Structure-function analysis of protein-protein interactions and protease-substrate pairs

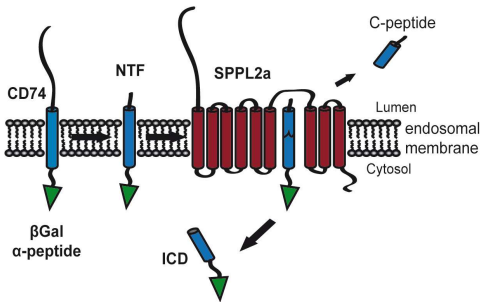
Our group works on intramembrane proteolysis which links protein degradation with signal transduction and thus represents an important regulatory mechanism for cellular homeostasis. We are especially interested in the SPP/SPPL family of intramembrane proteases, which are mechanistically related to the γ-secretase complex that is involved in Alzheimer disease. Our previous work has revealed that these proteases represent regulatory switches which can impact on cellular signal transduction as well as membrane trafficking. Altogether, the substrate spectrum of these proteases as well as their regulatory impact are insufficiently characterized, which we also study *in vivo* using mouse models. In particular, the integration of these proteases into alternative pathways for membrane protein degradation within the endocytic system (ESCRT, MVB pathway) is currently not well characterized and is one of our key interests.

Amongst other aspects, research efforts in our group aim at:

- Defining the substrate spectrum of SPP/SPPL proteases
- Analysing regulatory mechanisms of the proteases
- Analysing the functional impact of the cleavage events based on protein interactions and molecular functions of the respective substrates

In any of our individual projects, regularly questions arise regarding molecular determinants of protein-protein interactions. For example, this can be the interaction of substrate proteins with downstream mediators of signaling or trafficking. Furthermore, we have observed that our proteases of interest are part of larger protein complexes, of which we are currently trying to identify the interaction partners. Another continuous question in our lab are the mechanisms of substrate selection, which decide, why certain type II membrane proteins are cleaved by SPP/SPPL proteases and others are not. In all these cases, mutagenesis approaches are a powerful tool to narrow down which parts and determinants of a given protein are involved in a certain protein-protein interaction or turn a protein into a substrate of SPP/SPPL intramembrane protease. In the summer project you will perform a small mutagenesis project connected to an ongoing project. Thus, you will create a couple of mutants and will analyse these accordingly with the appropriate readouts. Therefore, you will be able to learn, apply and get confident in a broad spectrum of molecular biology, biochemical and cell biological techniques:

- Design of cloning strategies
- Molecular cloning of expression constructs
- Cell culture and transfections
- Western blotting
- Immunofluorescence analysis
- Co-immunoprecipitation



Feel free to get in touch, if you have further questions about the project!

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