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DISSERTATION SUMMARY

Transcriptional targets of *Drosophila* p53

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The tumor suppressor p53 is a sequence specific transcription factor which plays a crucial role in mammalian cells in safeguarding the integrity of the genome. The p53 protein regulates multiple cellular responses to DNA damage, including DNA repair, induction of apoptosis, cell cycle arrest, but the transcriptional targets that specify these processes are mostly unknown.

The *Drosophila* homolog of p53 (Dmp53) has been identified recently (Ollman et al. 2000). Dmp53 is required for the apoptotic response, but unlike mammalian p53, it appears unable to block the cell cycle in G1 phase (Ollman et al. 2000). Since in many aspects Dmp53 has similar function as its human counterpart, studying p53-associated functions in the genetically well traceable *Drosophila* system offers many advantages. In concert with this, the aim of my work is the identification of Dmp53 transcriptional targets activated upon different cellular stress responses. For this I use UV-C and X-ray to induce genotoxic stress and study the change of gene expression pattern between treated and untreated animals. After the optimalization of the dosage and the recovery time of UV-C and X-ray irradiation, I compared the expression of *Ark*, *Hid* and *reaper* genes, which are known targets of Dmp53 (Jassim et al. 2003; Brodsky et al. 2000), in third instar larvae by real time PCR. I observed that X-ray irradiation resulted in *reaper* induction, while the level of *Ark* mRNA was enhanced upon UV-C irradiation. *Hid* expression was upregulated under both stress conditions used. None of these genes showed altered expression in *Dmp53* null mutants, indicating that their expression was indeed the result of Dmp53 activation. As these observations indicated that my experimental system is suitable for the identification of Dmp53 regulated genes, I carried out genome-wide studies using DNA microarrays to compare the gene expression profile of UV-induced and non-induced animals in wild type and Dmp53 mutant background. In the microarray experiment I observed 29 transcripts upregulated and 38 transcripts downregulated upon UV-C irradiation. The expression of these genes remained unchanged in *Dmp53* null mutant animals suggesting that Dmp53 participates in the regulation of their transcription. One of these genes is an ubiquitin ligase with homology to the mammalian MDM2 and MDM4 proteins, which are the main regulators of p53 (Momand et al. 1992; Oren 1999). MDM2 is a transcriptional target of p53 and regulates the level of p53 protein in the „p53-MDM2 loop" (Oren 1999) A similar regulation of Dmp53 is unknown so far, therefore further studies of the identified MDM2-related protein might result in significant new findings in the mechanisms p53 exerts its many effects.

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