

## INVITED LECTURE H15

### Proteomics in the discovery of cell-surface markers on stem cells

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The concept of cell-based therapy has been advocated as a novel approach for treating diseases or conditions where regeneration of cells, tissue and/or potentially organs is required. A promising source for cell replacement therapies is stem cells, but the success of this approach will ultimately rely on the ability to isolate primary stem or progenitor cells. Cell surface protein markers will play a critical role in this step. Current methodologies for the identification of cell surface protein markers rely primarily on antibody availability and flow cytometry, but many cell surface proteins remain undetectable. Proteomic technologies now offer the possibility to specifically identify and investigate the cell surface subproteome in a quantitative and discovery-driven manner. We have developed a methodology for the multiplexed, quantitative, mass-spectrometric identification of cell surface glycoproteins, and their N-glycosites, which can be used to phenotype cells, including stem cells, without antibodies in an unbiased fashion, and without *a priori* knowledge. The cell surface capturing (CSC) technology allows for the isolation, identification and quantification of N-glycosites from the extracellular domains of cell surface proteins in a discovery-driven mode. Several hundred *bona fide* cell surface glycoproteins and their N-glycosites, including CD-annotated and novel proteins, can be identified in a single MS experiment. CSC technology enables a more comprehensive view of the cell surface glycoprotein landscape, and can detect glycoproteins as potential differentiation markers that are currently not accessible by other means. When integrated into existing stem cell research strategies, proteomic technologies offer a new avenue of investigation towards the molecular understanding of stem cell renewal and differentiation by scratching the surface of the cell.