

BIOGRAPHICAL SKETCH

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NAME: Creed Michael Stary

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

POSITION TITLE: Associate Professor

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
UC San Diego, La Jolla, CA	BS	06/1997	Animal Physiology, Neuroscience
UC San Diego, La Jolla, CA	BA	06/1997	Psychology
UC San Diego, Graduate School of Biomedical Sciences, La Jolla, CA	PHD	06/2006	Physiology
UC San Diego, School of Medicine, La Jolla, CA	MD	06/2008	Medicine
U. Hawaii Transitional Program, Honolulu, HI	Internship	06/2009	Medicine/Surgery
UC San Diego, Dept. Anesthesia, San Diego, CA	Residency	06/2012	Anesthesiology

A. Personal Statement

I am a clinical anesthesiologist and basic scientist, with 75% protected research time. My goal is to develop new treatments to improve neurologic outcome after brain injury. My focus is on decoding the epigenetic response to stroke. My prior and expanding expertise in mitochondrial bioenergetics, combined with my recent work demonstrating the roles of select microRNAs in altering levels of injury and their therapeutic potential as drug targets in experimental rodent models of brain injury, situates me ideally for the completion of these proposed Aims. In parallel, my laboratory focuses on cell-type-specific differences in the mechanisms of action of microRNAs. Building upon my expertise in microRNAs and rodent surgical models of cerebral ischemia injury, this project will extend our prior *in vitro* findings identifying miR-494 in retinal fibroproliferation to a clinically-relevant *in vivo* model for translational testing, including establishing novel *in vitro* models derived from human induced stem cells (iPSCs). The present proposal incorporates parallel histological, molecular and transcriptomics approaches *in vivo* to identify novel therapeutic targets. My relevant original research publications employing these techniques, including *in vitro* models derived from human iPSCs, are as follows:

- a. Sun, X, Hye Jung J, Arvola O, Santoso M, Giffard RG, Yang PC and **Stary CM**. (2019) Stem Cell-Derived Exosomes Protect Astrocyte Cultures from *in vitro* Ischemia and Decrease Injury as Post-Stroke Intravenous Therapy. *Front. Cell Neurosci.* 13:394. PMID: 31128240
- b. Arvola O, Kaidonis G, Xu L, Griffiths B, and **Stary CM**. (2019) Hippocampal Sub-Regional Differences in the MicroRNA Response to Forebrain Ischemia. *Mol Cell Neurosci.* 98:164-178. PMID: 31128240
- c. Alhadidi Q, Xu L, Sun X, Althobaiti YS, Almalki A, Alsaab HO, and **Stary C**. (2021) MiR-182 Inhibition Protects Against Experimental Stroke in Vivo and Mitigates Astrocyte Injury and Inflammation *in vitro* via Modulation of Cortactin Activity. *Neurochemical Res.* 47(12): 3682-3696. PMID: 34106941
- d. Leng, T, Kaidonis, G, Davda, P, Chang, H, Sun, X, Greer, M and **Stary, CM**. (2023) MicroRNA-494-3p targets p27 and augments fibro-proliferation with cell-type specificity in human retinal epithelial cells. *Frontiers in Ophthalmology, Frontiers in Ophthalmology Vol. 3* DOI: 10.3389/fopht.2023.1168650

Ongoing and Completed projects I would like to highlight include:

Ongoing Research Support

W911NF-24-2-0108

07/01/2024 - 06/30/2029

United States Department of Defense

“Creating a Safer Battlefield Anesthetic Based on a Newly Developed Anesthetic Class Specific to the GABAAR-slow Receptor Subtype.”

Major Goal: To develop novel anesthetics with improved cardiovascular stability and safety profile for field administration in the battlefield.

Role: Co-Investigator.

5R01NS112642

06/15/2020 - 03/31/2025

National Institute of Health

“Cofilin signaling in hemorrhagic stroke.”

Major Goal: To determine cofilin signaling mechanisms in the evolution of injury from hemorrhagic stroke.

