## BIOGRAPHICAL SKETCH

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NAME: Murray G Blackmore

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

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 |
|---|---|---|---|
| Stanford University | BS | 1996 | Environmental Science |
| University of Minnesota | PhD | 2005 | Neuroscience |
| University of Miami Miller School of Medicine | Post-Doc | 2006-09 | Neuroscience |

### A. Personal Statement

I am driven to understand molecular mechanisms of axon growth, with the ultimate goal of harnessing this information to enhance axon regeneration. This has been my research focus since I entered graduate school; my pre-doctoral HHMI fellowship in 2000 was titled “Neuron-intrinsic Limits to Axon Regeneration.” My lab, founded in 2011, is divided into two integrated components. The first focuses on basic molecular mechanisms, and employs bioinformatics and high content screening to continually expand the set of known growth-regulatory genes. The other half of the lab selects the most promising candidates from this discovery pipeline and then uses viral gene manipulation to test them in animal models of spinal cord injury. We employ a variety of injuries to query different aspects of axon growth (pyramidotomy, partial transection, complete crush), and have established a standard battery of outcome measurements. These start with simple histological assessment of axon growth, then move into a newly developed optogenetic/electrophysiological test for synapse formation, and ultimately into behavioral testing (pellet retrieval, horizontal ladder, tactile sensation, BMS). The lab’s integrated pipeline is designed to discover or acquire new concepts and technologies, and push them rapidly into *in vivo* testing for spinal injury. We have moved a variety of transcription factors, including the KLFs at the center of this grant, through this pipeline. This has yielded promising results, and has also identified limits to the single-factor approach. After careful consideration and broadly surveying the emerging options, we have selected interlocking strategies to overcome these limits. A new round of bioinformatics and high content screening has produced our best-ever cell culture phenotypes, while improved viral delivery systems and stem cell bridges now incorporate the very latest advances into our animal experiments. With these new gene combinatorial gene targets and new *in vivo* techniques, we stand poised to explore a novel multi-pronged strategy to improve outcomes after spinal injury.

### B. Positions and Honors

**Professional Experience**

| | |
|---|---|
| 2009-Sept 2011 | Research Assistant Professor, University of Miami Miller School of Medicine |
| Oct 2011 – Aug 2017 | Assistant Professor, Department of Biomedical Sciences, Marquette University |
| Sept 2017- | Associate Professor, Dept. of Biomedical Sciences, Marquette University |

**Memebership on federal review panels**

| | |
|---|---|
| 2015 | Ad hoc member, NIH ZRG1 DKUS G 90 Special Emphasis Panel |
| 2015, 2016 | Reviewer, DoD Spinal Cord Injury Research Program (SCIRP) |
| 2017 | Ad hoc member, NIH NDPR |
| 2016, -17, -18 | Ad hoc member, NIH CNNT |
| 2019 - | Standing member, NIH NDPR |

**Honors and Awards**

| | |
|---|---|
| 1996 | Award for highest GPA in major, Stanford University (4.0) |
| 2000 | University of Minnesota, Morris Smithberg Memorial Prize (top-performing neuroscience graduate student) |
| 2000-2005 | Howard Hughes Pre-doctoral Fellowship |
| 2010 | Cellome Award, Thermo Fisher, *"Best published peer-reviewed scientific paper using high-content screening in 2009"* |
| 2016 | Way Klingler Young Scholars Award, Marquette University |

## C. Contributions to Science

1. The first major research direction in my lab is the continual discovery of novel molecular mechanisms that regulate axon growth. We established high content screening technology in the lab, and use it to test the effect of gene overexpression or knockdown on axon growth in cultured neurons. This approach has led to the discovery of completely novel transcription factors that affect axon growth. In addition we focus on the adoption of cutting edge technology and concepts, for instance using CRISPR-mediated gene knockout in high content workflows, and exploring epigenetic as well as genetic modification. **The contribution of these studies is continued expansion of our understanding of the molecular control of axon growth**, a critical step toward the ultimate goal of fostering effective axon growth after CNS injury

    a. M. Simpson, I. Venkatesh, B. Callif, L. Thiel, D. Coley, K. Winsor, Z. Wang, A. Kramer, J. Lerch, **M. Blackmore**. (2015) The tumor suppressor HHEX inhibits axon growth when prematurely expressed in developing central nervous system neurons. *Molecular and Cellular Neuroscience* 68:272-83.

    b. Venkatesh, I., and **M.G. Blackmore**. (2016) Selecting optimal combinations of transcription factors to promote axon regeneration: Why mechanisms matter. *Neurosci Lett*. S0304-3940(16)30981-8

    c. Venkatesh, I., M.T. Simpson, D.M. Coley, and **M.G. Blackmore**. (2016) Epigenetic profiling reveals a developmental decrease in promoter accessibility during cortical maturation in vivo (2016) *Neuroepigenetics*. 8:19-26.

    d. B. Callif, B. Maunze, N. Krueger, M. T. Simpson, **M. G. Blackmore** (2017). The application of CRISPR technology to high content screening in primary neurons. *Molecular and Cellular Neuroscience* 80: 170-179.

    e. Venkatesh, I.; Mehra, V.; Wang, Z.; Califf, B.; **Blackmore, M. G**. Developmental chromatin restriction of pro-growth gene networks acts as an epigenetic barrier to axon regeneration in cortical neurons. Developmental Neurobiology (2018).

