One of the major challenges of modern medicine is tumour resistance developed in response to various types of treatment including chemotherapy. Cancer, persistently leading as the second cause of death despite geographic localisation, and chemoresistance claim millions of lives every year besides countless amounts of public money and scientists' efforts. One way to tackle this issue is to design adjuvant therapies consisting of several substances which effectively target different cellular processes and together have an enhanced toxic impact on tumour cells. **In this project we propose to add inorganic molecules known as metallacarboranes to the list of potential drug candidates that in combination with known cytostatics might magnify their action towards cancer.** Metallacarboranes are abiotic, man-made particles of one of the highest thermal and physical stability known to chemistry and consist of a wide range of derivatives. Recent biological studies with metallacarboranes have indicated their terrific potential in the antimicrobials' design - along with high antibacterial activity they display low toxicity against eukaryotic cells, although it is possible to modify primary molecules to have specific antitumor activity. Metallacarboranes have been a subject of intensive research in clinical oncology as well - they are used as a rich boron carrier in boron neutron capture therapy. Nowadays, researchers' interests concentrate on introducing boron clusters as novel drug delivery systems and potential drugs themselves with promising antimicrobial and antitumor activity.

**In this project, we plan to search for intriguing metallacarboranes-doxorubicin combinations for treatment of cancer cells in *in vitro* studies.** We will synthesise $[COSAN]^-$-doxorubicin ion pair and covalently-bound conjugate and examine if the lipophilicity of the obtained combinations increases. The impact of lipophilicity on the enhanced drug transport will be measured on three different membrane models: liposomes, blood cells and eukaryotic cells. In the next step we will study the effect of changes in lipophilicity on the combinations' antitumour activity in both doxorubicin-sensitive and doxorubicin-resistant cancer cell lines cultured as monolayers and 3D spheroids. To check if $[COSAN]^-$-doxorubicin combinations oppose resistance mechanism generated towards doxorubicin alone we will perform mechanistic molecular studies. They will involve cell cycle process analysis, cell death via apoptosis mechanism and reactive oxygen species formation which in excess lead to cell damage. **All the described experiments taken together will provide a solid basis for introducing metallacarboranes and their derivative entities into biological as well as biomedical context.** An additional effect of this project will be the deepening of knowledge on metallacarboranes' activity within eukaryotic cells as right now the available literature severely lacks such reports.

Facing the concern of tumour cells generating resistance to administered therapy and thereby having a chance to continue growth and metastasis, we believe that designing innovative, original treatment involving unconventional molecules might provide a solution. Therefore, we propose to introduce such molecules - metallacarboranes to already clinically administered cytostatics treatment protocols in order to search for their combined action towards various cancer cells in *in vitro* studies (in both conventional and 3D cultures) and describe molecular pathways in which these combinations might be involved. This interdisciplinary project from the interface of inorganic chemistry and medical biology gives an opportunity to rethink our approach to chemotherapy and cancer biology in general.