2 AIM OF THIS WORK

The degradation of plasma-membrane-derived ceramides takes place in the acidic compartments of the cell, the endosomes and lysososmes, and requires the action of the specific exohydrolase called acid ceramidase and saposins SapC or SapD as activator proteins. Although the general fold of activator proteins belonging to the saposin family is known, our understanding of the structural basis for their modes of interaction with biological membranes is still very limited. The aim of this work is to determine and analyze the crystal structures of human SapC and acid ceramidase, in order to understand their mode of lipid activation and catalytic mechanism, respectively.

The human acid ceramidase is a hydrolase, which consists of two subunits: α and β. An amino-acid sequence analysis of the β-subunit of acid ceramidase revealed that it is homologous to the bacterial enzyme choloylglycine hydrolase from *Clostridium perfringens* (CBAH). CBAH is proposed to be an Ntn-hydrolase and belongs herewith to the large family of amidecleaving enzymes, which play an important role in many diseases and in industrial processes. The aim of this work was to elucidate the three dimensional structure of CBAH. The protein structure should then be compared to acid ceramidase and other hydrolases in order to establish the relationship of CBAH to structural homologous enzymes.

In addition, co-crystallization of CBAH with different substrates should be performed. The resulting substrate-bound structures should be analyzed and their binding modes characterized. This structural information may then aid in the understanding of the molecular basis for the reaction mechanism in CBAH.