Differences in PRG3 and PRG5 folding and transportation

Cells rely on the ability to target proteins to specific cellular locations. They therefore possess an extensive protein sorting and quality control

machinery that directs functional proteins to the correct cellular compartment and retains or degrades defective proteins (Vincenz-Donnelly & Hipp, 2017). Most proteins directed to the plasma membrane are first targeted to the endoplasmic reticulum, and only once folded then travel to the Golgi apparatus and the plasma membrane. A dysfunction in these processes, can lead to reduced levels of functional proteins, as in Cystic Fibrosis, or to the accumulation of intra or extracellular protein aggregates, that is a hallmark of many neurodegenerative diseases (Hipp et al.,2019). A new class of transmembrane protein, named Plasticity-related genes (PRGs), have important functions in neuronal differentiation, aging, and de-/regeneration (Bräuer et al.,2003, Strauss and Bräuer, 2013). In particular, we are interested in identifying the machinery involved in transport and sorting of the proteins PRG3 and PRG5. Although their sequence is closely related, they promote different morphological changes in neurons. PRG3 promotes the formation of neurites in primary neurons (Verlmans et al.,2013), whereas PRG5 contributes to spine induction in immature neurons and to regulation of spine density and morphology in mature neurons (Coiro et al., 2014). Our studies have shown that for PRG3 and PRG5 the plasmamembrane localisation is important to induce morphology changes. Interestingly, these proteins do not contain classical ER signaling sequences, and both proteins exhibit short intracellular N- and C-termini with less than 50 amino acids. The aim of our basic and translational research project is to identify the machinery involved in sorting PRG3 and PRG5 to the plasma membrane as well as the characterization of the quality control machinery that interacts with these proteins en route to the plasma membrane.

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