

ABSTRACT

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Title of diploma thesis: **Synthesis and biological evaluation of purine inhibitors of phosphatidylinositol-3-kinases and related protein kinases II**

Cancer is a serious disease with an uncertain prognosis and difficult treatment. Nowadays, cancer is one of the most common causes of death worldwide. Options of therapies are evolving every year; nevertheless, we still do not have effective treatment available for all types of tumours. Patients often undergo conventional cytotoxic therapy or radiotherapy, which unfortunately have many side effects and they are not always effective. One of the highly researched ways how to make this treatment more effective is to disrupt corrective mechanisms of DNA damage, which are the essence of radiotherapy and some chemotherapeutics. For this purpose, phosphatidylinositol-3-kinase-related proteinkinases, especially DNA-dependent proteinkinase (DNA-PK) seem to be very useful, because they are highly involved in DNA repair. In this diploma thesis, 12 potential inhibitors of DNA- PK were prepared, from which 9 substances were tested alone on 9 tumour and 1 non-tumour cell lines. Two compounds were cytotoxic. The remaining 7 compounds has undergone to a chemosensitization test in combination with doxorubicin using the same cell lines. Only one compound (**33**) showed very significant chemosensitization of the tumour cells and will be subjected to further tests.