Abstract

Dispatched 3 (DISP3), sterol - sensing domain (SSD) – containing protein, is a key focus of our laboratory. It was described as a gene regulated by thyroid hormone and its expression is mainly localized within neural tissue. Our preliminary data suggested increased DISP3 expression in medulloblastoma, a highly common pediatric cerebellar tumour, therefore we wanted to examine DISP3 role in human cancer cells.

The aim of this thesis is to perform DISP3 overexpression and downregulation in human medulloblastoma cell lines and in mouse neural progenitors and analyse its effect on cell proliferation and differentiation. For this purpose, we chose DAOY and D341, human medulloblastoma cell lines with low and high expression of DISP3 and mouse multipotent neural progenitor cell line, C 17.2, with low DISP3 expression.

We showed, that DISP3 ectopic expression leads to increase in cell proliferation in both DAOY and C 17.2 cells. Next, we examined the ability of C 17.2 cells to differentiate into neurons and astrocytes and observed, that cells overexpressing DISP3 reveal delay in differentiation, what we proved by analysis of cell specific markers.

Using CRISPR-Cas9 targeting system, we reduced DISP3 expression within D341 cells and observed decrease in their proliferation. Finally, we analysed cell cycle profile of DISP3-downregulated D341 cells.

Key words: Dispatched 3 (DISP3), cancer, proliferation, differentiation