

# Membrane Stress Response Buffers the Harmful Effects of Lipid Disequilibrium

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Biological membranes comprise hundreds of different molecules called lipids, the compositions of which differ in different parts of the cell. It has recently become clear that maintaining these precise compositions is critical for health, and incorrect compositions have been associated with increasingly common pathologic conditions such as obesity, diabetes and liver failure.

To understand the underlying basis of lipid disequilibrium, Assoc Prof Davis Ng and his team applied advanced technologies to comprehensively and quantitatively profile the cellular lipid compositions, gene expression and protein compositions in a model of the disease state. Their work resulted in the most detailed map of a pathogenic state ever accomplished. To their surprise, the researchers discovered that cells can compensate for disturbed lipid compositions in a process they label ‘membrane stress response’ by remodeling the protein homeostasis network, a complex regulatory regime that has been extensively studied in search of potential therapeutic targets for diseases such as Alzheimer’s, Parkinson’s, Huntington’s and cystic fibrosis.

The findings offer new insight into an important disease state and, more importantly, suggest a potential path for therapeutic interventions in diseases such as diabetes and non-alcoholic steatohepatitis.

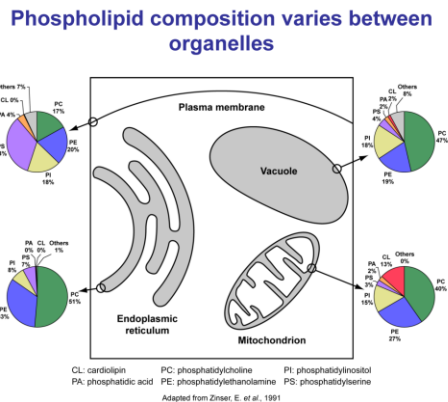


Figure 1. Variance in phospholipid composition between organelles.

## Protein changes linked to the Membrane Stress Response (MSR)

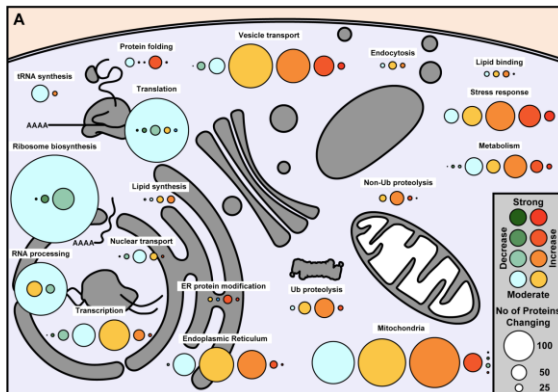


Figure 2: Range of protein changes linked to membrane stress response

### Publication:

Thibault, G., Shui, G., Kim, W., McAlister, G.C., Ismail, N., Gygi, S.P., Wenk, M.R. and Ng, D.T.W. The membrane stress response buffers the lethal effects of lipid disequilibrium by reprogramming the protein homeostasis network. *Molecular Cell* 48: 16-27 (2012). DOI: 10.1016/j.molcel.2012.08.016.