LIST ALL AUTHORS and AFFILIATIONS – underline presenting author
Farhad Dastmalchi¹, Aida Karachi¹, Hassan Azari¹, Duane Mitchell¹, Maryam Rahman¹

¹Preston A. Wells, Jr. Center for Brain Tumor Therapy, UF Brain Tumor Immunotherapy Program, Department of Neurosurgery, McKnight Brain Institute, University of Florida, Gainesville, FL, USA,

TITLE
Strategy to enhance DC migration for increased efficacy of dendritic cell vaccine immunotherapy

HYPOTHESIS:
Based on our previous publication in Nature, we have established that increasing dendritic cell (DC) migration in glioblastoma (GBM) patients treated with DC vaccination results in significantly improved survival.

BACKGROUND/AIMS:
In this project we evaluated the efficacy of using a non-toxic, naturally occurring metabolite called sarcosine to increase cellular migration in the setting of cellular immunotherapy.

METHODS:
In-vitro migration was analyzed with cytotoxic cell transfer membrane. In vivo migration was evaluated by vaccinating in a murine model. C57BL/6 mice received tetanus diphtheria (Td) toxoid vaccine prior to vaccination with DCs. After 48 hours post-vaccination, animals were culled for migration analysis of the dissociated lymph nodes through cytometry and immunofluorescence technique. This experiment was repeated to for spleen analysis as well.

RESULTS & CONCLUSIONS
Sarcosine did not alter DC growth or phenotype. DCs loaded with sarcosine demonstrated significantly increased migration in vitro. Mice treated with DC vaccination in the setting of sarcosine demonstrated increased DCs migration to draining lymph nodes and spleens after 48 hours. The migration percentage of cells to the draining lymph nodes were 7.5%, 18.3% and 25.3% for regular DCs, sarcosine loaded DCs and sarcosine plus PKH loaded DCs respectively (p<0.05). All analyses showed migration of DCs was further enhanced when sarcosine combined with PKH staining. Sarcosine in combination with PKH increased antigen specific CD8 T cells after vaccination compared to regular DC vaccination. Sarcosine is non-toxic and significantly increases DC migration after vaccination resulting in a more robust immune response to vaccination. The effects of outcomes in a brain tumor model are ongoing.