## Tubulohelical membrane arrays: Novel nonlamellar, nanoperiodic cell compartments of unknown function

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Cells respond to certain physiological and pathological conditions by pleomorphic reformation of their reticulated membranes. This may lead to the formation of highly ordered structures, such as stacks of organized smooth endoplasmic reticulum (OSER), or 3D-periodic cubic membranes [1]. By application of rapid microwave fixation to cell monolayerrs, we found lipid membrane arrays in the epithelial cell line PtK2 that are unique if compared with any of these highly ordered membrane specializations [2,3]. To emphasize their particularity, we named them "tubulohelical membrane arrays" (referred to hereafter as TUHMAs).

TUHMAs are organized around tubular, proteinaceous electron-dense cores of 80 nm in diameter (Figure 1). The interface between the core tubules and the lipid membrane displays characteristic helical threads. Depending on the cell status, up to 8 core tubules provide the basis for an intermingled, nonlamellar membrane scaffold of an overall length of  $3-5 \mu m$ . From our observations we conclude that TUHMAs are built according to a cellular "construction plan", which determines the relation between the proteinaceous, nucleoporincontaining, core tubules and the surrounding lipid membranes. The design principles seem to include the regulation of the number, ensuring that TUHMAs exist as single entities. Taken our initial observations together, TUHMAs can not be mistaken for aggregated membranes of ill-defined size, shape, and/or number.

TUHMAs could be observed in 5 t0 10 % of the cells of the asynchronously grown cell population. They are not locally fixed but dynamic structures which are transiently associated with the cell nucleus and the Golgi complex. If positioned next to the nucleus, they prefer polarized orientations either in parallel or perpendicularly to the nuclear membrane. The nuclear linkage is mediated via tubular membrane bridges. Since TUHMAs are also continuous with rough endoplasmic reticulum and annulate lamellae, we hypothesize a "life cycle" for them that is likely to be related to the pleomorphic reformation of the membrane reticulum.

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**Figure 1.** Tubulohelical membrane array (TUHMA). The membrane array is built up around darkly contrasted tubules of uniform diameter of ~80 nm, numbered 1-4. The tubules are confined by helical bands black in contrast. Note also a twisting pattern of the tubules within the plane of section and the size relation of the TUHMA in comparison with a mitochondrion, m. Bar, 500 nm. Insert showing a fluorescent tubular structure of the dimension of a TUHMA labeled with monoclonal antibody against nucleoporins. Note its orientation perpendicularly to the nucleus counterstained with Hoechst 33258. [2]