MPI-NAT SEMINAR SERIES


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ER remodelling in health and disease

The human body is in a continuous state of repair and renewal, from breaking down and reusing damaged or excess cell parts via the process of autophagy. The endoplasmic reticulum (ER) in the cell cytoplasm, critical to the synthesis and transport of cellular components, is no exception. ER-phagy is a major driver of ER remodelling, and ER-phagy receptors play central roles in this process. Loss-of-function mutations in ER-phagy receptors (FAM134b) result in autosomal recessive hereditary sensory and autonomic neuropathy (HSAN) in humans and dogs.

Within the last decades, several ER-resident membrane-shaping proteins with central reticulon homology domains (RHD) have been associated with hereditary axonal disorders as well, i.e. ATL1, ATL3, REEP1 and REEP2, SPAST, RTN2, and ARL6IP1. They can also cause hereditary spastic paraplegia/HSP, a neurodegenerative disorder characterized by progressive leg spasticity alone or in combination with loss of sensory and pain perception (HSAN). The underlying mechanisms of RHD-containing proteins functions as well as their contribution to pathogenesis of HSP and HSAN neuropathies remain largely elusive. I will discuss the role of ubiquitination and autophagy in controlling ER-phagy receptor clustering and efficient ER remodelling and renewal. Structural models of RHDs and intrinsically disordered regions (IRDs) located in the cytosolic loops of ER-phagy receptors will be elaborated. Moreover, mouse genetic data reveal how defects in ER-phagy pathways lead to neuronal cell death and sensory and motorneuron neuropathies.

Tuesday, 26.03.2024, 14:00 pm

Host: Sonja Lorenz

Fassberg Campus
Ludwig Prandtl Saal

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