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Bridging Structural and Systems Biology to investigate the root cause of neurodegeneration

Neurodegenerative diseases are very complex and a holistic understanding of the relation between structure and function requires the integration of molecular, cellular and systems biology. We applied 'omic' technologies to generate of a most complete protein interactome associated with Alzheimer's disease (1). The analysis of this network triggered insights on the mechanisms implicated in the disease such as the formation of amyloid plaques, which surround neurons affected by Alzheimer's, with the dysfunction of mitochondrial respiration (2). We examine the mitochondrial respiratory complex under amyloidogenic conditions by applying an integrative structural and cell biology approach. Deciphering the molecular mechanisms will advance our understanding of the disease etiology by unveiling the causal link between altered mitochondrial respiratory function and early amyloid formation as it may occur in pre-symptomatic stages (3).

References

- (1) Soler-López M, Zanzoni A, Lluís R, Stelzl U, Aloy P. Interactome mapping suggests new mechanistic details underlying Alzheimer's disease, *Genome Research*, 21:364-76, 2011.
- (2) Soler-López M, Badiola N, Zanzoni A, Aloy P. Towards Alzheimer's root cause: ECSIT as an integrating hub between oxidative stress, inflammation and mitochondrial dysfunction, *BioEssays*, 34(7):532-41, 2012.
- (3) Giachin G, Bouverot R, Acajjaoui S, Pantalone S, Soler-López M. Dynamics of Human Mitochondrial Complex I Assembly: Implications for Neurodegenerative Diseases, *Front Mol Biosci*, 3:43, 2016.

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