Abstract

This thesis investigates two different aspects of altered glutathione metabolism in two different model systems, zebrafish and the yeast Saccharomyces cerevisiae. The way in which we have altered glutathione metabolism is different in the two systems. This is because the objectives were different. In the case of zebrafish, we attempted to investigate how a glutathione degrading enzyme could alter the redox milieu and initiate calcium signaling during the development of zebrafish. In the case of the yeast experiments, we investigated the consequence of depleting intracellular glutathione levels to see if this would enable us to identify and investigate genes that affect the levels of NADPH/NADP + , a secondary redox couple. Owing to these two diverse aspects of altered glutathione metabolism I have introduced and presented the two parts of the thesis separately. In the first part (zebrafish experiments), I attempted to investigate how a glutathione degrading enzyme could alter the redox milieu and initiate calcium signaling during the development of zebrafish. Our study suggests that Chac1 and redox have a very crucial role in early embryonic development which is the first clear demonstration of a role for redox in development. It also added one more vital component to the regulators upstream of calcium. In the second part of this thesis, I investigated the consequence of depleting intracellular glutathione levels in Saccharomyces cerevisiae to see if this would enable us to identify and investigate genes that affect the levels of NADPH/NADP + , a secondary redox couple. We demonstrate the successful development of a genetic screen for genes affecting NADPH metabolism. It is expected that through this screen new insights will be obtained on enzymes and proteins influencing NADPH consumption and generation.