New insights into ER morphology dysregulation in HSPs

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Numerous common HSP proteins are involved in maintaining the structural organization of the ER -- an expansive, membrane-enclosed organelle implicated in diverse cellular functions, with complex structural elements. In most cells, the ER consists of the nuclear envelope interconnected with ribosome-studded perinuclear sheets and an extensive polygonal network of highly dynamic tubules and peripheral sheets. Employing a variety of emerging super-resolution imaging approaches to study the ER at high spatial and temporal resolution, we have identified a novel, energy-dependent form of ER motion involving rapid oscillations of tubules and active tubular junction dynamics. Peripheral “sheets” in many cases appear discontinuous, containing many spaces of subdiffraction-limited size with brief lifespans. Viewed using lattice light sheet-point accumulation for imaging in nanoscale topography (LLS-PAINT), sheet-like structures appear as tightly clustered three-way junctions of interconnected tubules, harboring proteins associated with tubule stabilization and junction formation. Together, our results demonstrate the highly dynamic nature of the peripheral ER and indicate that many structures historically defined as sheets are instead dense tubular matrices. We are currently adapting these and related optical approaches to the study of ER morphology and dynamics in axons of HSP iPSC-derived neurons. [*,#]Equal contributions