DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Melanoma is the most malignant skin cancer type. Early stages of the tumor are relatively easy to cure, but there are serious issues when melanoma is advanced or when metastasis occurs. The mortality of patients who suffer from metastatic melanoma rises 80%. The new generation of biological drugs caused that for the first time, the statistics concerning mortality have slightly improved. That moderate success makes very rational to continue research on expanding therapies focusing on cancer biology and targeting molecular pathways crucial for growth, metastasis and respond to the treatment. One of the way to interrupt cancer cell development is to inhibit metabolism of DNA synthesis. DNA consists of deoxyribonucleotides which are synthetized by nucleotide reductase from ribonucleotides. Crucial for reductase activity is one of its subunit – RRM2. The high expression of RRM2 in many tumors (including melanoma) is related to chemoresistance due to high efficiency of DNA damage repair what decrease efficiency of cytostatic drugs. RRM2 is controlled by cyclin F, which low expression – on the contrary to RRM2 expression – causes worse outcome. The cyclin F is important for DNA repair, and also maintain genome stability inhibiting cell cycle progression when DNA damage is detected. However, our knowledge about action of cyclin F is poor. The studies suggest that increase in cyclin F expression may reverse chemoresistance via RRM2 depletion. Moreover, the growth in cyclin F expression may restore proper functioning of cell cycle checkpoints what may enhance therapy efficiency. Realization of proposed project should give answers for following questions:

(I) Is there a significant difference in expression of cyclin F in primary and metastatic melanoma cell lines?
(II) Is a low cyclin F expression condition alter the chemoresistance of melanoma cells via RRM2 pathway?
(III) Is an increase in cyclin F expression make melanoma cells more susceptible for UV radiation and anticancer drugs such as cisplatin and temozolomide through decrease in DNA repair efficiency?
(IV) Is an altered expression of cyclin F affect the expression profile of antiapoptotic and pro-apoptotic proteins?
(V) Is an altered expression of cyclin F affect inhibition of cell proliferation induced with UV radiation and cytostatic drugs?
(VI) Is an altered expression of cyclin F influence the ability of melanoma cell to migration and its invasiveness profile?

If our hypothesis is correct, the results of the study will give the reason to consider therapy strategies based on cyclin F/RRM2 axis.