

# DANDRITE Topical Seminar

## Modulation of Cysteines upon cellular signalling

In this seminar, cysteine modifications will be introduced, including various tools for assessing these and various applications where we have used cysteine-specific proteomics to characterize important cysteine residues in key proteins for cellular signalling, such as T-cell activation and nerve-terminal stimulation.

Cysteine is a relatively low abundant amino acid that is present in almost all mammalian proteins (2.26% occurrence). However, more than 95% of all human proteins contain one or more cysteine residues. Cysteine contains a sulfhydryl group which makes it very reactive and can participate in several possible modifications making it a central amino acid in free radical driven processes. However, in normal proteomics workflows cysteine-containing peptides are used for identification and quantitation on an equal level compared to peptides without cysteines, as proteins conventionally are reduced and alkylated prior to digestion and quantitative analysis.

Conserved Cysteines are often located in active site of enzymes, such as Tyrosine phosphatases or Ubiquitylation ligases, as well as in the hydrophilic part where they are exposed to the cellular solvents and therefore capable of performing interactions with other molecules<sup>1</sup>. The reactive sulfhydryl group allows it to form irreversible (covalent) bond with groups such as sulfonic acid, in addition to making reversible (oxidative) bonds with several groups such as S-nitrosylation, S-sulfenylation, S-glutathionylation, S-sulfhydration, S-acylation as well as inter- and intra- disulphide bonds<sup>2</sup>. In a cellular context, cysteine can be modified with any of the above groups and attain unique functional capabilities, mostly in disulphide bond formation and metal binding. Moreover, it can make such reversible bonds very quickly and in response to sensitive factors such as change in pH or change in cellular oxidative state due to cellular activation with various factors. These attributes allow protein containing redox sensitive cysteine residues to function as oxidases, reductases, peroxidases, disulphide isomerases and transcription factors; critical for maintenance of redox homeostasis of the cell<sup>3</sup>. With its fast response and possibility to modulate protein structure and function one can imagine a significant role of redox sensitive cysteines in signal transduction processes.



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**Date:** Monday 8 July 2024  
**Time:** 13:00-13:30  
**Venue:** 1870-816  
**Address:** Universitetsbyen 81, 8000 Aarhus

**Host:** Poul Nissen

**OPEN TO ALL INTERESTED.**