# Baker’s yeast as a model for studying chronic diseases related to ER stress

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An increasing number of studies indicate that saturated lipids can be metabolically harmful and their role in inflammatory diseases such as type II diabetes is actively discussed [1]. Further there is collective evidence linking type II diabetes to chronic ER stress [2]. Using the baker’s yeast as a model, we provide evidence for a direct role of aberrant lipid compositions in the ER for the onset and progression of chronic ER stress. We show that increased lipid saturation causes chronic ER stress with direct consequences for the viability of cells. Our studies reveal that the so-called unfolded protein response (UPR) can perpetuate ER stress thereby contributing to dramatic changes in ER morphology. We seek to understand the molecular events and mechanisms that switch the UPR from a beneficial, homeostatic response to a detrimental, cell death inducing program. Our working hypothesis, supported by genetic, functional and lipidomic data is that

1) An overly saturated lipidome causes UPR activation
2) UPR activation upregulates lipid biosynthesis
3) Increased lipid synthesis leads to the production of even more saturated lipids which cause a perpetuation of the UPR forcing the cell to enter and be trapped in a vicious cycle that ultimately gives rise to the formation of non-fluid gel phases in the ER

Our studies reveal that the UPR may contribute to disease development, progression and the chronification there of by perpetuating a stress-inducing condition.

[1] Risérus, U., Willett, W. C., & Hu, F. B. (2009). Dietary fats and prevention of type 2 diabetes. *Progress in lipid research*, *48*(1), 44–51. https://doi.org/10.1016/j.plipres.2008.10.002
[2] Eizirik, D. L., Cardozo, A. K., & Cnop, M. (2008). The role for endoplasmic reticulum stress in diabetes mellitus. *Endocrine reviews*, *29*(1), 42–61. https://doi.org/10.1210/er.2007-0015