BIOGRAPHICAL SKETCH

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NAME: Banu, Matei Alexandru

eRA COMMONS USER NAME (credential, e.g., agency login): mateibanu

POSITION TITLE: Clinical Instructor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Carol Davila University of Medicine, Bucharest, Romania	MD	10/2005	9/2011	Medicine
Weill Cornell Medical College, New York, New York	Postdoctoral Fellowship	10/2011	02/2014	Glioma and stem cell biology
Columbia University Irving Medical School, New York, New York	Postdoctoral Fellowship	02/2014	06/2016	Molecular and computational biology
Columbia University/New York Presbyterian Hospital, New York, New York	Neurosurgery Residency	06/2016	06/2023	Neurological Surgery
University of Texas MD Anderson Cancer Center, Houston, Texas	Clinical Fellowship	07/2023	06/2024	Neurosurgical oncology
Stanford University, Palo Alto, California	Clinical Fellowship	07/2024	06/2025	Skull base neurosurgical oncology

A. Personal Statement

My career goal is to become an academic neurosurgeon with a clinical focus on brain tumors and a principal investigator of an NIH funded neuro-oncology laboratory, working to develop new therapeutic approaches for brain and skull base tumors. My specialized clinical training and my research experience in molecular and computational biology provide me with the necessary background to complete the proposed project and quickly translate the relevant findings into clinical trials. My current research focuses on understanding treatment resistance and recurrence in GBM and in skull base malignancies, such as clival chordomas, as well as investigating novel treatment strategies that are tailored based on molecular and imagistic biomarkers. Tumor cell subpopulations and non-neoplastic cells in the tumor microenvironment exhibit distinct molecular, epigenetic or metabolic vulnerabilities that can be therapeutically targeted. Understanding these vulnerabilities and using combined drug regimens are essential to increase treatment efficacy. I have recently identified distinct mitochondrial metabolic programs in a subset of neoplastic cell populations that can be leveraged therapeutically. Furthermore, I have employed a metabolic approach to target the immunosuppressive glioma microenvironment, using novel ferroptosis-inducing agents. I am currently investigating the potential of ferroptosis-inducing drugs to disrupt glioma cell-microglia crosstalk and target immunosuppressive T cell populations in order to obtain an effective and durable response to immunotherapy. Furthermore, I am currently working on developing a molecular, cellular and metabolomic atlas of the neoplastic cell states and tumor-associated cells in clival chordomas, a rare but aggressive tumor of the skull base with limited therapeutic

options. Specifically, I am comparing matched primary and recurrent chordoma samples to understand evolutionary trajectories of chordoma cells and the impact of radiation on the tumor microenvironment in these aggressive malignancies of the clivus. Overall, my goal is to identify novel treatment strategies tailored to tumor and patient specific characteristics that could be quickly translated to clinical practice. My projects are therefore also designed to identify potential molecular and metabolic biomarkers, that could be used to improve patient selection and to track response to treatment.

B. Positions, Scientific Appointments and Honors

2024- Clinical Instructor, Department of Neurosurgery, Stanford University, Palo Alto, California
2023-2024 Clinical Instructor, Department of Neurosurgery, University of Texas MD Anderson Cancer Center, Houston, Texas
2016-2023 Neurosurgery Resident, Department of Neurosurgery, Columbia University Irving Medical Center/New York Presbyterian Hospital, New York, New York
2020-2021 Post-doctoral Research Associate, Bartoli Brain Tumor Laboratory, Columbia University Irving Medical Center, New York, New York
2017-2018 Post-doctoral Research Associate, Bartoli Brain Tumor Laboratory, Columbia University Irving Medical Center, New York, New York
2014-2016 Post-doctoral Research Associate, Bartoli Brain Tumor Laboratory, Columbia University Irving Medical Center, New York, New York
2011-2014 Post-doctoral Research Associate/Laboratory Manager, Glioma and Stem Cell Biology Laboratory, Department of Neurosurgery, Weill Cornell Medical College, New York, New York

Other Professional Memberships

2020-present Member, North American Skull base Society
2020-present Member, Society for Neuro-oncology
2020-2023 Trainee Associated Member, Herbert Irving Cancer Center
2020-present NIH R38 Scholars
2019-2021 Member, Society of Immunotherapy in Cancer
2012-present Member, Congress of Neurological Surgeon
2012-present Member, American Association Neurological Surgeons

