BIOGRAPHICAL SKETCH

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NAME: Styliani-Anna (Stella) E. Tsirka

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

POSITION TITLE: Distinguished Professor of Pharmacology; Miriam and David Donoho Professor; Director, Scholars in Bio-Medical Sciences Program; Vice Dean for Faculty Affairs

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Aristotle U. Thessaloniki, Greece	B.S.	1984	Chemistry
Aristotle U. Thessaloniki, Greece	PhD.	1989	Biochemistry
U. of Cal. at San Francisco	Postdoc	1989-92	Molecular & Cell Biology
SUNY at Stony Brook	Postdoc	1993-97	Developmental Neurobiology

A. Personal Statement

My laboratory explores interactions and communication between the nervous and immune systems in physiological and neurodegenerative, pathological settings. Our initial venture into the CNS was through exploring the tissue plasminogen activator proteolytic cascade and its roles (please see contributions to science below). We focus on microglial functions in the CNS and their communications within the CNS environment (i.e., with neurons, astrocytes, oligodendrocytes, and neural stem cells) as well as with infiltrating cells, namely T cells and macrophages. In more recent years, we investigate mechanisms that control microglial activation and migration to sites of injury and that compromise the blood-brain-barrier and the CNS microenvironment in the context of neurological (glioma, epilepsy, multiple sclerosis) and neuropsychiatric (depression) disorders. We utilize culture, *ex vivo* and *in vivo* preclinical and translational models to investigate innate immune cell functions.

As an educator, I served as the Director of the Molecular and Cellular Pharmacology Training Program at SBU for 11 years, renewing the T32 training grant twice. I established and am currently the director of the Scholars in BioMedical Sciences Program (SBMS, a Molecular Medicine program), which is running its eighth year and was recently awarded a T32. Our laboratory provides a rigorous and nurturing environment to foster scholarship and independent scientific thought in the students trained. I have trained 33 undergraduate students (currently training 6), 4 MS students (currently training 3), 28 PhD students (currently training 4), 6 postdoctoral fellows, and 1 research scientist. All the graduate trainees and postgraduate scholars are engaged in research. I am very excited to serve as the co-PI of the LINCATS K12 program and help guide the scholars training and development in clinical and translational research.

As an administrator, I previously served for five years as the inaugural Vice Provost for Faculty Affairs. During that period, I collaborated across campus to facilitate a variety of initiatives, oversaw processes for academic personnel review, the Stony Brook Foundation Faculty Fellow Awards, the SUNY Distinguished Professor appointments, and the Outstanding Mentor Awards, developed the Faculty Affairs Guide posted on the Provost's Office website, an indispensable resource for faculty. I organized and coordinated the Senior Faculty Mentoring Group, a team of senior faculty across schools and colleges on campus who meet and provide guidance and support to junior and mid-career faculty. I spearheaded the creation of a Leadership Academy for associate professors and advancement opportunities for non-tenure track faculty. As a co-chair of the Faculty Diversity group, I co-organized the Preparing Future Faculty conference that provided guidance for young investigators aspiring to academic careers. I currently serve as the Vice Dean for Faculty Affairs in the Renaissance School

of Medicine, organizing the Clinical Leadership Academy for faculty in clinical departments, providing workshops on all aspects of academic life with an emphasis on research and scholarship and education.

Active support –

2020 – 2024	NASA 80NSSC19M0215: Remote, In situ and Synchrotron Studies for Science and Exploration 2 (RISE2) PI: Glotch, (Role: CoI)
2020 - 2024	NIH R01DA029718 "Calcium-related neurotoxicity of cocaine' (PI: Congwu Du); role CoI
2020 - 2025	NIH R01MH123093 A translational study of neuroinflammatory depression: Understanding mechanism and evaluation of a novel pharmacologic intervention (PI Parsey), Role: CoPI
2019 – 2022	NIH Inducer MARC T34 grant (PI Williams) Mentor
2021 – 2023	Walk for Beauty TRO – Establishing a metastatic niche in the brain
2022 – 2023	OVPR Seed Grant: AI Enhanced Multimodality Optical Platform to Image Tumor Microenvironment in Awake Brain (Pan, Tsirka, Du, MPIs)

Mentored funding

2021-2023 R01MH123093S1 predoctoral diversity supplement for Miguel Madeira
2021-2024 F30CA257677-01A1 NRSA for Daniel Radin

