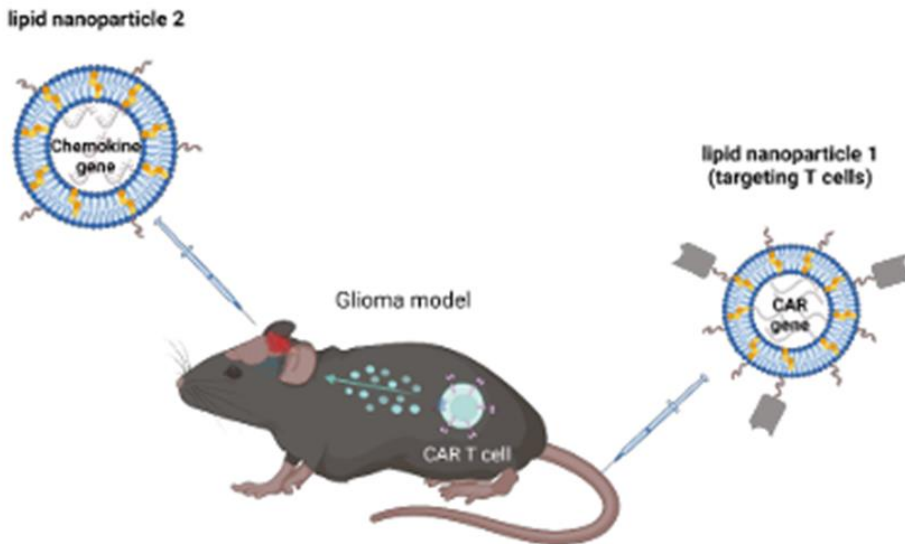


## Development of cell therapy for patients suffering from glioma



Glioma is the most aggressive brain tumor and one of the most lethal cancers. The current standard of care, which consists of surgery, radiotherapy and chemotherapy, is only able to modestly increase patient survival. There is therefore an urgent need to develop alternative treatment strategies. Recently, approaches that use the immune system to fight cancer, together known as immunotherapy, have shown to be efficient in several cancer types and are being developed for patients suffering from glioma.

Among immunotherapy approaches, cell therapy is using the patient's own immune cells, in particular T lymphocytes (also called T cells). T cells are white blood cells that have the capacity to make holes in the cells they recognize as abnormal and eliminate them. To use these cells against cancer, T cells are modified in the laboratory so that they recognize tumor cells. Among cell therapy approaches, one is called chimeric antigen receptor (CAR) T cell therapy. In that approach, an antibody that recognizes the tumor is selected and artificially inserted in the T cell, transforming it into a CAR T cell. This allows redirecting the T cells to the tumor and promoting tumor cell killing. The genetic information used to produce the CAR is introduced in the T cell via a delivery vector and CAR T cells then are amplified and infused to the patient. The CAR T cell approach is already being used successfully in patients with leukemia and lymphoma and is now in development for glioma.

Currently, the CAR T cell product is manufactured in the laboratory through a procedure that is a tedious, time-consuming and costly. In our proposal, we suggest to use lipid nanoparticles to deliver the genetic information required to make the CAR T cell directly to the patient. The lipid nanoparticles will be generated in the laboratory and will then be injected in the blood of the patient, where they will enter T cells and modify them (see Figure, right). This will allow generating CAR T cells in the body of the patient, in a simple, fast and inexpensive way.

In addition, in order for the CAR T cells to move from the blood to the tumor located in the brain, we will develop a second lipid nanoparticle that carries the genetic information to make proteins (called chemokines) that attract immune cells (see Figure, left). These lipid nanoparticles will be directly injected in the brain of the patient. In this way, we will develop a system to manufacture CAR T cells in the patient and help them go to their site of action.

In the current project, we will work with a mouse model of glioma, which will enable us to test our system and optimize it. Then, if successful, we will open a clinical trial for patients suffering from glioma. This project will thus potentially lead to the implementation of a novel treatment approach for patients and hopefully increase their survival and quality of life.