Role of *DIRC3* gene in development of thyroid cancer.

Differentiated thyroid cancer, one of the most common cancers of hormonal system, is diagnosed annually in 3000 patients in Poland, mostly in women. In developed countries its incidence is increasing rapidly, whereas in the United States the rise in its incidence is one of the highest among all cancer types. Although prognosis for most thyroid cancer patients is very good, in a few percent of cases tumor is growing aggressively leading to formation of metastasis and consequently patients' death. Currently the background of these events is poorly understood, however recent large-scale studies have revealed that certain hereditary genetic variants (so called polymorphisms) have a significant impact on thyroid cancer development and its aggressivity. One of the most interesting risk factors identified in these studies is a gene called *DIRC3*. Although its function remains unknown, there is rich evidence of its involvement in cancer biology. It has been shown that certain hereditary variants in *DIRC3* increase risk of thyroid cancer by approximately 40% and increase cancer related mortality by 60%. Mutations and polymorphisms in *DIRC3* have also been shown to contribute to familiar renal cancer and breast cancer development. *DIRC3* is classified as a gene producing "long noncoding RNA" (lncRNA), what describes its inability to produce proteins. In last few years lncRNA genes have become subjects of vigorous interest in cancer research with much evidence of their involvement in regulation of cancer cell growth, metastasis formation and other processes.

The aim of this project is to describe *DIRC3* function and identify its role in differentiated thyroid cancer progression. We utilized genetic material isolated from thyroid tumors to quantify *DIRC3* expression (production) what revealed abrogated *DIRC3* level. Next, we will characterize *DIRC3* function in *in vitro* experiments applying molecular biology methods capable of increasing or decreasing lncRNA activity. Thyroid cancer cells modified with these techniques will be tested in an effort to describe the effect of *DIRC3* perturbations on cancer cell growth and activity of its genes. We predict that understanding *DIRC3* function will not only explain the mechanisms in which the hereditary variants contribute to the thyroid cancer risk, but will also pinpoint significant alterations that shape more aggressive cases of this cancer type. These discoveries may be thus applicable for identification of patients requiring the most intensive care and treatment.