Honors and Awards

2021 New York Society for Neurosurgery Basic Science Research Award
2020-2021 Neurosurgery Research and Education Foundation (NREF) Research Fellowship Grant
2020-2021 NIH R38 Stimulating Access to Research in Residency (StARR) Training Grant
2018 NYS Neurosurgical Society Research Award
2017 New York Society for Neurosurgery Resident Research Award
2014-2015 Herbert Irving Cancer Center Interprogramatic Pilot Project
2011 *Summa cum laude* Carol Davila University of Medicine
2011 GlaxoSmithKlein Award for Excellence
2006-2011 National Merit Scholarship

C. Contributions to Science

1. **Dissected intratumoral heterogeneity in GBM and brain metastases.** We first started characterizing the cellular and molecular landscape in high grade gliomas using next generation sequencing, specifically bulk RNA-seq, on radiographically guided surgical specimens starting in 2014. This work identified for the first time that there are significant differences in cellular composition between the tumor core and the infiltrated tumor margins. This finding has important therapeutic implications as the core is removed during surgery whereas the margins lead to tumor recurrence and contain neoplastic subpopulations resistant to chemotherapy and radiation. More recently, we employed novel techniques such as single nuclei RNA-sequencing and spatial transcriptomics in conjunction with clinically relevant fluorescent dyes, such as 5-aminolevulinic acid, to further define the cellular landscape in GBM. These studies identified specific tissue states in the tumor microenvironment with important prognostic features and enriched in specific metabolic programs. Employing similar techniques on melanoma metastases we found that brain metastases adopted a specific neuronal-like state and were enriched in spatially dependent metabolic pathways compared to extracranial metastases. Furthermore, melanoma brain

metastases harbored large fractions of immunosuppressive cell populations such as macrophages and dysfunctional CD8+ T cells.

A. MRI-localized Biopsies Reveal Subtype-Specific Differences in Molecular and Cellular Composition at the Margins of Glioblastoma. Gill, B.J., Pisapia, D.J., Malone, H.R., Goldstein, H., Lei, L., Sonabend, A., Yun, J., Samanamud, J., Sims, J.S., **Banu, M.A.,** Dovas, A., Teich, A.F., Sheth, S.A., McKhann, G.M., Sisti, M.B., Bruce, J.N., Sims, P.A., Canoll, P. PNAS, August 2014 DS
B. Dissecting the Treatment-naive Ecosystem of Human Melanoma Brain Metastasis. Biermann, J., Melms, J.C., Amin, A.D., Wang, Y., Caprio, L.A., Karz, A., Tagore, S., Barrera, I., Ibarra-Arellano, M.A., Andreatta, M., Fullerton, B.T., Gretarsson, K.H., Sahu, V., Mangipudy. VS, Nguyen TTT, Nair A, Rogava M, Ho P, Koch PD, **Banu M.A.**, Humala, N., Mahajan, A., Walsh, Z.H., Shah, S.B., Vaccaro, D.H., Caldwell, B., Mu, M., Wünnemann, F., Chazotte, M., Berhe, S., Luoma, A.M., Driver, J., Ingham, M., Khan, S.A., Rapisuwon, S., Slingluff, C.L. Jr, Eigentler, T., Röcken, M., Carvajal, R., Atkins, M.B., Davies, M.A., Agustinus, A., Bakhoum, S.F., Azizi, E., Siegelin, M., Lu, C., Carmona, S.J., Hibshoosh, H., Ribas, A,. Canoll, P., Bruce, J.N., Bi, W.L., Agrawal, P., Schapiro, D., Hernando, E., Macosko, E.Z., Chen, F., Schwartz, G.K., Izar. B. Cell, July 2022
C. Re-convolving the compositional landscape of primary and recurrent glioblastoma reveals prognostic and targetable tissue states. Al-Dalahmah, O., Argenziano, M.G., Mahajan, A., Furnari, J., Paryani, F., Boyett, D., Save, A., Khan, F., Li, J., Lu, H., Sun, Y., Tuddenham, J., Goldberg, A., Dovas, A., **Banu, M.A.,** Sudhakar, T., Bush, E., Lassman, A., Bruce, J.N., Sims, P.A., Menon, V., Canoll, P. Nature Communications, May 2023
D. Single-cell analysis of 5-aminolevulinic acid intraoperative labeling specificity in glioblastoma. Liu, Z., Mela, A., Argenziano, M.G., **Banu, M.A.,** Furnari, J., Kotidis, C., Sperring, C.P., Humala, N., Mahajan, A., Bruce, J.N., Canoll, P., Sims, P.A. Journal of Neurosurgery, September 2023

