True Cell Simulations Inc.
cell blog
Oct/1/2025, Kazuhisa Ichikawa

17. Real intracellular structure 4

— Dynamics of endoplasmic reticulum —

Organella, including Endoplasmic Reticulum (ER) and mitochondria, move[1]. They move at the expense of ATP molecules, as was discussed in Blog 10. Still, they should move for some requirement. Molecular mechanisms for ER to move are getting clearer. Here, the dynamics and their mechanisms are discussed.

1) Until several tens of years before, organellar movement was called protoplasmic streaming collectively, due mainly to the limited resolution in microscopic observation of each organelle.

Morphological change of ER: Fig. 1 shows the temporal change in ER morphology over approximately 25 minutes (Takakura, H., et al., Nat. Biotech, 2017; HeLa cell). This shows time at 0 and 24min 44sec after the start of the recording on the left and right, respectively. ER sheets are found among the tubular ER networks. Both change their morphology significantly during 25 minutes. If we look carefully, we can find local morphological changes among global areal changes. The change is not random, but organized in a way that the upper right part is moving toward the upper right, the lower right toward the lower right, and the lower left toward the lower left. Among these, local changes for both tubular ER and ER sheets proceed. Morphological oscillation of ER was reported (Perkins, H.T., et al., Cells, 2021). In fact, modulated movement of the tubular ER is found among areal changes. Generation/enlargement/reduction of ER sheets, and elongation/shortening of ER tubules are also observed. Generation of fenestrated ER sheets is also seen (Schroeder, 2019).

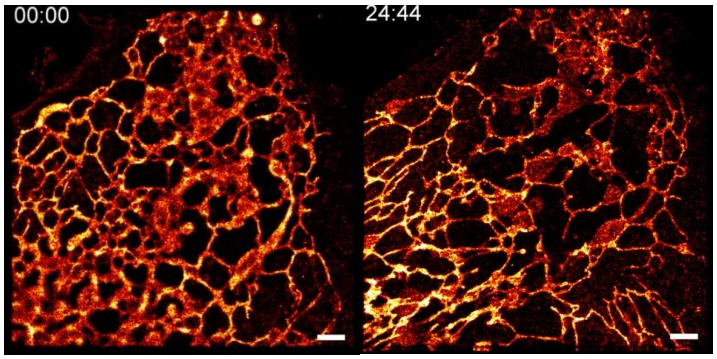

Fig. 1. ER dynamics (modified from Takakura, H., et al., Nat.Biotech, 2017). The movie is downloaded from https://pmc.ncbi.nlm.nih.gov/articles/PMC5609855/#_ad93_.

Molecular mechanisms of ER dynamics: ER moves along microtubules (MT), on which the elongating front end of ER is attached. Nonmoving tubular ER was reported to be isolated from MT (English, A.R., et al., Curr.Opin. Cell Biol., 2009). There are two mechanisms of ER movement, TAC (Tip Attachment Complex) dynamics and sliding (English, A.R., et al., Curr.Opin. Cell Biol., 2009). In TAC dynamics, the front end of ER attaches to the + end of non-acetylated MT, while in sliding, the front end of ER attaches to the halfway point on acetylated MT. The majority of ER movement proceeds by sliding, which is faster than the TAC dynamics (English, A.R., et al., Cold Spring Harb.Perspect.Biol., a013227, 2025).

Motor proteins contributing to the sliding are kinesin-1 and dynein. Since kinesine-1 and dynein transfer a cargo to the + and – ends of an MT, respectively, ER can move both to + and – ends on the MT in the sliding. In contrast, in the TAC mechanism, the tip of the ER connects to the + end of MT

via the STIM1 protein of the ER and the EB1 protein on the MT. Thus, in the TAC mechanism, ER moves according to the movement of MT (Pendin, D., et al., Curr.Opin. Cell Biol., 2011). Finally, fusion of tubular ER was reported, in which a GTPase protein atlastin is involved (Friedman, J.R., et al., Trends Cell Biol., 2011).

Molecular mechanism of ER stress response: As was discussed in Blog 16, UPR (unfolded protein response) leads to the degradation of ER (ER-phagy). UPR-accumulated ER region is recognized by CALCOCO1 and C53 of ER-phagy receptor, leading to the phagocytosis directly by a lysosome without the help of autophagosomes (Almanza, A., et al., FEBS J., 2019; Gubas, A., et al., Mol.Cell, 2022; Mochida, K., et al., EMBO Rep., 2022). FAM134B is thought to be a receptor for the ER-phagy, in which Ca^{2+}/calmodulin-dependent phosphorylation of FAM134B by CAMK2B is a key step (Yamanaka, T., et al., Front. Neurosci., 2018).

ER dynamics and related function: What functions are ER-moving responsible for? The function that ER obeys seemed unclear in 2021. But some postulated that ER oscillation facilitated the movement of substances on ER sheets and tubes (Perkins, H.T., et al., Cells, 2021). If the relation between ER movement and protein secretion, lipid synthesis, and Ca^{2+} homeostasis becomes clear, we will have a much clearer view of the ER dynamics (Friedman, J.R., et al., JCB, 2010). Although movement of the ER is ultimately required for making contact with other organelles and the cell membrane, the movement may be of no use after the contact formation. Instead, the dynamic nature of ER is essential if the environmental change requires the destruction and creation of old and new contacts.

In this blog, we discussed ER dynamics and its molecular mechanisms. Anyway, every organelle moves. Is there any cellular environment in which organellar movement stops? Does it move even in an environment where no net inward and outward flows via the plasma membrane exist? If so, the movement of organella may be driven by intrinsic, in addition to extrinsic factors. ER dynamics are caused by STIM1, EB1, and kinesin-1/dynein. If ER movement can be stopped specifically by manipulating these proteins, it is highly expected that we will find the role of ER movement in a cell by observing what is happening to it. In addition, if TAC dynamics are specifically inhibited at a specific region in a cell, we will have more information on the relationship between ER movement and its function in a cell. However, questions remain: How is the direction of ER movement chosen, and how is it sensed? These should be proved too. In addition, how is the ratio between the ER sheet and tube determined? The ER occupies 35% of the cytoplasmic volume. To what extent is this volume the obstacle to signal transductions? Or is a cell dynamically and adaptively utilizing this obstacle as a barrier for a localized signal transduction? These are interesting questions to be answered.