DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Currently, cancer is becoming the leading cause of death. There are several reasons that might be underlying this state. The majority of scientists consider immortality of malignant tumour cells as one of them. According to this assumption, malignant tumour cells do not undergo senescence and, contrarily to normal ones, their death occurs solely under influence of toxic chemical compounds or ionizing radiation. This view is often found in textbooks. Research conducted by the applicant indicates that this theory is relevant in case of minority of cancer cells that may be stabilized *in vitro* as cell lines. This leads to a paradox – majority of cancer cells cannot be cultured *in vitro* under conditions considered as optimal. Therefore *in vitro* studies are conducted using a small percentage of specialized cells that possess the ability to adapt to *in vitro* conditions. Most of the scientists are not aware of the fact that experimental models constitute marginal representation of *in vivo* conditions. In case of glioblastoma, the most malignant primary brain tumor, only 10% of patient-derived cells can be cultured *in vitro*.

According to research conducted by the applicant, one of the reasons for the negative selection is senescence, occurring earlier in cancer cells than in case of normal stromal cells infiltrating the tumor. Paradoxically, normal cells adjust to *in vitro* culture conditions far better than cancer cells, commonly believed not to undergo senescence. Recently it has been proven that these cells are also subjected to programmed cell death that accompanies cells divisions (mitotic cell death) under optimal culture conditions. Thus, another opinion regarding the reasonability of induction of apoptosis with toxic chemical compounds or ionizing radiation in tumor cells has been undermined. Nevertheless, it brings hope that processes observed *in vitro* could be used in therapeutic purposes.

Research conducted by the author of the application demonstrated that the limited availability of stable glioblastoma models with specific oncogene alterations results from their inability to stabilize *in vitro*. The aim of the project is to determine the cause of the inability of *in vitro* culture of cancer cells with *EGFR*, *PDGFR*, *MET*, *MDM2*, *CDK4* and *EGFRvIII* amplicons, the ones that do not have stable cell line counterparts. Extrachromosomal amplicons are fragments of genome, in which a gene facilitating carcinogenesis is present in several copies. They are frequently observed *in vivo* (even over 50%, e.g. *EGFR* amplification in glioblastoma), while *in vitro* they are very rare. Identification of the causes of amplicon loss will enable to establish suitable *in vitro* culture conditions for successful maintenance and studies of their biology. On the other hand, determination of specific mechanisms of amplicon-containing cancer cells negative selection might be a basis of new therapeutic approaches.