Role: Co-Investigator.

B. Positions and Honors

Employment

7/2020-

Associate Professor, Dept. Anesthesiology, Perioperative & Pain Medicine, Stanford

7/2016-6/2020

Assistant Professor, Dept. Anesthesiology, Perioperative & Pain Medicine, Stanford

7/2012-6/2016

Clinical Instructor, Dept. Anesthesiology, Perioperative & Pain Medicine, Stanford

7/2012-6/2014

Postdoctoral Scholar, Rona Giffard, Advisor

Dept. of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine

9/2011-3/2012

Research Fellow, David Roth/Hemal Patel/Brian Head/Piyush Patel, Advisors

Dept. Anesthesia, University of California, San Diego

6/1997-9/2000

Staff Research Associate, Division of Physiology, Department of Medicine, UC San Diego

7/1994-6/1997

Laboratory Assistant, Division of Physiology, Department of Medicine, UC San Diego

Board Certifications

5/2014 -

American Board of Anesthesiology, Certification

Teaching

7/2012-6/2016

Clinical Instructor, Dept. Anesthesia, Stanford University School of Medicine

2003

Teaching Assistant, Mammalian Physiology, UC San Diego, Dept. Biology

1997

Teaching Assistant, Comparative Physiology, UC San Diego, Dept. Biology

1995-2005

Teaching Assistant, Organ Physiology Laboratory, UC San Diego, School of Medicine

Service on Study Sections

2024

NIH AGCD-1 (NIA K99 charted panel, 2/2024)

2023

NIH AGCD-1 (NIA K99 charted panel, 10/2023)

2023

NIH AGCD-1 (NIA K99 charted panel, 6/2023)

2023

NIH AGCD-1 (NIA K99 charted panel, 2/2023)

2022

NIH AGCD-1 (NIA K99 charted panel, 10/2022)

2022-

European Science Foundation, ad hoc reviewer

2021

NIH Director's New Innovator Award Program (DP2)

2021

NIH 2021/05 ZRG1 EMNR-H RFA-OD19-029: The Intersection of Sex and Gender Influences on Health and Disease

2017-

Royal College of Surgeons in Ireland (ERB), ad hoc reviewer

2017-

Dutch Cancer Society (KWF), ad hoc reviewer

2015-

International Anesthesia Research Society, IMRA study section participant

Professional Memberships

American Physiological Society, American College of Sports Medicine, Society for Experimental Biology and Medicine, American Society of Anesthesiology, Society for Neuroscience in Anesthesiology and Critical Care, Society for Neuroscience, American Heart Association, Association of University Anesthesiologists

Awards

2015	Young Investigator Award, American Heart Association
2014	Travel Award, Best Abstract, Association of University Anesthesiologists
2013	Stanford Department of Anesthesia, Best T32-funded Research Project
2012	Western Anesthesia Residents Conference, Best Clinical Science Poster
2012	Western Anesthesia Residents Conference, Best Basic Science Presentation

C. Contributions to Science

1. Assessment of mitochondrial function

I completed my pre-doctoral training with Dr. Michael Hogan at UC San Diego developing techniques to assess bioenergetic changes in living, single skeletal muscle cells in response to stress. I have more recently adapted my expertise in mitochondrial function and metabolism to study changes in mitochondrial function in the brain in response to stroke and most recently in a model of select ischemic CA1 neurodegeneration.

- a. **Stary CM**, Hogan MC (2000). Impairment of Ca^{2+} -release in single *Xenopus* muscle fibers fatigued at varied extracellular PO_2 . *J Appl Physiol*. 88: 1743-8. PMID: 10797138.
- b. **Stary CM**, Hogan MC (2000). Phosphorylating pathways and fatigue development in contracting *Xenopus* single skeletal muscle fibers. *Am J Physiol Regul Integr Comp Physiol*. 278: R587-91. PMID: 10712276.
- c. Li L, Voloboueva L, Griffiths BB, Xu L, Giffard RG, **Stary CM**. (2021) MicroRNA-338 inhibition protects against focal cerebral ischemia and preserves mitochondrial function *in vitro* in astrocytes and neurons via COX4I1. *Mitochondrion*. 2021 Apr 30;59:105-112. PMID: PMC8292173
- d. Griffiths B, Xu L, Sun X, Greer M, Murray I, **Stary CM**. (2022) Inhibition of miR-200c preserves astrocyte sirtuin-1 and mitofusin-2 and protects against hippocampal neurodegeneration following global cerebral ischemia in mice. *Frontiers in Molecular Neuroscience*. Nov 16;15:1014751. PMID: PMC9710226

