Abstract

MCC/eisosomes are yeast plasma membrane microdomains that respond to changes in both extracellular and intracellular conditions and activate important stress-related signaling pathways. In this study, we investigated the function of MCC/eisosomes under the conditions of chronic glucose depletion. We found that MCC/eisosomes regulate mRNA decay under these conditions. Specifically, we demonstrated that the sequestration of the evolutionarily conserved Xrn1 exoribonuclease at MCC/eisosomes leads to the attenuation of its enzymatic activity. Modulation of activity by the enzyme localization may represent a novel and effective mechanism in regulation of biochemical pathways. Moreover, our results suggested that an MCC protein Nce102 might play a role in vacuolar fusion and lipid droplets degradation. We demonstrated that prolonged chronic glucose depletion induces the translocation of Nce102 from MCC to sterol-enriched microdomains in the vacuolar membrane. Deletion mutants lacking Nce102 and its functional homologue Fhn1 exhibited significant delay in vacuole maturation and in turnover of a lipid droplet marker Erg6.

The function of MCC/eisosomes in the stress response have been demonstrated in many fungal species. Similar to the microdomain function, also individual protein components of MCC/eisosomes are widely evolutionarily conserved. To further characterize this phenomenon, we tested the compatibility of *Saccharomyces cerevisiae* (*S. cerevisiae*) MCC/eisosome with MCC/eisosomal proteins from phylogenetically distant species *Schizosaccharomyces pombe* (*S. pombe*; *Sp*). We found that *S. cerevisiae* Pil1 and its homologue *Sp*Pil1 compete with each other and *Sp*Pil1 is able to substitute for Pil1 function in organizing *S. cerevisiae* MCC/eisosomes in cells lacking endogenous Pil1 protein. Similarly, Nce102 and its homologue *Sp*Fhn1 are competitors, albeit Nce102 is more effective than *Sp*Fhn1 in binding both Pil1- and *Sp*Pil1-organized eisosomes. In contrast, *S. pombe* homologue of the eisosome stabilizer Seg1, *Sp*Sle1, did not recognize Pil1 at the plasma membrane of *S. cerevisiae*, while it strongly interacted with its natural interaction partner *Sp*Pil1 under the same conditions. These observations shed not only the new light on principles of the MCC/eisosome organization, but also allowed us to reconstitute *S. pombe* MCC/eisosome in the plasma membrane of *S. cerevisiae*, which was capable to attract endogenous MCC proteins. Further tests would be necessary to prove whether the imported *S. pombe* microdomain preserves also its function in the stress response.