Projekat prof. dr Vladimira Dobričića

1. **Naslov**: Utilization of interplay between inflammation and cancer in the development of compounds with anticancer activity;
2. **Akronim**: InfCanPlay;
3. **logo projekta**: u prilogu mejla;
4. **budžet**: 284.759,87 eura (33.601.664,66 dinara).

2. **Sastav tima sa Fakulteta**: prof. dr Vladimir Dobričić (PI), prof. dr Zorica Vujić, prof. dr Olivera Čudina, prof. dr Mara Aleksić, prof. dr Jasmina Brborić, prof. dr Bojan Marković, prof. dr Branka Ivković, doc. dr Milkica Crevar, doc. dr Jelena Savić, asistent Jelena Rupar, istraživač saradnik Jelena Bošković;

3. **Apstrakt**: It is estimated that up to 20% of cancer-related deaths are linked with inflammation. Inhibition of inflammatory enzymes COX-2 and 5-LOX impacts cancer cells directly, or indirectly via tumor microenvironment. Wider anticancer potential was evaluated for a small group of COX-2 inhibitors, while there are no such data for dual COX-2 and 5-LOX inhibitors. In addition, COX-2 inhibitors show cytotoxicity not only to cells expressing COX-2, which implies that "non-COX-2" mechanisms are involved but still remain underexplored. The main aim of the Project is to select the most promising anticancer drug candidates from a group of 50 COX-2 and dual COX-2 and 5-LOX

   inhibitors (newly synthesized and those previously synthesized in our laboratory). New compounds will be designed (using structure-based and ligand-based in silico methods) and synthesized. Cytotoxicity will be evaluated towards 4 cancer cell lines by MTT assay. Wider anticancer potential of 5 selected compounds will be analyzed (synergism with conventional chemotherapy (MTT assay) and radiotherapy (clonogenic assay), inhibition of angiogenesis (on zebrafish embryos) and activity towards multidrug resistant cancer cells (direct cytotoxicity and sensitization to conventional chemotherapy using MTT assay)) and lead compounds will be identified. Mechanisms of action will be proposed for two lead compounds using bioinformatics analysis of genes expression. In vitro evaluation of passive gastrointestinal absorption (PAMPA and BMC), binding to human serum albumin (HPLC and electrochemistry) and metabolism (human liver microsomes) will be performed. QSPR, QSRR and QSMARt models will be created and, together with analysis of metabolism, will be used for the optimization of structures of lead compounds. The Project will result in the development of new anticancer candidates,

make new and strengthen previously established scientific collaborations and give starting point for further clinical evaluations of lead compounds.