Prevention of protein aggregation by competitive ß-sheet binders (Extension)

Initiative: Konformationelle Kontrolle biomolekularer Funktionen (beendet)

Bewilligung: 05.04.2004

Laufzeit: 2 Jahre

In the second phase of the project, emphasis will be placed on the synthesis of ß-sheet binders with optimized solubility, efficiency and specificity for certain pathological proteins, above all the Alz- heimer's protein Aß and the prion protein. The Schrader group will use the whole repertoire of solution and solid phase protocols developed in the first phase, and will also introduce a combinatorial approach in combination with a solid-phase binding assay based on fluorescence detection, which should greatly facilitate the search for efficient and specific ligands. In addition it will be tried to elucidate the structure and conformation of the complexes between the proteins (mainly Aß) and the ß-sheet ligands by various methods (CD, ultracen- trifugation). Detailed kinetic investigations with the optimized ß- sheet binders (ESI-MS, FCS) will be aimed at a better understanding of the mechanism of aggregation prevention and its enhancement. The Ries- ner group will also examine the new ligands in assays aimed at revert- ing seeded aggregation processes and even disaggregation of existing plaques, both with Aß and Prion precipitates. Furthermore, it will strive to better understand and control this process with new specifi- cally designed ß-sheet ligands. All biophysical results will automati- cally feed back into the design and synthesis of optimized ligands.

Projektbeteiligte

Prof. Dr. Detlev Riesner
Universität Düsseldorf
Institut für Physikalische Biologie
Düsseldorf

Prof. Dr. Thomas Schrader
Universität Marburg
Fachbereich Chemie
Marburg