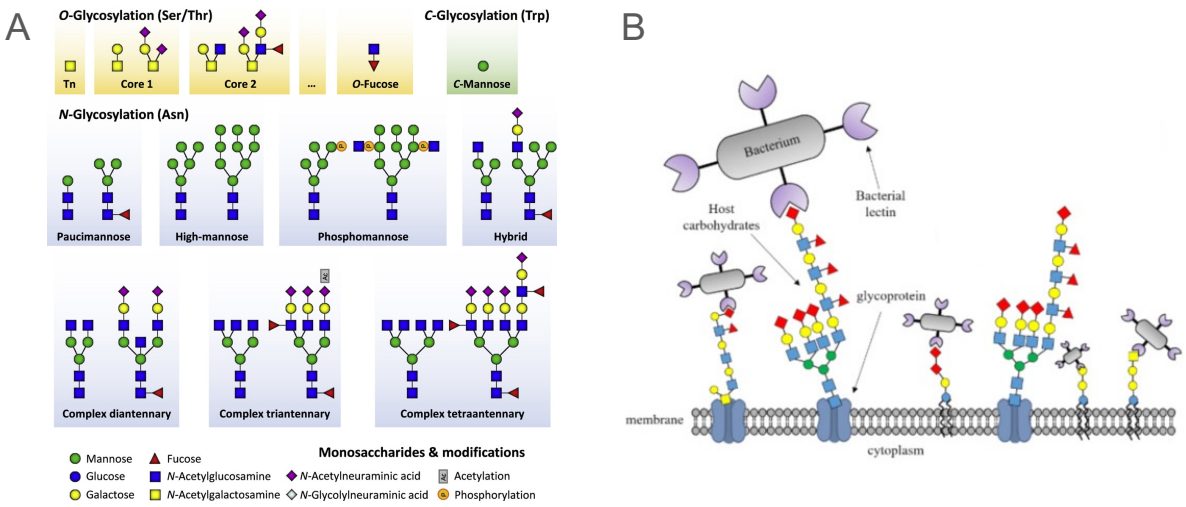

Figure 1 Glycosylation and its role in attachment of pathogens onto cell surface

A. Glycosylation encompasses dozens of different types of sugar residues arranged in various fashions (image from (1)).

B. Schematic representation of interactions in bacterial pathogenesis with specific glycans on host cell (image adapted from (4)).

Cell surface glycan structures of the host cells undergo dynamic changes that reflect cell types and states (5, 6). Understanding the dynamics of glycosylation at the cell surface might therefore be crucial for getting deeper insights into the process of viral and bacterial infection. Glycans are also involved in the host immune reaction to pathogens: trafficking of leukocytes from blood stream to the site of inflammation is heavily dependent on the interaction between glycans present on leukocytes and the endothelium of the blood vessel (7). The adaptive immune activation is also affected by glycosylation: the proper function of T lymphocytes is determined by their surface receptors, which in turn are glycosylated (8).

Despite its significance, a method for precise prediction of glycan structures based on gene expression profiles has not been established yet. Similarly, the quantification of glycosylation levels at the single cell level has only rarely been addressed until now, despite its important role in the infection and immune response process.

To enable the analysis of cell surface glycosylation in individual single cells, Singleron has developed a unique multi-modal ProMoSCOPE™ single cell sequencing technology. ProMoSCOPE allows for chemoenzymatic labelling of the N-acetyllactosamines (LacNAc), disaccharides commonly found in the cell surface glycans, using a dedicated ProMoSCOPE tag. Combined with Singleron's SCOPE-chip® technology for high-throughput single cell transcriptome profiling, ProMoSCOPE simultaneously detects glycosylation levels and gene expression in the same single cells. The LacNAc quantification results obtained with ProMoSCOPE technology were confirmed by flow cytometry (Figure 2), demonstrating that our approach provides reliable detection of LacNac levels on the cellular surface. The unique combination of transcriptomics information together with glycosylation quantification at single cell resolution provides a new tool to understand host-pathogen interactions and host immune defense in infectious diseases.

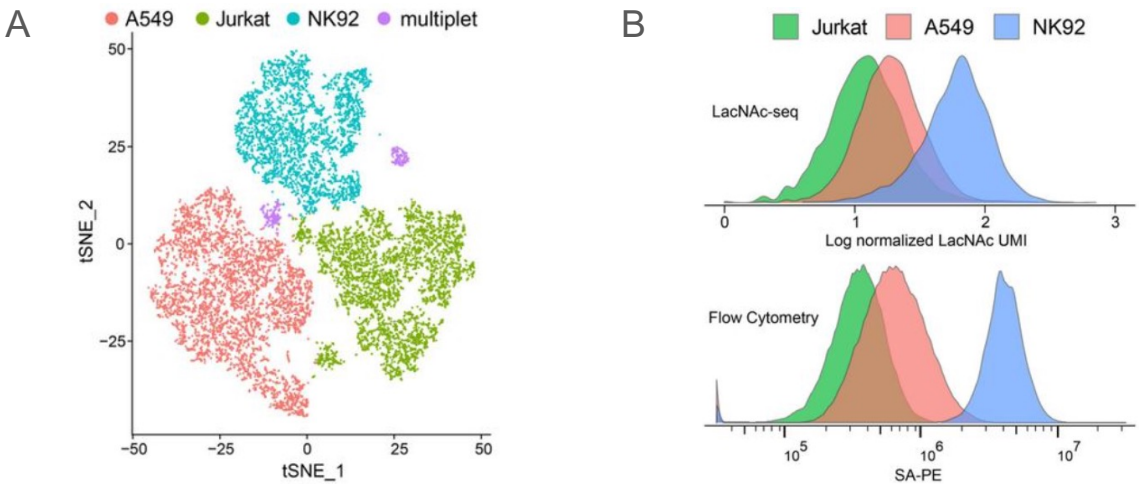

Figure 2. ProMoSCOPE enables simultaneous transcriptome profiling and detection of cell surface LacNAc at single cell level

A. Cell mixtures of Jurkat, NK-92, A549 cell lines were processed with ProMoSCOPE technology. t-SNE plot shows transcriptome-based clustering of 12,343 cells (image from (9)).

B. Histograms showing LacNAc density of Jurkat, NK-92, A549 cell lines barcoded with ProMoSCOPE tags (up) and labeled with GDP-fucose-biotin probe, followed by streptavidin-APC staining for quantification by flow cytometry (bottom) (image from (9)).

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