

Nesprin roles at the nuclear envelope

Enaptin/Nesprin-1 and NUANCE/Nesprin-2 are giant proteins with an F-actin binding site at the amino terminus with which they interact with the cytoskeleton and a single transmembrane domain at their carboxyl terminus (KASH-domain) which anchors them in the nuclear envelope (NE). At the NE they can interact with the inner nuclear membrane protein SUN, with emerin and with lamins. Through these interactions a tight network is established which connects all these components with each other and provides a link between the nucleus and the cytoplasm. Mutations in several of these proteins lead to severe disease states such as muscular dystrophy or premature aging. Furthermore, Nesprins exist in many isoforms that are found in many cellular compartments in addition to the nuclear envelope and presumably have a wide variety of roles.

In this project we would like address the roles of Nesprin-2 in the nucleus and the cytoplasm and through which mechanisms it contributes to the various diseases. Specifically, we will search for binding partners using individual domains of Nesprin-2 for pull down experiments employing cytosolic fractions and nucleoplasmatic fractions, identify the proteins and confirm the interactions. This will reveal the processes Nesprin-2 is involved in. In the current model that is supported by analysis of Nesprin-2 Giant deficient cell lines Nesprin-2 stabilises the nucleus, contributes to its position within the cell and affects centrosome positioning.

References:

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