Understanding molecular control of functional amyloidogenesis.

https://www.neurodegenerationresearch.eu/survey/understanding-molecular-control-of-functional-amyloidogenesis/

Name of Fellow

Prof Stephen Matthews

Institution
Funder

Wellcome Trust

Contact information of fellow
Country

United Kingdom

Title of project/programme

Understanding molecular control of functional amyloidogenesis.

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The project/programme is most relevant to:

Neurodegenerative disease in general

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Research Abstract

In contrast to human disease-associated amyloidogenesis that underlie neurodegenerative disorders like Alzheimers and Parkinsons disease, many microbial organisms possess

elaborate molecular machineries that facilitate the assembly of amyloid fibres in a highly regulated, non-cytotoxic manner. The resulting polymeric structures are multifunctional, often enabling biofilm formation in extreme environments, modulating host cell adhesion and contributing to pathogenicity during infection. We aim to unravel the molecular processes that control the assembly of functional amyloids and biofilm formation, which may also offer clues to controlling pathogenic amyloids in humans. Crucial to our understanding is a deep atomic and mechanistic knowledge of how amyloid subunits are safely transported across membranes and between cellular compartments. Although the amenability of microbial systems to manipulation and functional readouts means they are important model systems, there have been rela tively few in-depth studies on the pathways of amyloidogenesis control. Our approach engages multi-disciplinary and complementary methods that aim to marry biological insight with quantitative data. In addition to employing a diverse array of molecular and high resolution structural tools, we are developing new nuclear magnetic resonance methods to assist in mapping structural, dynamic and interactional changes in large protein assemblies, including membrane proteins. Studying key molecular p rocesses used by pathogenic microorganisms not only provides insights into disease pathways, it often illuminates fundamental cell biology in higher eukaryotes and will provide a foundation for future translational activities.

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Fellowships

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