ET-02. THERAPEUTICALLY ENGINEERED INDUCED NEURAL STEM CELLS ARE TUMOR-HOMING AND INHIBIT PROGRESSION OF GLIOBLASTOMA
Adolfo Alfonso-Pecchio, Juli Bago’, Onyinyechukwu Okolie, Raluca Dumitru, and Shawn Hingtgen; The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Transdifferentiation (TD) is an exciting new advancement in somatic cell reprogramming that eliminates the pluripotent intermediate stage to create cells that are ideal for personalized cell transplant therapy. Induced neural stem cells (iNSCs) are the newest cell type created by TD. Here we begin to define the efficacy of iNSC therapy for central nervous system disorders. We developed the first iNSC-based drug deliver vehicles, and show that engineered iNSCs are tumor-homing drug delivery vehicles with significant anti-cancer effects in models of glioblastoma (GBM). After genetically engineering iNSCs with tumoricidal or diagnostic transgenes, we observed that the modified iNSCs proliferated and differentiated into astrocytes and neurons with the same efficiency as unmodified cells. Non-invasive serial imaging revealed that engineered iNSCs implanted into the parenchyma of mice survived more than 1 month. In vitro time-lapse motion analysis showed iNSCs exhibit tumor-homing properties similar to brain-derived NSCs, while iNSCs implanted into the frontal lobe of mice migrated through the brain homing to invasive GBM cells. iNSCs engineered with the anti-cancer molecule TRAIL (iNSC-sTR) stably released the tumoricidal agent and killed co-cultured human GBM cells. We evaluated iNSC-sTR therapy in orthotopic mouse models of solid and patient-derived diffuse GBM. We found that iNSC-sTR therapy reduced GBM volumes 20- to 230-fold and doubled the survival of tumor-bearing mice compared to control mice. These data provide the first evidence that tumoricidal iNSCs can be used to efficaciously treat brain cancer, and provide a foundation for the continued development of iNSC-based therapies.