Huntington’s disease: deciphering the key molecular level processes of toxic amyloid aggregates

https://neurodegenerationresearch.eu/survey/huntington%c2%92s-disease-deciphering-the-key-molecular-level-processes-of-toxic-amyloid-aggregates/

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Country

Denmark

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Huntington’s disease: deciphering the key molecular level processes of toxic amyloid aggregates

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2

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Research Abstract

Huntington’s disease is a highly-debilitating neurodegenerative disorder which remains currently incurable. However, the responsible pathogenic protein has been identified: huntingtin (Htt). Despite Htt fibrils and inclusions being commonly found in patients’ brains, evidence from recent studies implicates Htt oligomers as the most toxic species. Understanding their role, the overall self-assembly process and the structural features of pathogenic aggregates is thus crucially important in deciphering the cytotoxicity mechanisms underlying the etiology of Huntington’s

diseases. In this project, we aim to progress beyond a bulk level description of Htt aggregation towards a mechanistic understanding of the key molecular level processes that are responsible for the formation of oligomers and define their properties. We will address this challenge through the development and application of an array of new biophysical techniques based on a microfluidic platform capable of following the aggregation process from the very early stages (i.e. nucleation and growth phenomena) up to the final phases (i.e. fibril and inclusion formation), and to use these techniques in conjunction with nanomechanical property mapping to explore the physical properties and heterogeneity at a single aggregate level. This work will shed light on the fundamental molecular level determinants and processes underlying pathological Htt aggregation.

Further information available at:

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Investments < €500k

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Denmark

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