2. Investigating mechanisms of sexual dimorphism in cerebral ischemia

My relevant recent work has focused on how biological differences in gene regulation between males and females contribute to sexual dimorphism in injury and development.

- a. **Stary CM**, Xu L, Li L, Sun X, Ouyang YB, Xiong X, Zhao J, Giffard RG. (2017) Inhibition of miR-181a protects female mice from transient focal cerebral ischemia by targeting astrocyte estrogen receptor- α . *Mol Cell Neurosci*. 2017 May 15;82:118-125. PMID: PMC5561665
- b. **Stary CM**, Xu L, Voloboueva LA, Alcántara-Hernández M, Arvola OJ, Idoyaga J, Giffard RG. (2019) Nursing markedly protects postpartum mice from stroke: associated central and peripheral neuroimmune changes and a role for oxytocin. *Front Neurosci*. Jul 8;13:609. PMID: PMC6637858
- c. Griffiths BB, Madden AMK, Edwards KA, Zup SL, **Stary CM**. (2019) Age-dependent sexual dimorphism in hippocampal cornu ammonis-1 perineuronal net expression in rats. *Brain Behav*. May;9(5):e01265. PMID: PMC6520292
- d. Xu, L, Sun, S, Griffiths, B, Voloboueva, L, Valdes, A, Dombrowski, M, Jeong-Jin Min, and **Stary CM**. (2023) Sexual dimorphism in brain sirtuin-1 and m6A methylated sirtuin-1 mRNA, and in protection with post-injury anti-miR-200c treatment, after experimental stroke in aged mice. *Aging and Disease*. Jun 1;14(3):892-903 PMID: PMC10187686

3. Establishing novel single cell techniques

Cell-type heterogeneity represents a confounding variable in assessing the molecular regulation of cellular processes. My doctoral thesis established a novel modification of the reverse transcription quantitative polymerase chain reaction assay for measurement of transcriptional activation in single skeletal muscle cells in response to stress. My recent work describes novel approaches to assess cell-type specific gene expression patterns after brain injury. The present proposal will utilize emerging technology to establish a model of single cell spatial transcriptomics after cerebral ischemia.

- a. **Stary CM**, Walsh BJ, Knapp AE, Brafman D, Hogan MC. (2008) Elevation in heat shock protein 72 mRNA following contractions in isolated single skeletal muscle fibers. *Am J Physiol Regul Integr Comp Physiol.* 295; R642-8. PMID: 18525012. PMCID: PMC2519928.
- b. **Stary CM** and Hogan MC (2016). Cytosolic calcium transients are a determinant of contraction-induced HSP72 transcription in single skeletal muscle fibers. *J. Appl. Physiol.* 2016 Feb 11: PMID: 26869714. PMCID: PMC4867320.
- c. Arvola O, Kaidonis G, Xu L, Griffiths B, **Stary CM**. (2019) Hippocampal sub-regional differences in the microRNA response to forebrain ischemia. *Mol Cell Neurosci.* Jul;98:164-178. PMID: 31128240
- d. Arvola O, Griffiths B, Rao A, Xu L, Pastroudis IA, **Stary CM**. (2021) Expression of miR-200c corresponds with increased reactive oxygen species and hypoxia markers after transient focal ischemia in mice. *Neurochem Int.* Oct;149:105146. PMCID: PMC8387456

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Stary+C%5BAuthor%5D>