Non-Research / Graduate Training

NIH T32GM0075186 Training Grant in Pharmacological Sciences (PI: Styliani-Anna E. Tsirka until 2015)
NIH T32 1T32GM127253 Scholars in BioMedical Sciences Training Program (PI: Styliani-Anna E. Tsirka) (2018-2023)

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2020 -	SUNY Distinguished Professor, Dept of Pharmacological Sciences, Stony Brook University, NY
2008- 2020	Professor, Dept of Pharmacological Sciences, Stony Brook University, NY
2004- 2008	Associate Professor, Dept of Pharmacological Sciences, SUNY Stony Brook, NY
2000- 2003	Assistant Professor, Dept of Pharmacological Sciences, SUNY Stony Brook, NY
1998- 2000	Res. Asst. Professor, Dept of Psychiatry, SUNY Stony Brook, NY
1995-1997	Instructor, Dept of Pharmacological Sciences, SUNY Stony Brook, NY
1993-1994	Postdoc Res. Associate, Pharmacology, SUNY Stony Brook, N.Y. (Advisor: Dr. S. Strickland)
1992	Lecturer, Dept of Biochemistry, University of Athens, Greece
1989- 1992	Postdoc fellow, Microbiology and Immunology, UCSF (Advisor: Dr. P. Coffino)

Other Experience and Professional Memberships

2020 -	Vice Dean for Faculty Affairs, Renaissance School of Medicine at Stony Brook University
2017 -	Member Group on Institutional Planning (GIP), American Association of Medical Colleges (AAMC)
2014 - 2019	Vice Provost for Faculty Affairs, Stony Brook University
2012 -	Director of Stony Brook University Scholars in BioMedical Sciences (Med-into-Grad) Program
2011 -	Chair, Stony Brook University IACUC
2011 -	Interim Director, Stony Brook University Hellenic Studies Center
2007- 2010	Dean's Leadership Advisory Group
2004 - 2010	Scientific advisory board of National Parkinson Foundation
2003- 2014	Director, Molecular and Cellular Pharmacology Graduate Program, SUNY Stony Brook, NY
1998-	Member of SUNY Stony Brook IACUC

Study Sections: Grant Reviewer for Alzheimer's Association (2002-present); AHA-EIA (2011); NIH/NSC-C (2004); NIH/NST2 (2005-2009); NIH/SRB-M (2006); NIH/BDCN-90L/BINP (2004-2010, 2011); ZHD1 DRG-D

(2011); AHA-Brain 1 (2007-); NIH-TWDA (2014-2018); NSF-GRFP (2014-); ZRG1 BDCN-B (02) SEP (2018 -) and currently F03A.

Honors

2020 -	Miriam and David Donoho Professor
2019	Dr. Herbert and Nicole Wertheim Leadership in Healthcare and Medicine Lectureship, Florida International University
2019	AAAS elected Fellow
2018	Andrea Hunter Memorial Lecture in Pharmacology, East Carolina University
2018 - 2019	Secretary/Treasurer, Division for Neuropharmacology ASPET
2016	Chancellor's award for Excellence in Faculty Service, SUNY
2015	Center for Inclusive Education Distinguished Faculty award, SBU
2007	Dean's award for excellence in service to Graduate Education by a graduate program director
2006- 2010	Established Investigator Award of the American Heart Association (National)
2002- 2004	Carol M. Baldwin Breast Cancer Research Award
1998–1999	Targeted Research Award, SUNY Stony Brook (Neurological Disease)
1994-1995	IHFSPO Postdoctoral Award
1993	NIH-NIDDKD Postdoctoral Award
1986-1989	Predoctoral Fellowship from IKY (The Greek Foundation of Fellowships)

C. Contributions to Science: 135 publications, h-index = 55
http://www.ncbi.nlm.nih.gov/sites/myncbi/styliani-anna.tsirka.1/bibliography/41163883/public/?sort=date&direction=ascending

