ABSTRACT

Charles University in Prague
Faculty of Pharmacy in Hradec Králové
Department of Pharmacology and Toxicology

Candidate:	Markéta Syslová
Supervisors:	Prof. Keiko Funa, Erik Johansson, Ph.D., Doc. PharmDr. Petr Pávek, Ph.D.
Title of diploma thesis:	Regulation of TLX expression by p53 family members

The p53 mutation is associated with poor therapeutic response and prognosis, being observed in almost 60% of human cancers. p53 is kept at low steady-state levels in the absence of cellular stress. In response to various stress, p53 becomes activated. It binds DNA in a sequence specific manner to activate the transcription of a number of genes mostly belonging to cell cycle inhibitors and apoptosis inducers. When p53 is mutated it cannot fulfil its function and regulate target genes. p73, analogue of p53, has two different isoforms with two different functions. In neuroblastoma, TAp73, as well as p53, is infrequently mutated but overexpression of DNp73 is connected with poor prognosis.

TLX (also called NR2E1) is an orphan nuclear receptor, a member of a highly conserved family in both vertebrates and invertebrates. TLX is an essential transcriptional regulator of maintenance and self-renewal of neural stem cells.

In this study I investigated if there is a functional link between p53 family members and TLX. In this thesis is showed that p53 binds the TLX promoter and regulates its activity in both cell lines we tested. These results suggest that TLX interacts with the p53 signalling pathway and is able to regulate the activity of postnatal neural stem cells.