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	Completion Date	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 late 2011, is divided into two integrated components. The first focuses on basic molecular mechanisms of regeneration, 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).

B. Positions and Honors

Professional Experience

Oct 2009-Sept 2011	Research Assistant Professor, University of Miami Miller School of Medicine
Oct 2011-Aug 2017	Assistant Professor, Dept. 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)
2016, 2017	Ad hoc member, NIH CNNT
2017	Ad hoc 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. Contribution to Science

1. My early publications addressed the importance of neuron-intrinsic factors, as opposed to cell-extrinsic inhibition, in blocking axon regeneration in the central nervous system. I used the developing brainstem-spinal projection in the chick as a model system, taking advantage of a well-characterized transition from early success at axon regeneration to failed regeneration just prior to hatching. At the time, the axon regeneration field was strongly focused on extracellular inhibition. I developed an age-mismatched culture system that allowed me to vary independently the age of the brainstem neurons attempting to regenerate, and the age of the spinal cord tissue. The key finding was that the age of the regenerating neuron, and not the age of the spinal cord (or the presence of myelin) best predicted regenerative success. The importance of these studies was to demonstrate a major contribution of neuron-intrinsic changes to the failure of axon regeneration. I then went on to examine specific cell-intrinsic mechanisms (adhesion and local protein synthesis in axons) that could potentially contribute to neuron-intrinsic regenerative ability. Overall these studies, along with others, contributed to a shift in focus in the field toward cell intrinsic mechanisms that regulate regenerative success.

   a. M. Blackmore and P. Letourneau (2006). Changes within maturing neurons limit axonal regeneration in the developing spinal cord. *Journal of Neurobiology* 66: 348-60.

   b. M. Blackmore and P. Letourneau (2006). L1, beta1 integrin, and cadherins mediate axonal regeneration in the embryonic spinal cord. *Journal of Neurobiology* 66: 1564-83.

   c. M. Blackmore and P. Letourneau (2007). Protein synthesis in distal axons is not required for axon growth in the embryonic spinal cord. *Developmental Neurobiology* 67: 976-86.

2. As the importance of neuron-intrinsic control of axon regeneration became clear, a key goal was to identify genes that act in neurons to control regenerative ability. As a post-doctoral fellow, I helped establish a system of high content screening to test large numbers of candidate genes for effects on axon growth in primary neurons. One important outcome of these studies was the identification of the KLF family of transcription factors as key regulators of regenerative ability in the CNS. The central contribution of this work was to identify novel genes that help explain different regenerative ability between cell types.

   a. D. L. Moore*, **M. Blackmore***, Y. Hu, K. H. Kaestner, J. L. Bixby, V. P. Lemmon, and J. L. Goldberg (2009). KLF family members regulate intrinsic axon regeneration ability. *Science* 5950: 298-301.
   *These authors contributed equally

   b. **M. Blackmore**, D. L. Moore, R. P. Smith, J. L. Goldberg, J. L. Bixby, and V. P. Lemmon (2010). High content screening of cortical neurons identifies novel regulators of axon growth. *Molecular and Cellular Neuroscience,* 44(1):43-54.

3. As an independent PI, the first major research direction has been continued 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. Callif, B.L., B. Maunze, N.L. Krueger, M.T. Simpson, and **M.G. Blackmore** (2017). The application of CRISPR technology to high content screening in primary neurons. *Mol Cell Neurosci*. 80:170-179.

4. A major research goal as an independent PI 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 corticospinal tract 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. A major effort has been to create optogenetic methods to verify the synaptic connectivity of regenerated axons. **Overall, the key contribution of these studies is to identify novel gene manipulations that succeed in promoting axon regeneration in adult CNS neurons, and to verify synaptic connectivity.**

   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. 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.

   d. 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.

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. Other Research Support

Ongoing Research Support

R01NS083983 Blackmore (PI) 7/2013-5/2018
Functional Testing of KLF7 in Spinal Cord Injury: An Optogenetic Approach

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.

R21NS093278 Blackmore (PI) 4/2016-3/2018
Novel Gene Targets at the Intersection of Spinal Injury and Cancer Biology
The goal of this grant is to perform high content screening of transcription factors previously linked to cancer biology for their effects on neurite outgrowth; no overlap with the current proposal.

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). It ends prior to the start of this current application, thus avoiding overlap.

R01NS091234 (Co-I) 7/2014-5/2019
Inhibitory feedback mechanisms that couple circadian clock neurons in mammals
I am lending my viral expertise to this circadian project by creating Cre-dependent overexpression and knockdown constructs for small peptides in the suprachiasmatic nucleus. No overlap with the current proposal.

Previous Research Support

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

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.

Bryon Riesch Foundation Blackmore (PI) 4/2013-3/2015
Genome Editing of Novel Gene Targets for Spinal Cord Injury
The goal of this pilot grant is to develop a CRISPR-based approach to silence growth inhibitory gene targets in a mouse model of spinal cord injury.