Signaling in excitable cells in health and disease

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Main Research Area

The group of Martin R. Larsen is focusing on the application of **biological** mass spectrometry in proteomics, especially the characterization of post-translational modifications in proteins and their influence on biological systems and diseases. The current focus in the group is to study cellular signaling in excitable cells, such as pancreatic beta-cells and neurons, and their function in health and disease. One unique new cell model used in the group is brain organoids which is a novel 3D cell system that is able to mimic early human brain development.



Post-translational modifications (PTMomics)

Post-translational modifications (PTMs) are the attachment of small molecules (e.g. phosphate or acetyl) or smaller proteins to proteins after they are synthesized in the cell. PTMs modulate the proteins function, activity, interaction with other biomolecules and location. As such, PTMs are essential for the function of cells, migration of cells and communication between cells.



- More than 400 PTMs are known.
- Approximately 5% of all proteins in the human proteome encode an enzyme for PTM modulation (e.g. 536 kinases and 200 phosphatases that modulate protein phosphorylation.
- Signaling dependent processes in early brain development
 - Neurogenesis \geq
 - Synaptogenesis > Synapse formation **Neural migration**
 - Axonal guidance

Proteomics and PTMs

Brain organoids ("mini-brains") from stem-cells

Day 2 **Patient cells** Study signaling events in: Reprogramming Early brain development Human nerve terminal Day 72 Human neurological diseases Peripheral blood Induced Alzheimer's Disease mononuclear pluripotent stem Parkinson Disease cells (PBMCs) cells (iPSCs) Schizophrenia

Signaling in Nerve Terminals (synaptosomes) in health and disease







endocytosis

Changes in phosphorylation, glycosylation and Lysine-acetylation after 10 sec depolarization of rat synaptosomes **Phosphorylation** Sialylation (glycosylation) Lysine-acetylation