2. **Identified molecular and metabolic vulnerabilities in neoplastic cell subpopulations to design novel therapeutic approaches in GBM.** Glioma cells adopt a variety of cell states by activating neurodevelopmental transcriptional programs. Some of these programs can lead to synthetic lethality. Targeting these vulnerabilities can lead to novel cell state specific therapeutic approaches. I have investigated several such transcriptional pathways in GBM models, including the GSK3B/PP2A and the STAT3/SRC/EGFR pathway, both of which induced effective and tumor specific cell death. More recently, I have identified specific mitochondrial metabolic programs which are intimately linked to specific cell states, such as the quiescent astrocytic cell state. These metabolic programs also lead to a cell state specific vulnerability to ferroptosis, either via pharmacologic or genetic inhibition of the hydroperoxidase GPX4 or via cysteine and methionine deprivation. Additionally, we have proven that a simple diet can further sensitive neoplastic cells to induction of ferroptosis. Furthermore, I found that modulating mitochondrial function can lead to several types of cell death including apoptosis and ferroptosis. Importantly, we have recently discovered that stalling cells in quiescence via kinesin inhibitors can induce profound changes in cell states as a mechanism of resistance and that this can be mitigated via therapeutic drug combinations.
   A. Tight Regulation Between Cell Survival and Programmed Cell Death in GBM Stem-like Cells by EGFR/GSK3B/PP2A Signaling. Gursel, D.B., **Banu, M.A.,** Kobylarz, K., Berry, N., Marongiu, R., Burkhardt, JK., Kaplitt, M.G., Rafii, S., Boockvar, J.A. Journal of Neuro-oncology, October 2014
   B. Inhibition of Mitochondrial Matrix Chaperones and Antiapoptotic Bcl-2 Family Proteins Empower Antitumor Therapeutic Responses. Karpel-Massler, G., Ishida, C.T., Bianchetti, E., Shu, C., Perez-Lorenzo, R., Horst, B., **Banu., M.A.**, Roth, K.A., Bruce, J.N., Canoll, P., Altieri, D.C., Siegelin, M.D. Cancer Research, July 2017
   C. Induction of Synthetic Lethality in IDH1-Mutated Gliomas through Inhibition of Bcl-xL. Karpel-Massler, G., Ishida, C.T., Bianchetti, E., Zhang, Y., Shu, C., Tsujiuchi, T., **Banu., M.A.**, Garcia, F., Roth, K.A., Bruce, J.N., Canoll, P., Siegelin, M.D. Nature Communications, October 2017
   D. Protein kinase C$_{\iota}$ and SRC signaling define reciprocally related subgroups of glioblastoma with distinct therapeutic vulnerabilities. Kenchappa, R., Liu, Y., Argenziano, M., **Banu, M.A.**, Mladek, A., West, R., Luu, A., Quinones-Hinojosa, A., Hambardzumyan, D., Justilien, V., Leitges, M., Sarkaria, J.N., Sims, P.A., Canoll, P., Murray, N., Field, A., Rosenfeld, S. Cell Reports, November 2021
   E. Activation of STAT3 through Combined SRC and EGFR Signaling Drives Resistance to a Mitotic Kinesin Inhibitor in Glioblastoma. Kenchappa, R., Dovas, A., Argenziano, M., Meyer, C.T., Stopfer,

L., **Banu, M.A.**, Pereira, B., Griffith, J., Mohammad, A., Talele, S., Haddock, A., Zarco, N., Elmiquist, W., White, F., Quaranta, V., Sims, P.A., Canoll, P., Rosenfeld, S. Cell Reports, June 2022

