

Imaging the Nature of Protein Aggregation *in vitro* and *in vivo*

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We show using lifetime imaging microscopy and polarisation resolved imaging of fluorescently tagged amyloidogenic proteins that the degree of aggregation of such proteins and the nature of the resulting species are closely correlated with the value of the excited state lifetime and the emission anisotropy of the attached fluorophores both *in vitro* and *in vivo*. This finding provides a robust means to monitor in real time the populations of different types of aggregates formed *in vivo* and to relate them directly to similar species characterised in detail *in vitro* by conventional biophysical methods. We have used this approach to reveal the close similarity of the nature and mechanism of self-association reactions taking place *in vitro* and *in vivo* for several amyloidogenic proteins linked to Parkinson's, Alzheimer's and Huntington's diseases opening the door to identifying the nature of the pathogenic agents in these and other protein misfolding diseases.