

## **Intraoperative Mass Spectrometry for Personalized Treatment of Brain Tumors**

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### **2010 Project Accomplishments**

The long-term goals of this project are to introduce MALDI (Stoeckli, M, 2001) and Desorption ElectroSpray Ionization (DESI) mass spectrometry imaging (Wiseman, JM, 2006 and 2008) analyses of surgical tissue in image-guided therapy to contribute to both the accurate identification of brain tumors, and the specific identification of their boundaries to healthy tissue. Both MALDI and DESI tissue analysis can also provide direct detection of drugs and their metabolites, potentially contributing to refine the deployment of clinical trials for selected targeted therapies. The inclusion of these novel approaches could contribute extensive molecular information in real time to assist in the tailoring of personalized treatment, from surgery to administration of select adjuvant chemotherapy.

This initial year allowed us to establish and adapt the laboratory methodologies. MALDI imaging was used to characterize meningioma progression and results were published in the journal *Analytical Chemistry* as an Accelerated Article. DESI imaging was used to study astrocytomas, and the results supported the concept of using DESI mass spectrometry to rapidly provide diagnostic information. In this case, grades of astrocytomas were distinguished based on lipid signatures, and the study was reported in the journal *Angewandte Chemie*. DESI mass spectrometry was also used for the analysis of tumor cell concentration, which could be used to inform the neurosurgeon in delineating tumor margins. The study report was accepted for publication in the journal *Neurosurgery*. Methodologies for the preparation of tissue for MALDI mass spectrometry imaging were published, as well as justification for the use of high field FTICR mass spectrometry for the imaging of small molecules and mathematical approaches to data analyses.

The project was made possible by support from the Brain Science Foundation, and from invaluable collaborations with groups at BWH, DFCI, Brandeis University, Purdue University, Georgia Institute of Technology, and Prosolia Inc. Our laboratory also welcomed two new members this year: Isaiah Norton and Dr. Murat Karabacak.

### **Peer-reviewed Manuscripts**

- 1) Agar, N.Y.R., Malcolm, J.G., Mohan, V., Yang, H.W., Johnson, M.D., Tannenbaum, A., Agar, J.N., and Black, P.M. (2010) *Analytical Chemistry*. **Accelerated Article**. Imaging of Meningioma Progression by Mass Spectrometry. *Selected as a Highlight by the Editor*. PubMed: 20196536; NIHMSID: 184740
- 2) Karabacak, N.M., Easterling, M.L., Agar, N.Y.R., Agar, J.N. (2010) *J. Am. Soc. Mass. Spectrom.* 21(7): 1218-1222 Transformative Effects of Higher Magnetic Field in Fourier Transform Ion Cyclotron Resonance Mass Spectrometry. PMID: 20444622
- 3) Agar, N.Y.R., Kowalski, J.M., Kowalski, P.J., Wong, J.H., and Agar, J.N. (2010) *Methods in Molecular Biology*. 656: 415-431. Tissue preparation for the in situ MALDI MS imaging of proteins, lipids, and small molecules at cellular resolution. PMID: 20680605
- 4) Eberlin, L.S., Dill, A.L., Golby, A.J., Ligon, K.L., Wiseman, J.M., Cooks, R.G., and Agar, N.Y.R. (2010) *Angewandte Chemie*. 49(34):5953-5956. Discrimination of Human Astrocytoma Subtypes by Lipid Analysis using Desorption Electrospray Ionization Imaging

Mass Spectrometry. PMID: 20602384 Highlight by Nature Publishing Group *Science-Business eXchange*. Published online July 29, 2010. SciBX 3(29); doi:10.1038/scibx.2010.910.

- 5) Agar, N.Y.R., Golby, A.J., Ligon, K.L., Norton, I., Mohan, V., Wiseman, J.M., Tannenbaum, A., and Jolesz, F.A. (In press) *Neurosurgery*. Development of Stereotactic Mass Spectrometry for Brain Tumor Surgery.

#### **Proceedings of Meetings (full-length manuscripts)**

- 6) Mohan, V., Kolesov, I., Jolesz, F.A., Agar, N.Y.R., and Tannenbaum, A. (2010) *Mathematical Theory of Networks and Systems (MTNS)*. Intraoperative prediction of tumor cell concentration from Mass Spectrometry Imaging.
- 7) Mohan, V., Huang, J., Agar, N.Y.R., and Tannenbaum, A. (2010) *Medical Image Computing and Computer Assisted Intervention (MICCAI), Computational Imaging Biomarkers for Tumors (CIBT)*. Automatic classification of glioma subtypes and biomarker identification using DESI Mass Spectrometry Imaging.

#### **Patent**

International Application, Filing Date: April 01, 2010. U.S. Provisional Patent Application No.: 61/165635, "Method and System for Surface Sampling". Applicant: Prosolia Inc., and Brigham and Women's Hospital. Inventors: Agar, N.Y.R., and Wiseman, J.M.

#### **New Funding**

##### ***National Institutes of Health (NIH)- NIH Director's New Innovator Award***

Real-Time Stereotactic Mass Spectrometry Tissue Analysis for Intraoperative Neurosurgical Guidance  
*PI, Nathalie Y.R. Agar*

##### ***Brain Science Foundation***

On-Chip Characterization of Brain Tumor Heterogeneity by Single Cell Mass Spectrometry  
*PI, Nathalie Y.R. Agar, Ph.D., Department of Neurosurgery, BWH*  
*Co-PI, Philip De Jager, M.D., Ph.D., Department of Neurology, BWH and Broad Institute of MIT and Harvard*  
*Co-PI, J. Christopher Love, Ph.D., Department of Chemical Engineering, Massachusetts Institute of Technology*

##### ***Center for Integration of Medicine and Innovative Technology (CIMIT)***

Intraoperative Stereotactic Molecular Imaging of Tumor Boundaries by Mass Spectrometry  
*PI, Nathalie Y.R. Agar*

***Thank you to the Brain Science Foundation!***