F. Dietary restriction of cysteine and methionine sensitizes gliomas to ferroptosis and induces alterations in energetic metabolism. Upadhyayula, P., Higgins, D.M.O., Mela, A., **Banu, M.A**., Dovas, A., Zandkarimi, F., Patel, P., Mahajan, A., Humala, N., Nguyen, T.T.T., Chaudhary, K., Liao, L., Argenziano, M.G., Sudhakar, T., Sperring, C., Shapiro, B., Ahmed, E., Kinslow, C., Ye, L., Siegelin, M., Cheng, S., Soni, R., Bruce, J.N., Stockwell, B., Canoll, P. Nature Communications, March 2023

G. A cell state specific metabolic vulnerability to GPX4-dependent ferroptosis in glioblastoma. **Banu, M.A.***, Dovas, A.*, Argenziano, M.G.*, Zhao, W.*, Grajal-Cuervo, H., Higgins, D.M.O., Ye, L., Mahajan, A., Humala, N., Upadhyayula, P., Nguyen, T.T.T., Al-Dalahmah, O., Wu, P., Zandkarimi, F., Karan, C., Razavilar, A., Furnari, J., Siegelin, M., Kitajewski, J., Bruce, J., Stockwell, B., Sims, P.A., Canoll, P. bioRxiv April 2023

H. Multiplexed single-cell lineage tracing of mitotic kinesin inhibitor resistance in glioblastoma. Cheng, Y., **Banu, M.A.**, Zhao, W., Rosenfeld, S.S., Canoll, P., Sims, P.A. accepted Cell Reports, March 2024

3. **Developed drug delivery methods and cancer models to study personalized therapeutic approaches in neuro-oncology.** Accurate and realistic cancer models are critical for preclinical studies. Over the past ten years I have collaborated with multiple groups on developing models that can be used as precision medicine platforms, including several mouse models, a large animal model and patient-derived organotypic slice cultures. All these models were used to study a variety of therapeutics. These studies demonstrated cell state specificity of various drugs and revealed mechanisms of resistance and therapeutic evasion. We also developed a set of tagged monoclonal antibodies that can be used to track delivery both in cell and mouse models and in future clinical trials. Recently, we developed a drug delivery system for brain tumors using an implantable pump for long term intratumoral convection enhanced delivery which we successfully tested in a Phase 1b clinical trial.

   A. Multifunctionalization of Cetuximab with Bioorthogonal Chemistries and Parallel EGFR Profiling of Cell-lines using Imaging, FACS and Immunoprecipitation Approaches. Reschke, M.L., Uprety, R., Bodhinayake, I., **Banu, M.A.**, Boockvar, J.A., Sauve. A.A. Biochim Biophys Acta, August 2014

   B. Validation of an Effective Implantable Pump-infusion System for Chronic Convection-enhanced Delivery of Intracerebral Topotecan in a Large Animal Model. D'Amico, R.S., Neira, J.A, Yun, J., Alexiades, N.G., Banu, M.A., Englander, Z.K., Kennedy, B.C., Ung, T.H. Rothrock, R.J., Romanov, A., Guo, X., Zhao, B., Sonabend, A.M., Canoll, P., Bruce, J.N. Journal of Neurosurgery, August 2019

   C. Ex-Vivo Multi-Electrode Analysis Reveals Spatiotemporal Dynamics of Ictal Behavior at the Infiltrated Margin of Glioma. Gill, B.J.A., Khan, F.A., Sosunov, A.A., Liou, J.Y., Dovas, A., Eissa, T.L., **Banu, M.A.,** Bateman, L.M., McKhann, G.M. 2nd, Canoll, P., Schevon, C. Neurobiology of Disease, February 2020

   D. Deconvolution of Cell Type-specific Drug Responses in Human Tumor Tissue with Single Cell RNA-seq. Zhao, W., Dovas, A., Spinazzi, E.F., Levitin, H.M., **Banu, M.A**., Upadhyayula, P., Suhakar, T, Marie, T., Otten, M.L., Sisti, M.B., Bruce, J.N., Canoll, P., Sims, P.A. Genome Medicine, May 2021

