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MEDGENET Guest Lecture

Identification of molecular pathogenic mechanisms through protein-protein interaction networks. The example of the polyQ protein ataxin-1

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START: 10.00

Protein-protein interaction (PPI) networks offer information on the formation of protein complexes and subsequently, their function. This information is extremely useful in the case of mutant proteins involved in human diseases with genetic aetiology. Therefore, identification of aberrant PPIs of a mutant protein may lead to the characterization of molecular mechanisms involved in the pathogenesis of such diseases. In this project, we studied the effect of proteins interacting with mutant polyQ ataxin-1 on its toxicity and aggregation using high-throughput cell-based and cell-free assays. We indicate that the coiled-coil (CC) domain of MED15, an ataxin-1 binding partner is crucial for polyQ protein aggregation and proteotoxicity. We propose a molecular mechanism through which proteins with CC enhance the pathogenicity of a polyQ protein. Finally, we describe the generation of human stem cell models resembling the characteristics of polyQ protein aggregation and discuss their potential application in the design of novel anti-aggregating strategies.

More information HERE.

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