

| | |
|---|---|
| Title: | Conformational Switching and Nanoscale Assembly of Human Prion Protein into Polymorphic Amyloids via Structurally Labile Oligomers |
| Authors: | Arya, S. (/jspui/browse?type=author&value=Arya%2C+S.)<br>Bhattacharya, M. (/jspui/browse?type=author&value=Bhattacharya%2C+M.)<br>Mukhopadhyay, S. (/jspui/browse?type=author&value=Mukhopadhyay%2C+S.) |
| Keywords: | Peptides and proteins<br>Oligomers<br>Sodium dodecyl sulfate<br>Nanofibers |
| Issue Date: | 2015 |
| Publisher: | American Chemical Society |
| Citation: | Biochemistry, 54(51) |
| Abstract: | Conformational switching of the prion protein (PrP) from an α-helical normal cellular form (PrPC) to an aggregation-prone and self-propagating β-rich scrapie form (PrPSc) underlies the molecular basis of pathogenesis in prion diseases. Anionic lipids play a critical role in the misfolding and conformational conversion of the membrane-anchored PrP into the amyloidogenic pathological form. In this work, we have used a diverse array of techniques to interrogate the early intermediates during amyloid formation from recombinant human PrP in the presence of a membrane mimetic anionic detergent such as sodium dodecyl sulfate. We have been able to detect and characterize two distinct types of interconvertible oligomers. Our results demonstrate that highly ordered large β-oligomers represent benign off-pathway intermediates that lack the ability to mature into amyloid fibrils. On the contrary, structurally labile small oligomers are capable of switching to an ordered amyloid-state that exhibits profound toxicity to mammalian cells. Our fluorescence resonance energy transfer measurements revealed that the partially disordered PrP serves as precursors to small amyloid-competent oligomers. These on-pathway oligomers are eventually sequestered into higher order supramolecular assemblies that conformationally mature into polymorphic amyloids possessing varied nanoscale morphology as evident by the atomic force microscopy imaging. The nanoscale diversity of fibril architecture is attributed to the heterogeneous ensemble of early obligatory oligomers and offers a plausible explanation for the existence of multiple prion strains in vivo. |
| Description: | Only IISERM authors are available in the record. |
| URI: | https://pubs.acs.org/doi/abs/10.1021/acs.biochem.5b01110 (https://pubs.acs.org/doi/abs/10.1021/acs.biochem.5b01110)<br>http://hdl.handle.net/123456789/2712 (http://hdl.handle.net/123456789/2712) |
| Appears in Collections: | Research Articles (/jspui/handle/123456789/9) |

Files in This Item:

| File | Description | Size | Format |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Need to add pdf.odt (/jspui/bitstream/123456789/2712/1/Need%20to%20add%20pdf.odt) | 8.63 kB | OpenDocument Text | View/Open (/jspui/bitstream/12345 |

Show full item record (/jspui/handle/123456789/2712?mode=full)

(/jspui/handle/123456789/2712/statistics)