Protein Misfolding and Disease

https://neurodegenerationresearch.eu/survey/protein-misfolding-and-disease/

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Country

Sweden

Title of project or programme

Protein Misfolding and Disease

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4

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Research Abstract

Impaired protein folding and aggregation plays a key role in a wide variety of diseases. One of the most intriguing aspects of these diseases is the auto-catalytic conformational conversion process dictating amyloid proliferation. In this context my research focus on replication of amyloidogenic proteins associated with neurodegeneration in Alzheimer's disease, the prion disease Creutzfeldt-Jakob disease and familial amyloid polyneuropathy. Despite half a century of research there are inadequate treatments, diagnostics, and prognostics for people suffering from protein aggregation diseases while the number of patients is increasing. Many drug companies have surrendered this field despite the growing need. I ascribe this paradox to the topics described in this proposal. I submit that we understand very little about protein aggregate dynamics. Protein misfolding is plastic and affords hard-to-target diverse shape shifting species. In vivo there is a constant tug-of-war for substrate recruitment into the amyloid state and

degradation of misfolded proteins. The fittest amyloid state will prevail in this process. The described project is a long term investigation with obvious high risk, given the difficulties so far. To understand the basics of protein misfolding processes and how misfolded proteins proliferate we study a number of proteins associated with these neurodegenerative diseases, i.e. Amyloid-beta, Prion protein, Transthyretin and Tau using a variety of biophysical techniques. Now we embark on studies of protein aggregates, their dynamics, their specific molecular interfaces, and the energy barriers involved. What provide me with some confidence that we can succeed are our previous achievements. Our discoveries of novel molecular probes and assays and that our proof-of-concept studies of rare mutations laid the foundation for the first drug to be developed against an amyloid disease, are signs that we are on the right track.

Further information available at:

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