DESCRIPTION FOR THE GENERAL PUBLIC

In Poland, bladder cancer is in fourth place of morbidity and fifth of mortality in men. Therefore, it is important to understand the molecular mechanisms associated with this pathological state. One of the unusual tumor suppressor genes, whose function has not been fully understood in bladder cancer at the molecular level is *WWOX* gene. Studies have shown that its expression in the bladder cancer could be regulated by methylation of the promoter and exon 1 and loss of heterozygosity, which can be related to cigarette smoking. One of its protein partner is AP2γ transcription factor, which activity is inhibited in the cytoplasm by sequestration through interaction with WWOX.

Preliminary results based on bioinformatics analysis of the risk of recurrence based on the *WWOX* expression level in the interaction with *TFAP2A* and *TFAP2C* revealed different roles of *WWOX* gene (suppressor or oncogene gene). The results indicate a lower risk of recurrence in patients with low *WWOX* /high *TFAP2C* and a high level *WWOX* /high *TFAP2A*. Furthermore, *in silico* analysis suggests that in the above mentioned cell models other transcription factors can be regulated by WWOX. Therefore, in this project will be created two cell models in three bladder cancer cell line with different status of differentiation (grade 2,3,4). We will use retroviral or adenoviral system to increase expression genes and CRISPR-Cas9 system to knock out gene.Then, we will perform gene expression analysis at the level of the transcriptome and promoterome and its biological effects on processes adhesion, invasion, proliferation, apoptosis, anchorage-independent growth, growth in 3D. Analysis of protein collocation of the WWOX with AP-2α and AP-2γ transcription factors allow to know their direct interaction in specific cellular compartments.