The Role of Reticulon 4b in the Structure of Mammalian Endoplasmic Reticulum

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Endoplasmic reticulum (ER) is a large, dynamic cellular organelle that stretches around the whole cell. It has multiple functions including protein folding and modification, lipid biosynthesis and regulation of cytoplasmic calcium concentration. Traditionally ER has been divided into 3 subdomains: rough and smooth ER (RER, SER) and nuclear envelope (NE). A more current approach is to discuss ER structure based on its morphology: where NE and perinuclear RER consist of sheet like cisternae, the peripheral ER and SER are observed as tubular network. Interestingly, our recent studies show that ER undergoes dramatic changes in its morphology during cell division as the sheet like structures are transformed into tubular network in mammalian fibroblast cells [1].

We are interested in the maintenance of sheet and tubule structures of ER in mammalian cells. The ER morphology is affected by the Reticulon 4 proteins (Rtn4) which belong to the large protein family with C-terminal Reticulon Homology Domain (RHD) as the common factor. The RHD of all Reticulons anchors the proteins into membranes and within this anchor-region two hairpin-like folds are formed. It is now believed that these hairpin structures incorporate additional membrane curvature to the area where it localizes, namely the tubular regions of the ER [2]. Additionally, Rtn4 proteins have been shown to oligomerize and this phenomenon is hypothesized to induce the formation of the tubular ER [3]. Reticulon 4 gene encodes three main splice variants (a,b and c) which all associate with the ER but with different expression profiles and functions.

Our aim is to obtain information about the influence of Reticulon proteins to ER morphology during different stages of mammalian cell cycle. This will be executed by first studying the localization and structural effects of different expression levels of Rtn4 splice variants in mammalian cell lines by confocal microscopy and transmission electron microscopy (TEM). Further studies will be done with 3D electron tomography (ET) to gain further insight to the division between sheet and tubule profiles.

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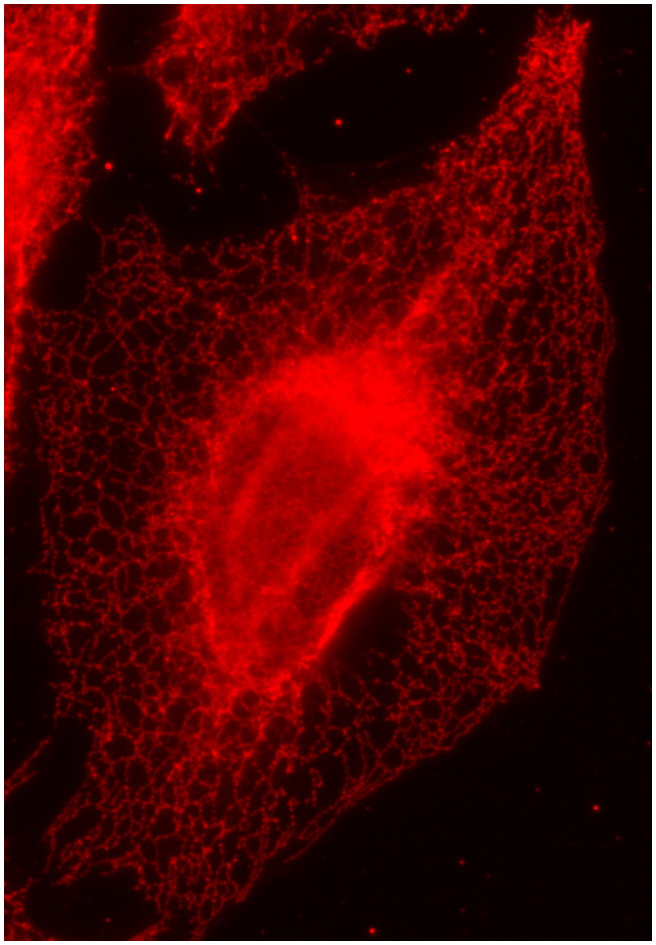

Figure 1. Immunofluorescence image of endoplasmic reticulum of U-2 OS cell stained with Reticulon 4b antibody and visualized with Rhodamine Red secondary antibody.

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