To the Heart of IFs Function: Do they Aggregate on Purpose?

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Background: One of the molecular hallmarks in the development of heart failure (HF) is loss of ultrastructure within the cardiac myocyte. In addition, HF is increasingly recognized as a proteinopathy characterized by the accumulation of misfolded proteins similar to Alzheimer and Parkinson disease. However, despite its increasing prevalence and poor prognosis, the advances in the pharmacological treatment of HF have been limited, highlighting an urgent need for the discovery of new therapeutic targets.
We reported a consistent accumulation of mono-phosporylated desmin in experimental and clinical models of HF. We also demonstrated how mono-phosphorylated desmin is more prone to cleavage and aggregation in isolated cardiac myocytes. Therefore, if on the one hand desmin cleavage could easily explain the loss of a cardiac myocyte's ultrastructure, its high abundance and propensity to aggregate make it an ideal candidate as the seed generating pre-amyloid-oligomers (PAOs) and amyloid fibrils in the heart.
Methods: Using a combination of novel and established protein biochemistry techniques, we aimed at demonstrating desmin's identity as the seed starting the nucleation process which leads to the formation of cardiac PAOs and amyloid fibrils.
Results: Desmin displayed common features shared by other established PAOs and fibrils (e.g. tinctorial properties) in experimental and clinical models of HF.
Conclusions: The inherent propensity of intermediate filaments to aggregate, combined with the use of cardiac tissue as a model for repeated mechanical stretch, suggest that intermediate filaments aggregation could be used as a way to dissipate/scavange mechanical as well as chemical stress. We will therefore use the highly organized structure of cardiac myocytes to infer IFs function in mammalian cells.