Our goal is to engineer a microglia cell to seek and destroy the cancer-initiating cells in glioblastoma multiforme. The engineered microglia will act as a modular machine with many future applications.

Abstract

Glioblastoma multiforme (GBM) is one of the most common forms of primary brain cancer which usually results in mortality. To date, it has been difficult to overcome primary brain cancer resulting from GBM, primarily because the cancer-initiating cells are suspected to be highly resistant to current cancer therapies. Specifically, CD133+ cells have shown resistance to hypoxia, irradiation, and some forms of chemotherapy. CD133+ hunting machines will be created by genetically engineering microglial cells (BV-2) with mamalian expression vectors. The project will also take advantage of inherent qualities of the microglia such as constant environmental sensing and quick motility. The engineered BV-2s will be equipped to locate the specific CD133+ GBMs and label the targeted cells with a tat-GFP fusion protein. It is the goal of this study to show an alternative approach to cancer treatment, and to emphasize the power of biologically available options to fight the disease.

Background

According to the WHO, glioblastoma multiforme (GBM) is a grade 4 tumor. Glioblastoma contain multiple types of cells, making them difficult to treat. Current methods for tumor removal include: surgery, ultrasonic aspiration and polymer wafers, stereactactic radiosurgery, radiotherapy, and chemotherapy. Microglia are brain macrophages located in the parenchymal space. They share many, if not all, of the properties of macrophages in other tissues, but they have a "ramified", or branching out, morphology when in the resting state. Cell-penetrating peptides (CPPs) are short peptide sequences that have the ability to penetrate the plasma membrane, allowing for the uptake of molecules. Molecules can range in size from nanoparticles to proteins, including even fragments of DNA. The first CPP discovered is known as transactivating transcriptional activator (tat). It was discovered while studying HIV-1. In this study, a fusion protein will be created by combining tat and green fluorescent protein (GFP) to act as a labeling mechanism of the CD133+ cells.