Ice2p has properties of a SERINC-like regulator of membrane function, not an ER-plasma membrane tether

Ganiyu Alli-Balogun[1], Tim Levine[1*]

[1]UCL Institute of Ophthalmology, 11-43 Bath Street, London EC1V 9EL, United Kingdom

* **Corresponding author:** tim.levine@ucl.ac.uk

Communication between organelles is facilitated by molecular tethers that bring them into proximity. Numerous tethers have been described on the basis that their deletion reduces contact and their over-expression increases contact. However, the effect of a protein on contact might be entirely indirect. Here we looked at Ice2p, an integral endoplasmic reticulum (ER) membrane protein named “ICE” because deletion reduces the inheritance of cortical ER. Ice2p has been reported to be involved in the mobilisation of neutral lipids, and to use a cytoplasmic loop to bridge from the ER to the surface of lipid droplets. To support the link to lipid droplets, 4 amphipathic helices in the cytoplasmic loop all resemble lipid droplet-binding sequences. Ice2p has also been reported to be an ER-plasma membrane tether, because levels of the protein correlate with the amount of contact between these two compartments. However, our *in silico* analyses reveal that Ice2p is homologous to SERINCs (serine incorporators), which are eukaryotic proteins that carry out an as yet unknown function. The absence of bridging capacity from ER to plasma membrane and the presence of a conserved function together suggest that the effect of deleting Ice2 on the inheritance of cortical ER is indirect via its action as a SERINC-like protein. Study of Ice2 in the future may be a way to understand SERINCs in other systems, such as in HIV infection.

Key words: membrane contact site, intracellular communication, neutral lipid, lipid droplet