Polyglutamine and neurodegeneration

Annalisa Pastore

King's College, London, UK

Abstract:

Amyloids are insoluble protein fibrillar aggregates. The importance of characterizing their aggregation has steadily increased because of their link to human diseases. Misfolding and aggregation of Josephin domain of ataxin-3 is implicated in spinocerebellar ataxia-3. I am going to discuss how this protein sets a new paradigm of aggregation behaviour. Infrared nanospectroscopy, simultaneously exploiting Atomic Force Microscopy and Infrared Spectroscopy, can characterize at the nanoscale the conformational rearrangements of proteins during their aggregation. Here, I will demonstrate that, using this technique, we can *individually* characterize the oligomeric and fibrillar species formed along the amyloid aggregation. I will show how this technique may be used to describe secondary structure, monitoring at the nanoscale an alpha-to-beta transitions. Our results allow us to suggest a new mechanism of aggregation in which self-assembly proceeds from the monomer state to the formation of intermediates with a native structure which only successively evolve into misfolded aggregates and into the final fibrils. These results provide new important perspectives into the way misfolding diseases may be approached.

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Room PH 127

Contact: Matthias Rief, matthias.rief@mytum.de, phone: 089-289-12471