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Chemical chaperones for an experimental theraphy of Niemann-Pick disease - investigation in a new strategy for a pharmacological treatment of an inborn metabolic disorder

Initiative: Konformationelle Kontrolle biomolekularer Funktionen (beendet)

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Proper folding of proteins often is achieved with the help of so-called molecular chaperones. Chemical chaperones are synthetic small molecules which can exhibit similar functions to specific target proteins. They have raised vivid attention in connection with lysosomal storage disorders which result from genetic defects of the genes for lysosomal lipid hydrolases. Reduced enzyme activity is often a result of protein misfolding right after synthesis. A rational approach to chemical chaperones is the synthesis of substrate-analogues or competitive inhibitors binding to the active site of an enzyme. The aim of the project is to develop chemical chaperones for acid sphingomyelinase, an enzyme deficient in Niemann-Pick Disease (NPD). It is planned to synthesize potential chaperones and to conduct functional studies in cells derived from NPD-patients. NMR studies of variant and wildtype sphingomyelinase are supposed to provide a deeper understanding of the molecular mechanisms of chemical chaperone action. Moreover, the SAP domain of acid sphingomyelinase shall be examined biophysically for the first time.

Projektbeteiligte

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