BRIAN D. SILBER
MEMORIAL FUND
STRIVING TO CURE SPINAL TUMORS
18 HEATH ROAD | PEABODY, MA 01960
(978) 535-4788 | INFO@BRIANSILBERFUND.ORG

Research Updates at the Brian D. Silber Spine Tumor Clinic, Massachusetts General Hospital
April 2021

William T. Curry, Jr, MD
Co-Director, MassGeneral Neuroscience
Director of Neurosurgical Oncology, Mass General Cancer Center
Adeline Rose Wydotis Professor of Neurosurgery, Harvard Medical School

Safer and Faster Diagnosis of Spinal Cord Tumors

Liquid Biopsy and Rapid Diagnosis of Tumors in the Brain or Spinal Cord

A tumor in the brain, the brainstem, or in the spinal cord can present with loss of function, such as weakness, numbness, or difficulty with speech and language. A patient has an MRI and is referred to a specialist. At that point, typically, many questions remain. Is this a tumor, an infection, or inflammatory disease such as multiple sclerosis? Modern MRI results, while often highly suggestive of one diagnosis or another, are not specific enough to make these determinations with sufficient confidence to begin treatments such as radiation, chemotherapy, or powerful anti-inflammatory agents. Even if we were absolutely certain that the image on the MRI represented a tumor, we need to know more. What kind of tumor is it? Is it high-grade or low-grade? In this era of molecular classification and therapeutics, what are the mutations in the tumor DNA that drive prognosis, dictate treatment decisions, and might be directly targetable? Usually, a biopsy must be performed, which in the brain or spinal cord is not only invasive but also can be risky and require a recovery period. Furthermore, the time between referral and full diagnosis can be significant, delaying important treatment. Overcoming these challenges, risks, and delays would be a great advantage for patients with spinal cord tumors. The details of the tumor are so critical for our decision-making, but a biopsy of the spinal cord is a significant and high-risk procedure.

At Mass General, we are working on new technologies to rapidly obtain tumor diagnostic results from body fluids such as blood or cerebrospinal flood (CSF) – bypassing the need for biopsy. A team led by neurosurgeon Ganesh Shankar, MD, PhD has developed a technique by which small amounts of tumor tissue or cerebrospinal fluid, taken by lumbar puncture, can be processed. The presence of tumor-specific DNA can be confirmed within 30 minutes to 2 hours – a dramatic shift in both the accuracy and pace of our diagnostics, not to mention a significant cost reduction. This technique, recently published in the high-impact journal *Blood*, has been validated for lymphoma and glioma in the brain, and we now aim to validate it for patients specifically with apparent tumors in the spinal cord. Given the rarity of spinal cord tumors, we will partner with other academic medical centers and pool our resources. The continued support of the Brian D. Silber Memorial Fund makes this collaboration possible.

Capitalizing on Artificial Intelligence for Noninvasive Diagnosis of Tumors in the Central Nervous System

Similarly, artificial intelligence and machine learning have the potential to overcome the need for invasive biopsy. An MRI actually contains huge amounts of data that are not discernible by human inspection or quantification but are potentially detectable by computer algorithms. We are working with colleagues in the Martinos Center for Biomedical Imaging to correlate MRI findings with tumor-specific diagnoses, including predicting the molecular changes that exist within those tumors. We have established these methods and are seeing exciting results for accurate prediction of certain subtypes of brain tumors. With the support of the Brian D. Silber Fund, we will be able to create an international, multicenter database of spinal cord tumor scans, pathologies, and outcomes in hopes of detecting an artificial intelligence-enabled, non-invasive but accurate predictor of pathology.

Understanding the Microenvironment of Spinal Cord Tumors Can Drive Rational Immunotherapy for Spinal Cord Tumors

Drugs or biologics that drive a patient's immune system to effectively attack cancer cells (known as immunotherapy) represent an exciting advance against many kinds of cancer. Clear success has yet to be seen in tumors of the brain and spinal cord, in part, because we do not have a full understanding of which immune cells can get into these tumors, how they traffic there, and how the nervous system affects their function. Both in mouse models of tumors and using human tissues, we are performing detailed analyses of how the immune system responds to spinal cord tumors with different mutations, guided by work previously supported by the Silber Fund. We will then perform preclinical (mouse) experiments utilizing a variety of immune-targeting approaches, tailoring them to what we have learned about the baseline immune responses. We are doing this work in the Neurosurgery Translational CNS Tumor Laboratory in collaboration with colleagues in the Mass General Cancer Center.