Slow-cycling tumor stem cell based immunotherapy for malignant glioma

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Glioblastoma (GB), the most common primary malignancy of the central nervous system, is almost universally fatal despite aggressive therapies. Considering the diffuse nature of GB, targeting residual cells after surgical resection of the primary tumor mass is a daunting challenge. The ability of the immune system to recognize altered tumor cells while also preserving the surrounding normal tissue offers a critical advantage over the nonspecific nature of conventional treatments.

Our lab is developing novel immunotherapy strategies based on the use of specific subpopulations of GB cells such as cancer stem cells as activator of immune effector cells. The goal of the proposed project is to establish the immunogenic ability of a specific GB cancer stem cell compartment compared to the rest of the tumor population, and to investigate the ability of a dendritic cell-based vaccine to target this clinically relevant subpopulation of cancer-propagating cells.

Medical students will participate in isolating nucleotides from the different GB subpopulation of cells and assess their ability to activate dendritic cells to stimulate the antitumor activation of effector T-cells. T-cell functional stimulation will be determined using a Th1/Th2 cytokine release assays (cytometric bead array). The students will also participate in experiments assessing functionally the efficacy of this specific dendritic cell-based vaccine to inhibit the expansion capacity, and hence, the tumor-propagating ability of the different subpopulations of GB cells. Using a syngeneic tumor model, medical students will contribute to quantify and compare cell death, expansion rates and frequencies in the different GB cell populations, determined via flow cytometry, sphere forming frequency assay and in vivo limiting dilution transplantation assay, respectively.

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References