1. ***Tissue plasminogen activator and cell death*.** As a postdoctoral fellow, I explored the expression of the serine protease tissue plasminogen activator (tPA) in the developing embryo and found high levels of expression in the central nervous system (CNS). Based on these findings, I probed tPA expression and function in the adult CNS and found that it is a critical mediator of excitatory cell death in the mouse hippocampus (*a*, which has been cited over 500 times) through cleavage of its substrate plasminogen (b). As an independent investigator, I then demonstrated that the activation of microglia through tPA, which occurs non-proteolytically via binding to annexin A2 on the microglial surface, is critical for the excitotoxic death progression (c). More recent studies have investigated the molecular paths involved in this process in other experimental models of cell death, such as spinal cord injury (d), and are still continuing.
   a. Tsirka SE, Gualandris A, Amaral DG, Strickland S (1995) Excitotoxin-induced neuronal degeneration and seizure are mediated by tissue-type plasminogen activator. ***Nature*** 377:340-344.
   b. Tsirka SE, Rogove AD, Bugge TH, Degen JL, Strickland S (1997) An extracellular proteolytic cascade promotes neuronal degeneration in the mouse hippocampus. ***J. Neurosci****.* 17: 543-552
   c. Siao CJ, Fernandez SR, Tsirka SE. (2003) Cell type-specific roles for tissue plasminogen activator released by neurons or microglia after excitotoxic injury, ***J Neurosci*****.** 23: 3234-3242
   d. Bukhari N, Torres L, Robinson JK, Tsirka SE. (2011) Axonal regrowth after spinal cord injury via chondroitinase and the tissue plasminogen activator (tPA)/plasmin system. ***J Neurosci*****.** 31(42):14931-43. PMCID:PMC3206287

2. ***Microglia in excitotoxicity and CNS pathology.*** To further our understanding of microglial functions, we have developed tools to modulate their activity. Our initial approaches using excitotoxic paradigms revealed contribution of microglia to neurotoxicity (a) through their recruitment to the injury site (b). We have also used other models of disease (some listed in more detail below), including glioma and spinal cord injury to define pathological roles for microglia. Our investigations have revealed that microglia have complex, dynamic roles that are modified during course of the pathological event. For example, microglia initially respond with an immune attack to insults (c), but then undergo a shift to anti-inflammatory cytokine secretion and sometimes become co-opted by the pathologic events (c,d). Our current investigations focus on fine-tuning these responses to define therapeutic windows critical for each disease setting.
   a. Rogove AD, Tsirka SE. (1998) Neurotoxic responses by microglia elicited by excitotoxic injury in the mouse hippocampus. ***Curr.Biol***.8: 19-25.

b. Rogove AD, Lu W, Tsirka SE. (2002) Microglial activation and recruitment, but not proliferation, suffice to mediate neurodegeneration. ***Cell Death Differ.*** 9: 801-806.

c. Zhai H, Heppner FL, Tsirka SE. (2011) Microglia/macrophages promote glioma progression. ***Glia***. 59:472-85. PMCID:PMC3080032

d. Thompson KK and Tsirka SE (2020) Guanabenz modulates microglia and macrophages during demyelination, ***Sci. Reports****,* 10(1):19333.

3. ***Experimental allergic Encephalomyelitis/ Multiple Sclerosis.*** As a prototype neuroimmune disease, Multiple Sclerosis (MS) and one of its animal models, Experimental Allergic Encephalomyelitis (EAE), became a focal point for our research. We defined that tPA (both through its proteolytic properties and its microglial activation properties) affects different aspects of disease symptom progression (a). Narrowing in on microglia, we demonstrated that inhibition of microglial activation attenuates activation of proinflammatory helper Th1 cells, whereas use of the activating tetrapeptide tuftsin shifts microglial activation to an M2 anti-inflammatory state and induces a switch in the immune response to anti-inflammatory Th2 and an expansion of immunosuppressive regulatory T cells (Tregs) (b). On the molecular level, this is accomplished through binding to and activation of Neuropilin-1, NRP1, and the associated transforming growth factor beta receptor 1, TGFβR1. NRP1-mediated long lasting cell-cell interactions between microglia and Tregs allow for the establishment of an immunosuppressive environment in EAE (c). Dr Tsirka's lab is now investigating combinatory therapies between disease-modifying drugs and remyelinating agents to promote repair after EAE/MS (d).

   a. Lu W, Bhasin M, Tsirka SE. (2002) Involvement of tissue plasminogen activator in both onset and effector phases of experimental allergic encephalomyelitis, ***J Neurosci***: 22: 10781-10789.

