

Psychiatry and Neuroscience Seminar Series 2026

Dr. David Rubinsztein

***Cambridge Institute for Medical Research and UK
Dementia Research Institute, University of Cambridge***

(Host Thierry Galli)



**Strategies for enhancing toxic protein
clearance in neurodegenerative diseases**

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Room D. Levy, 102 rue de la santé - 75014 Paris

Intracellular protein aggregation is a feature of many late-onset neurodegenerative diseases, including Parkinson's disease, tauopathies (including Alzheimer's disease and frontotemporal dementia), and polyglutamine expansion diseases (like Huntington's disease). Many of these mutant proteins cause disease via toxic gain-of-function mechanisms. Therefore, the factors regulating their clearance are crucial for understanding disease pathogenesis and for developing rational therapeutic strategies. We showed that autophagy induction reduces the levels of proteins causing Huntington's disease, Parkinson's disease and forms of dementia and attenuates their toxicity in cellular/neuronal, *Drosophila*, *zebrafish* and mouse models. In this talk, I will discuss how understanding the processes regulating autophagosome formation have helped us delineate the functions of BIN1, a major Alzheimer's disease risk gene. I will describe how our work on cellular nutrient sensing has helped us understand how autophagy is compromised by alpha-synuclein, a major toxic protein causing Parkinson's disease. Finally, I will describe recent work suggesting that one may also be able to lower the levels of such intracellular proteins by stimulating lysosomal secretion and that there may be FDA-approved drugs that can be used to ameliorate tauopathies via this mechanism.

Stay tuned!