Converging pathways in the occurrence of endoplasmic reticulum (er) stress in Huntington's disease

Vidal, R.

Caballero, B.

Couve, A.

Hetz, C.

A variety of neurological diseases including Huntington's disease (HD), Alzheimer's disease and Parkinson's disease share common neuropathology, primarily featuring the presence of abnormal protein inclusions containing specific misfolded proteins. Mutations leading to expansion of a poly-glutamine track in Huntingtin cause HD, and trigger its misfolding and aggregation. Recent evidence indicates that alterations in the secretory pathway, in particular the endoplasmic reticulum (ER), are emerging features of HD. Although it is not clear how cytoplasmic/nuclear located mutant Huntingtin alters the function of the ER, several reports indicate that mutant Huntingtin affects many essential processes related to the secretory pathway, including inhibition of ER-associated degradation, altered ER/Golgi vesicular trafficking and axonal transport, disrupted autophagy and abnormal ER calcium homeostasis. All these alterations are predicted to have a common pathological outcome associated to dist