   E. Chronic Convection-enhanced Delivery of Topotecan for Patients with Recurrent Glioblastoma: a first-in-patient, single-centre, single-arm, Phase 1b Trial. **Banu, M.A**.* **(co-first author),** Spinazzi, E.F.*, Argenziano, M.G.*, Upadhyayula, P.S.*, Neira, J.A., Higgins, D.M.O., Wu, W.B., Pereira, P., Mahajan, A., Humala, N., Al-Dalahmah, O., Zhao, W., Save, A., Gill, B.J.A, Boyett, D.M, Marie, T., Furnari, J.L., Sudhakar, T.D., Stopka, S.A., Regan, M.S., Catania, V., Good, L., Zacharoulis, S., Behl, M., Petridis, P., Jambawalikar, S, Mintz, A., Lignelli, A., Agar, N.Y.R., Sims, P.A., Welch, M.R., Lassman, A.B., Iwamoto, F.M., D'Amico, R.S., Grinband, J., Canoll, P., Bruce, J.N. Lancet Oncology, November, 2022

4. **Used radio-anatomical biomarkers for selection of surgical approaches in intra-axial and skull base pathologies.** Personalized surgical approaches are critical in improving outcomes in neuro-oncology. I have developed several anatomical classification systems that were then successfully employed in the clinical setting to decide on the best surgical approach based on local anatomy and pathology. Preoperative imaging can guide therapeutic decisions even before the surgery. Understanding the limits of the approach based on specific radio-anatomical landmarks increased safety and extent of resection. Furthermore, I found that using patterns of pneumocephalus on postoperative

imaging can accurately identify patients with an active CSF leak which would require invasive interventions.

A. Impact of Skull Base Development upon Endonasal Endoscopic Surgical Corridors. **Banu, M.A**., Guerrero, A., McCrea, H.J., Souweidane, M.M., Anand, V.J., Heier, L., Schwartz, T.H., Greenfield, J.P., Journal of Neurosurgery Pediatrics, February 2014
B. Corridor-Based Endonasal Endoscopic Surgery for Pediatric Skull Base Pathology with Detailed Radioanatomical Measurements. **Banu, M.A.,** Rathman, A., Patel, K.S., Souweidane, M.M., Anand, V.J., Greenfield, J.P., Schwartz, T.H., Neurosurgery, June 2014
C. The Pattern of Post-operative Pneumocephalus Following Endonasal Endoscopic Skull Base Surgery as a Predictor of Post-operative CSF Leak. **Banu, M.A.,** Szentirmai, O., Mascarenhas, L., Salek, A.A., Anand, V.K., Schwartz, T.H. Journal of Neurosurgery, October 2014
D. Endoscopic-Assisted Endonasal versus Supraorbital Keyhole Resection of Olfactory Groove Meningiomas: Comparison and Combination of Two Minimally Invasive Approaches. **Banu, M.A.,** Szentirmai, O., Ottenhausen, M., Patel, K., Fraser, J., Tsiouris, J.A., Anand, V., Schwartz, T.H. Journal of Neurosurgery, August 2015
E. Efficacy and Outcomes of Facial Nerve-sparing Treatment Approach to Cerebello-pontine Angle Meningiomas. D'Amico, R.S.*, **Banu, M.A.* (co-first author)**, Petridis, P., Bercow, A., Malone, H., Praver, M., Wang, T.J.C., Isaacson, S.R., Sisti, M.B. Journal of Neurosurgery, February 2017
F. Endoscopic Endonasal Resection of Epidermoid Cysts Involving the Ventral Skull Base. Forbes, J.A., **Banu, M.A**., Lehner, K., Ottenhausen, M., La Corte, E., Alalade, A.F., Ordonez-Rubiano, E.G., Greenfield, J.P., Anand, V.K., Schwartz, T.H. Journal of Neurosurgery, June 2018
G. Endoscopic Endonasal Approach for Suprasellar Meningiomas: Introduction of a New Scoring System to Predict Extent of Resection and Assist in Case Selection with Long Term Outcome Data. Youngerman, B.E., **Banu, M.A.,** Gerges, M.M., Odigie, E., Tabaee, A., Kacker, A., Anand, V.K., Schwartz, T.H. Journal of Neurosurgery, July 2020

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