Cancer is one of the leading causes of death in the world, and the number of new cases continues to increase year by year. High mortality often results from too late diagnosis, which is associated with the advanced stage of the disease, and localization of the tumor in hard-to-reach areas, which makes effective treatment difficult using conventional methods, such as chemotherapy, radiotherapy or surgical resection. Other reasons are the high toxicity and side effects of chemotherapeutic agents, as well as the tumor resistance to treatment. As a result, intensive research is being carried out around the world to find new alternative anti-cancer therapies that show better efficacy than traditional treatments. One of the most promising targeted radiotherapy is boron neutron capture therapy (BNCT). The basis of BNCT is the introduction into the patient's body of boron-rich compounds, which are selectively targeted to the tumor tissue. In the next stage, the tumor site is irradiated with a neutron beam, and the cancer cells in which the boron has accumulated in high concentration are destroyed. Due to the precise delivery of boron to the tumor, adjacent cells are not damaged. Research on this therapy has been going on since the 1950s, but it is still at the stage of clinical trials. One of the reasons is the lack of efficient boron carriers that will selectively deliver the appropriate concentration of this element to cancer cells. In recent years, many modified peptide derivatives, sugars, lipids, as well as boron clusters, polymers and liposomes as potential boron carriers have been tested. However, boron carbide deserves special attention, mainly due to the high content of boron in its structure, low toxicity tested in many *in vitro* and *in vivo* tests, as well as the possibility of synthesizing small-sized nanoparticles.

The project is part of the research on the search for new carriers enabling the selective delivery of the boron to the tumor environment. The main objective of the project is to obtain carriers based on macrophages obtained from the bone marrow of healthy mice capable to uptake the boron carbide in the form of nanoparticles up to 100 nm. As immune cells, macrophages have a natural ability to phagocytose and infiltrate the tumor microenvironment. Therefore, they are more and more often used in anti-cancer therapies to deliver therapeutic compounds. The project proposes to compare three macrophage cell populations – unpolarized (M0), classically activated (M1) and alternatively activated (M2) macrophages, in order to select the one that will be the most efficient in delivering boron to cancer cells. Depending on the type, macrophages show stronger or weaker phagocytic and migrating abilities as well as tropism to hypoxia and the ability to infiltrate the tumor tissue. The use of carriers based on cells isolated from a living organism in research, rather than on commercially available cell lines, enables a better imitation of the conditions prevailing *in vivo*. The "cellular carriers" obtained in the project will be characterized in terms of surface phenotype, cytokine production, migration ability, as well as the cytotoxic effect of boron carbide and its degree of uptake.

BNCT is used to treat patients with hard-to-reach tumors that are resistant to conventional treatment, such as glioblastoma multiforme, melanoma, and other head and neck cancers. In the case of brain tumors, a major obstacle to effective boron delivery is the blood-brain barrier, which is impermeable to many substances. Therefore, the next objective of the project is to develop an *in vitro* model to assess the ability of the obtained boron carbide-loaded macrophages to migrate towards murine GL-261 glioma cells through the murine bEnd.3 brain endothelial cells, which are part of the blood-brain barrier *in vivo*. In addition, the migration of bone marrow-derived macrophages enriched in boron carbide through the collagen layer, which is one of the many components abundantly present in the tumor microenvironment, will be investigated.

The results of this project will determine the effectiveness of bone marrow-derived macrophages in delivering boron carbide to tumor cells across endothelial cells as well as extracellular matrix components. The results will also form the basis for extended research on the use of phagocytic cells as boron carriers in boron neutron capture therapy.