Instituts thématiques

Inserm

Institut national
de la santé et de la recherche médicale

PhD-position

Investigating the toxic species in amyloid diseases: a structural perspective from solution scattering

Project description:
Protein fibrillation is associated with fatal amyloid diseases (e.g. Alzheimer's and Parkinson's diseases). Protein fibrils may damage tissue and is an unwanted reservoir of inactive protein. However, the neuro-degenerative effect observed for the mentioned diseases does not arise from the presence of fibrils, but rather from transiently formed non-native soluble oligomeric species. The structural events leading to these functionally central species pass through several un- and re-folding events that remain poorly understood. This is mainly because such non-native structures are formed only in equilibrium with native and fibrillated protein forms and hence structural investigation is a significant challenge. In this PhD-project, we will further advance our previously developed Small-Angle X-ray Scattering data analysis approach (see Langkilde & Vestergaard (2012) *Meth. Mol. Biol*. for details) for a better understanding of the species involved in fibril formation, their mechanism of transformation, and the kinetics of the process. The candidate will develop an automated decomposition procedure, and apply it to several data-sets from different fibrillating proteins that are available in-house, supplemented with new experiments from the recently developed state-of-the-art synchrotron facilities. Protein systems related to Parkinson's, Alzheimer's and eukaryotic prion diseases will be investigated.

The candidate:
We are seeking a strong English-speaking candidate with a background in biostructural studies. Experience with software development and/or small angle scattering data analysis is considered highly advantageous. We welcome applications from all suitably qualified candidates.

The research environment:
The project is a collaboration between the BioSAXS group at the section of Biostructural Research; University of Copenhagen, Denmark (see www.farma.ku.dk/br), and the Centre de Biochimie Structural in Montpellier, France (see www.cbs.cnrs.fr). The candidate will be employed by the *Institute de la Santé et de la recherche Médicale* (INSERM), and will spend approximately half time in each of the two countries. The candidate will also obtain profound experience with high-quality SAXS data collection at the international large-scale infrastructures. The project is financed in concert by the Danish Council for Independent Research; Medical Sciences (Sapere Aude programme) and the INSERM.

HOW TO APPLY:
Applications - in English - must include:

- Cover Letter, detailing your motivation and background for applying for the PhD project
- CV
- Diploma and transcripts of records
- Other information for consideration, e.g. list of publications, peer reviewed and other
- Personal Recommendations if available

Please submit the application by email to Dr. Pau Bernadó at the following mail-address:
pau.bernado@cbs.cnrs.fr. Please mark the mail subject line with 'SAXS/fibrillation'
Deadline: October 15, 2012. Any applications received after the deadline will not be considered.
Expected project start: December 1st 2012.
Interested candidates are welcome to direct any questions to either Associate Professor Bente Vestergaard (bente.vestergaard@sund.ku.dk; +45 35 336 403) or Associate Professor Pau Bernadó (pau.bernado@cbs.cnrs.fr; +33 467417912