

*New Funding from Abbie's Army Foundation*

Abbie's Army Foundation (<http://www.abbiesarmy.co.uk>) has granted funding to the Monje Lab to support a project entitled "Towards a multi-pronged approach for DIPG therapy: targeting BDNF-TrkB signaling in the DIPG microenvironment"

Successful treatment of diffuse intrinsic pontine glioma (DIPG) will likely require a multi-pronged approach, targeting intrinsic vulnerabilities of DIPG cells, blocking key signals from the microenvironment of the developing childhood brain that fuel DIPG growth, and directing the immune system to attack the cancer.

DIPG hijacks mechanisms of development and plasticity in the childhood brain. Neuronal activity is a key regulator of brain development and plasticity, and we have recently shown that active neurons in the tumor microenvironment robustly promote DIPG growth. A growth factor called "brain-derived neurotrophic factor" (BDNF) is secreted in response to brain activity and plays numerous roles in childhood brain development. BDNF is also important for the adaptability of the brain necessary for learning and changing in response to experience. We have identified BDNF as a molecule that promotes DIPG proliferation, and hypothesize that DIPG subverts BDNF signaling to promote cancer growth. In the proposed experiments, we seek to determine the therapeutic potential of blocking BDNF signaling in DIPG, cutting off what we hypothesize is a key microenvironmental factor fueling DIPG growth.

The majority of the proposal focuses on BDNF, a leading candidate for microenvironmental therapy in DIPG. Parallel work from our group has focused on developing an effective immunotherapy for DIPG and included in the proposed work is a discrete set of experiments seeking to advance our mechanistic understanding of a promising immunotherapeutic strategy using chimeric antigen receptor T cells (CAR T cells). Ultimately, we hope to combine immunotherapy with complementary strategies like targeting microenvironmental determinants of DIPG growth. This sort of "one-two punch" approach, hitting the cancer from different angles, may move us closer towards the goal of defeating DIPG.