   b. Nissen JC, Tsirka SE. (2016) Tuftsin-driven experimental autoimmune encephalomyelitis recovery requires neuropilin-1. ***Glia***. 64(6):923-36. PMCID: PMC4833601

   c. Thompson KK, Nissen JC, Pretory A, Tsirka SE. (2018) Tuftsin Combines With Remyelinating Therapy and Improves Outcomes in Models of CNS Demyelinating Disease. ***Front Immunol.*** 9:2784 PMCID: PMC6283261

   d. Thompson KK, Tsirka SE (2020) Immunosuppression in Multiple Sclerosis and other Neurologic Disorders, Pharmacology of Immunosuppression (***Handbook of Experimental Pharmacology***), *in press*

4. ***Glioma and the Tumor microenvironment.*** A focus in our lab is to determine the immune environment around glioma, define the roles of glioma-associated microglia/macrophages (GAMs) in the microenvironment of preclinical glioblastoma and study their interactions with the adaptive immune system as they modify the glioblastoma landscape. The approaches we use are both pharmacological and genetic. Our recent work has identified a subset of microglia at the tumor border, the peritumoral glioma associated microglia (PGAM) in collaboration with Dr Moffitt. We continue to investigate the roles that microglia undertake in the tumor microenvironment over time, in models of the initial and recurrent glioma.

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   a. Miyauchi JT, Chen D, Choi M, Nissen JC, Shroyer KR, Djordevic S, Zachary IC, Selwood D, Tsirka SE. (2016) Ablation of Neuropilin 1 from glioma-associated microglia and macrophages slows tumor progression. ***Oncotarget***. 2016 7:9801-14. PMCID: PMC4891085

   b. Miyauchi JT, Caponegro MD, Chen D, Choi M, Li M, Tsirka SE. (2018) Deletion of neuropilin 1 from microglia or bone marrow-derived macrophages slows glioma progression, ***Cancer Res***, 78(3):685-694 PMCID: PMC5887044

   c. Caponegro MD, Moffitt RA, Tsirka SE (2018) Expression of neuropilin-1 is linked to glioma associated microglia and macrophages and correlates with unfavorable prognosis in high grade gliomas. ***Oncotarget****.* 9:35655-35665.

   d. Caponegro MD, Oh K, Madeira MM, Radin D, Sterge N, Tayyab M, Moffitt RA, Tsirka SE. (2021) A distinct microglial subset at the tumor-stroma interface of glioma. ***Glia***. 69(7):1767-1781. PMCID: PMC8113099

5. ***Physiological roles for microglia***. We have recently focused on the roles that microglia play in the physiological CNS. Initial evidence for such investigations came from work we did in pathology, specifically epilepsy (a). In that experimental setting we discovered that elimination of microglia from the tissue resulted

in exaggerated seizure intensity, functioning to regulate the extent of neuronal stimulation. Following from that we explored physiological roles of microglia and discovered that they function to regulate apoptosis in neurogenesis (b) and neuronal activity dynamically by modulating the number of active synapses and frequency of neuronal firing (c), which proceeds in part through effects on the stability of synapses and synaptic adhesion molecules. We are further pursuing the effects of microglia on physiological CNS functions and behavior (d).

a. Sierra A, Encinas JM, Deudero JJP, Chancey JH, Enikolopov G, Overstreet-Wadiche LS, Tsirka SE, Maletic-Savatic M (2010) Microglia shape adult hippocampal neurogenesis through apoptosis-coupled phagocytosis. ***Cell Stem Cell***, 7(4):483-95. PMCID:PMC4008496

b. Ji K, Akgul G, Wollmuth LP, Tsirka SE. (2013) Microglia actively regulate the number of functional synapses. ***PLoS One***. 8(2):e56293. PMCID:PMC3564799

c. Torres L, Danver J, Ji K, Miyauchi JT, Chen D, Anderson ME, West BL, Robinson JK, Tsirka SE. (2016) Dynamic microglial modulation of spatial learning and social behavior. ***Brain Behav Immun***. 55:6-16. PMCID: PMC4779430

d. Kokkosis A, Tsirka SE (2020) Sexual Dimorphism in Neuropsychiatric Disorders: the role of microglia, ***J Pharmacology Exp. Therapeutics***, *10.1124/jpet.120.266163*