I am examining the role of the molecular complex cyclinD1-CDK4 in the development of glioma. This complex drives the proliferation of glial tumor cells and permits their unfettered growth. Therapeutics to inhibit this complex are available and are currently in clinical trial for other malignancies. My work is showing the importance of this complex to glial tumor development and indicating that therapeutics used for other malignancies should be considered for glioma.

Current treatment regimens provide little overall survival benefit to patients suffering from brain tumors. Demonstrating that the molecular complex of cyclinD1-CDK4 is a viable target in glioma means potentially adding the CDK inhibitory drugs currently available to the arsenal we use to combat these aggressive tumors.

Adilia Hormigo

Title: Understanding the Role of CD133+ Stem Cells in the Brain

Currently there are only a few drugs with a rather limited success for the treatment of high-grade gliomas. We provided new insight on CD133-expressing cells in the brain and in tumors. This knowledge is important for the development of new strategies to control of tumor growth.

CD133 is a surface antigen considered the universal marker of normal stem cells in many tissues, including the brain, and potentially of cancer stem cells including those found in malignant gliomas. We were able to study the distribution and characterize the type of cells that express CD133 in the brain, resolving the inconsistent detection with antibodies that recognize ill-defined glycolysated epitopes of the protein. Furthermore, we were able to characterize these cells in malignant glioma and within the vascular niche. This could pave the way in the identification of novel targets for the discovery of new drugs to be used in preclinical studies.

Michael R. McDevitt

Title: Targeting Tumor Vasculature with a Self-Assembling Synthetic Infarct

Glioblastoma multiforme (GBM) is a malignant astrocytoma and one of the most common glial tumors. It is also one of the most rapidly fatal and incurable cancers, for which novel therapeutic approaches are needed. The standard of care for newly diagnosed GBM is a three-pronged regimen to treat the disease: (i) surgical resection (ii) whole-brain or stereotactic external-beam radiotherapy, and (iii) chemotherapy. However, all three of these modalities have limitations regarding untoward damage from excision and radiotoxicity to normal brain, and the probability of recurrence is nearly universal.

Novel multimodal nanomaterials can be designed and implemented to diagnose and treat GBM and may potentially afford clinical methods to specifically target and bind to the angiogenic and aberrant vascular endothelium in tumor; locally irradiate those vessels and the adjacent cancer stem cell niche with cytotoxic high-energy alpha particles; and provide for diagnostic follow-up for recurrence and retreatment if necessary. Such an agent could potently eradicate tumor while sparing normal tissue and simultaneously report the dose delivered and the extent of disease. The proposed theranostic agent is an innovative nanomaterial that is based on a multimodal carbon nanotube platform and may impact the way GBM is treated.

The proposed theranostic agent is designed to perform the following treatment tasks: (i) target the GBM vascular network and specifically bind to the tumor vascular endothelium; (ii) deliver a cytotoxic dose of short-ranged, high-energy alpha-particle emissions to these cells and also to their local microenvironment via the decay of the radionuclide; (iii) report the amount of agent delivered, its residence time, and precise location within the GBM via incorporation of a positron-emitting radionuclide; and (iv) accomplish a diagnostic follow-up to look for recurrence of disease and retreat if necessary. Each of these features could be rapidly translated into human application, and we have a track record of successfully translating similar novel targeted theranostic drugs from the bench to clinical trials.

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