2. Another major research goal has been to test *in vivo* the efficacy of various gene manipulations in promoting CNS axon regeneration. We focus on viral-mediated gene delivery to cortical neurons in a mouse model of spinal injury. We have now shown that forced expression of two transcription factors, a modified KLF7 and Sox11, can promote CST axon growth in the injured spinal cord. Importantly, these gene manipulations are performed in fully adult animals, and in the case of Sox11 were even administered many weeks after injury, a therapeutically relevant timeframe. **Overall, the key contribution of these studies is to identify novel gene manipulations that succeed in promoting axon regeneration in adult CNS neurons.**

a. **M. Blackmore***, Z. Wang, D. Motti, J. L. Goldberg, V. P. Lemmon, and J. L. Bixby (2012). KLF7 engineered for transcriptional activation promotes axon regeneration in the adult corticospinal tract. *Proceedings of the National Academy of Sciences* 109(18) 6845-6851.
* Corresponding Author

b. Z. Wang, A. Reynolds, A. Kirry, C. Nienhaus, **M. Blackmore**. (2015) Overexpression of Sox11 Promotes Corticospinal Tract Regeneration After Spinal Injury While Interfering With Functional Recovery. *Journal of Neuroscience* 35(7): 3139-45.

c. Z. Wang, V. Mehra, M.T. Simpson, B. Maunze, A. Chakraborty, L. Holan, E. Eastwood, **M. G. Blackmore**, Venkatesh I (2018) KLF6 and STAT3 co-occupy regulatory DNA and functionally synergize to promote axon growth in CNS neurons. Sci Rep 8:12565.

d. I. Venkatesh, V. Mehra, Z. Wang, M. T. Simpson, E. Eastwood, A. Chakraborty, Z. Beine, D. Gross, M. Cabahug, G. Olson, **M. G. Blackmore** (2020) Computational approaches identify novel transcription factor combinations that promote corticospinal axon growth after injury *bioRxiv* 146159; doi: https://doi.org/10.1101/2020.06.12.146159

**3.** We have developed a range of techniques and viral-based approaches to study and improve structural plasticity in the central nervous system. These include a first-ever use of optogenetics to monitor synapse formation by regenerating axons, creation of viral tools to degrade peri-neuronal nets with engineered chondroitinase, characterization of Retro-AAV2 as a potential tool for therapeutic gene delivery, and a recent application of this retrograde approach to the problem of spinal injury. **The key contribution of this work is the development of <u>new viral approaches</u> to manipulate gene expression and improve axon growth in injured neurons.**

a. N. Jayaprakash, Z. Wang, B. Hoeynck, N. Krueger, A. Kramer, E. Balle, D. S. Wheeler, R. A. Wheeler, **M. G. Blackmore**. (2016) Optogenetic Interrogation of Functional Synapse Formation by Corticospinal Tract Axons in the Injured Spinal Cord. *Journal of Neuroscience,* 36(21):5877-90.

b. Wang, Z., K. Winsor, C. Nienhaus, E. Hess, and **M.G. Blackmore**. (2016) Combined chondroitinase and KLF7 expression reduce net retraction of sensory and CST axons from sites of spinal injury. *Neurobiol Disease*. 99:24-35.

c. Z. Wang Z, B. Maunze, Y. Wang, P. Tsoulfas, **M. G. Blackmore** (2018) Global connectivity and function of descending spinal input revealed by 3D microscopy and retrograde transduction. J Neurosci 38(49):10566-10581

d. N. Jayaprakash, D. Nowak, E. Eastwood, N. Krueger, Z. Wang, **M.G. Blackmore** (2019) Restoration of Direct Corticospinal Communication Across Sites of Spinal Injury *bioRxiv* 546374; doi: https://doi.org/10.1101/546374

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/murray.blackmore.1/bibliography/47793126/public/?sort=date&direction=descending

**D. Additional Information: Research Support and/or Scholastic Performance**
**<u>Ongoing Research Support</u>**

R01NS083983 Blackmore (PI) 7/2013-6/2023
**Combinatorial Manipulation of Transcription Factors to Promote CNS Regeneration**
This grant has established the ability of KLF and other transcriptional interventions to promote axon regeneration, and created an optogenetic-based strategy to assess synaptic connectivity in regenerated axons.

R01NS107807 Blackmore (PI) 7/2018-6/2023
**Strategies to Optimize the Function of Regenerated Corticospinal Tract Axons**
This grant explores rehabilitation and neural stimulation approaches to improve behavioral outcomes in animals with stimulated axon regeneration.

R21NS106309 (NCE) Blackmore (PI) 9/2018-8/2021
**Regulation of CNS Regeneration by Chromatin Accessibility and Pioneer Factors**
This grant aims to profile chromatin accessibility in corticospinal tract neurons and harness pioneer transcription factors to improve accessibility at loci that control axon growth.

**Previous Research Support**

R21NS093278 Blackmore (PI) 4/2016-3/2018
**Novel Gene Targets at the Intersection of Spinal Injury and Cancer Biology**
This grant funded high content screening of transcription factors previously linked to cancer biology for their effects on neurite outgrowth.

R21NS095276 Blackmore (PI) 9/2015-8/2017
**The transcription factor HHEX as a novel regulator of CNS axon regeneration**
The goals of this grant were to identify transcription targets of a transcription factor called HHEX, and to test whether HHEX knockdown promotes axon regeneration in the corticospinal tract.

Bryon Riesch Foundation Blackmore (PI) 4/2016-3/2018
**Combined Gene Therapy and Stem Cell Grafting for Spinal Cord Injury**
This pilot grant supported experiments to produce preliminary data for this application (KLF6/stem cell combinations).

International Spinal Research Trust Blackmore (PI) 4/2013-3/2016
**Transcriptional Control of Axon Growth in the Chronically Injured Spinal Cord**
The goal of this project is to test combined treatment of KLF7 and Sox11 for the ability to promote CST axon regeneration in the chronic injury environment.