Age-dependent changes of membrane contact sites

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Virtually all organelles are connected by membrane contact sites (MCS), and such direct physical interactions facilitate interorganellar communication and the integration of compartmentalized processes by the exchange of small metabolites, lipids, and ions. While it is known that the functionality of MCS affects fundamental cellular processes such as apoptosis, autophagy, ion homeostasis, and general organelle function, a lot is to be learned regarding the molecular architecture and regulation of the tethering complexes forming the distinct MCS, in particular during aging. We have identified a novel regulator and component of the MCS connecting the perinuclear ER and the vacuole, termed **n**uclear -**v**acuolar **j**unctions (NVJs). We find this protein to concentrate at NVJs in old but not in young yeast cells, thereby affecting autophagy, lipid homeostasis and aging, and show that its absence abrogates NVJ formation. Moreover, we find a physical interaction not only with key components of the NVJs, but also with several enzymes involved in fatty acid elongation. In line, we observe distinct changes in the cellular lipid profile in cells lacking this novel NVJ component, in particular a shift towards longer-chain fatty acids incorporated into different lipid species. Pointing towards an important role of deregulated fatty acid elongation in the cellular defects observed in these cells, we find that additional deletion of *ELO2*, coding for a fatty acid elongase, provides cytoprotection. Thus, we identified a novel component of NVJs that seems to contribute to age-dependent changes in organellar connectivity and the regulation of fatty acid elongation in the ER