



INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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SHORT ABSTRACT

Ageing is a necessary evil experienced by all living organisms. It results in a progressive decline in the normal functioning of cells and eventually culminates with the death of the organism. Budding yeast has emerged as an appropriate model organism for ageing research and is used to study two aspects of ageing namely replicative and chronological ageing. Various studies have emphasized the function of subcellular organelles in the regulation of yeast ageing. One such organelle that is ubiquitously present in all eukaryotic cells is the peroxisome. β -oxidation of fatty acids and metabolism of reactive oxygen species are the conserved functions of peroxisomes. The proliferation of this organelle is extensively studied in various model organisms. However, the molecular mechanisms that link peroxisomes with ageing are still under investigation. Our study sought to comprehend the alterations in peroxisome dynamics during replicative and chronological ageing to understand their role in yeast ageing. The changes in peroxisome number and morphology upon were first investigated in wild type (WT) cells cultured in peroxisome-inducing oleic acid (OA) and non-inducing glucose (YND) media conditions. An increase in peroxisome number was observed in early replicatively aged wild type (WT) cells in both media. However, the increase was higher in OA as compared to the YND medium. Upon chronological ageing, the cells displayed increased mean and maximal CLS in OA medium. We also observed a change in phenotype of peroxisomes from punctate to cytosolic with the progression of ageing. Interestingly, OA grown cells displayed delayed change in the phenotype. This suggests an intricate link between the morphology/protein import of peroxisomes and chronological ageing. Further to address the effect of reduced peroxisome number upon yeast ageing, we investigated *pex11*, *pex25* and *pex11pex25* cells which lack proteins involved in peroxisome fission. Among these, *pex11pex25* cells had the most reduced peroxisome number. Reduction in peroxisome number had no effect on the replicative age of the yeast cells, as there was no significant difference in the number of bud scars between WT and deletion cells. But there was a surprising increase in catalase activity and reduced ROS in the deletion cells. Also another interesting observation was mitochondrial fragmentation and reduced mitochondrial membrane potential in the replicatively aged cells. On the other hand, upon chronological ageing, the deletion cells exhibited increased oxidative stress and lipotoxicity and thereby reduced chronological lifespan as compared to WT. In conclusion, our study offers some interesting perspectives on the relationship between peroxisomes and yeast ageing and reveals a previously uncharacterized role of the fission proteins in both replicative and chronological ageing of yeast. However, if the effect on ageing observed in our study, can be attributed solely to the altered peroxisome number and function needs further investigation. In line with this, we also report altered mitochondrial function and lipid droplet number upon ageing. Future work needs to look into organelle communication and their shared functions that may be affected due to the lack of fission proteins.