BIOGRAPHICAL SKETCH

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NAME: EMERY, BEN

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

POSITION TITLE: Associate Professor, Neurology

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
University of Melbourne, Australia	B.S.(Hon)	05/2001	Biological Sciences
University of Melbourne, Australia	Ph.D.	01/2005	Neurobiology
Stanford University, California, USA	Postdoctoral	02/2005-12/2009	Neurobiology

A. PERSONAL STATEMENT

The myelination of axons is a vital aspect of the development of the central nervous system, allowing for the rapid and energy-efficient conduction of action potentials. In addition, myelination is increasingly appreciated as a form of neuroplasticity and as a vital component of the repair process in diseases such as Multiple Sclerosis. Following my doctoral training at the University of Melbourne, during which I investigated ways to promote oligodendrocyte survival in the context of autoimmune attack, I took up a postdoctoral position at Stanford University. During this time I became interested in the transcriptional mechanisms underlying glial development and function in the CNS, performing both transcriptional profiling experiments on different cellular populations from the brain and investigating the transcription factors that regulate oligodendrocyte development. I have been an independent investigator since 2010; first at the University of Melbourne and more recently at Oregon Health & Science University. The goal of my laboratory is to understand the intrinsic and extrinsic mechanisms that regulate the development of oligodendrocytes and their myelination of axons in both health and disease. We use a number of approaches including genome-wide expression profiling, genetic mouse models (including conventional knock-in, transgenic and conditional knockout approaches as well as CRISPR/Cas9 mutants), *in vitro* myelination assays and biochemical techniques. My current research focuses include the transcriptional regulation of myelination and the bidirectional interplay between neural activity and myelination.

B. POSITIONS AND HONORS

Positions and Employment

1998-1999 Honors Student, University of Melbourne, Advisor: Sandra Rees
1999 Research Student, Walter and Eliza Hall Institute, Advisor: Dr. Helen Cooper
2001-2005 Graduate Student, University of Melbourne, Advisor: Prof. Trevor Kilpatrick
2005 Postdoctoral Fellow, University of Melbourne, Advisor: Prof. Trevor Kilpatrick
2005-2009 Postdoctoral Fellow, Stanford Medical School, Advisor: Prof. Ben A. Barres
2010-2014 Senior Research Fellow, University of Melbourne and Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

2015-2017 Assistant Professor, Jungers Center, Dept. of Neurology, Oregon Health & Science University
2017- Associate Professor, Jungers Center, Dept. of Neurology, Oregon Health & Science University

Fellowships and Awards

1997 Dean's Honor List, Faculty of Science, University of Melbourne
2001-2004 Australian Postgraduate Award
2004 Student Poster Prize (commendation), *Australian Neuroscience Society*
2004 Young Investigators Prize, *Progress in MS Research Meeting,* Melbourne
2006 NHMRC CJ Martin Postdoctoral Fellowship (Grant Number 400438)
2011-2015 NHMRC Career Development Fellowship
2012 Australian Neuroscience Society A.W. Campbell Award
2012 Australian Institute of Policy and Science Victorian Tall Poppy Award
2014 American Anatomical Association Young Investigators Award in Morphological Sciences
2015 Warren Distinguished Scholar in Neuroscience Research

Professional Activities

2005- Regular external reviewer for journals including *Nature, Science, Cell, PLOS Biology, Journal of Neuroscience, Journal of Cell Biology, Neuron, Brain, Glia* and *Genes & Development*.
2010- External reviewer for funding bodies including: The Wellcome Trust (UK), the Australian Multiple Sclerosis Research Association, the United Kingdom Alzheimer's Society, the UK Medical Research Council, the Craig H. Neilsen Foundation (U.S.A.) and the European Leukodystrophy Association
2012-2015 External reviewer for the Australian National Health and Medical Research Council
2012-2013 Grant Review Panel member for Australian National Health and Medical Research Council
2013- Editorial board member for *Brain Plasticity* (IOS press)
2013-2014 Faculty member of Florey Institute of Neuroscience and Mental Health
2013-2014 Research Management Council member for Multiple Sclerosis Research Australia (MSRA)
2015 Co-organizer of Myelin Satellite to International Society for Neurochemistry meeting, Fitzroy Island, Australia
2015- Editorial board member for *Glia* (Wiley press)
2013, 2016 Advisory Committee member for NMSS "Fast Forward" program
2016 *Ad hoc* Member for NMSS Fellowship Review Committee
2016 *Ad hoc* Member for NMSS Pilot Grant Review Committee
2017- Member of NMSS Biomedical Research Committee

Teaching and student supervision

2010- Primary supervisor of four PhD students (two graduated) and one honours student, co-supervisor of one PhD student (graduated)
2015- Guest lecturer for OHSU Neuroscience Graduate Program (cell culture and gene targeting)
2012-2014 Lecturer for 3rd year Developmental Neurobiology course, University of Melbourne
2010- Member of 15 PhD advisory committees (University of Melbourne and Florey Institute)
2010-2012 Research Higher Degree coordinator for Centre for Neuroscience, University of Melbourne

Professional Memberships

2003-2014 Member, Australian Neuroscience Society
2005- Member, Society for Neuroscience
2014- Member, International Society for Neurochemistry
2014- Member, American Anatomical Association

C. CONTRIBUTION TO SCIENCE

1. Development of a transcriptome database for the neuroscience community.

During my postdoctoral research at Stanford University, I co-developed a database mapping gene expression for the major types of cells within the brain. To develop this database, co-investigators and I developed new methods for isolating neurons and the different glial cell types from the mouse brain. We then used these cells as the basis for a gene profiling study, measuring the expression levels of over 20,000 genes in each type of

cell within the brain. The resulting paper and the accompanying online dataset have been extensively used by the neuroscience community to understand how different cell types within the brain interact. Reflecting the widespread use and importance of this dataset, the paper was highlighted in the Faculty of 1,000 website at the time of its publication and has been cited well over 1,000 times since.

a. *Cahoy JD[#], **Emery B**[#], Kaushal A[#], Foo LC, Zamanian JL, Christopherson KS, Xing Y, Lubischer JL, Krieg PA, Krupenko SA, Thompson WJ, Barres BA. A transcriptome database for astrocytes, neurons, and oligodendrocytes: a new resource for understanding brain development and function. J Neurosci. 2008 Jan 2;28(1):264-78. [#]Equally contributing authors.

2. Identification of a critical regulator of CNS myelination, Myelin Regulatory Factor

Based on the above transcriptome database of CNS cells, I was able to identify a previously uncharacterized gene as being a vital regulator of myelination during development. This gene, previously known as *gene model 98* (mouse) and *C11Orf9* (human) and now known as Myelin Regulatory Factor (Myrf), is highly specific to postmitotic oligodendrocytes within the CNS, though it is also expressed by some peripheral tissues. My research demonstrated that it is critically required in order for oligodendrocytes to fully mature and myelinate; in its absence oligodendrocytes stalled at the pre-myelinating stage and failed to myelinate, leading to a lethal dysmyelination. Conversely, forced expression of Myrf in oligodendrocyte progenitors promotes their differentiation, suggesting manipulation of Myrf levels may be a viable strategy to promote remyelination in MS. Subsequent work within my laboratory demonstrated that not only is Myrf required for the formation of myelin during development, but that it is equally important in the adult CNS for the maintenance of myelin. Conditional ablation of Myrf in mature oligodendrocytes in the adult causes a rapid loss of myelin gene expression followed by a considerably more delayed demyelination. These findings not only highlight the importance of continued oligodendrocyte transcriptional support of the extant myelin sheath, but also provide a robust genetic model for inducible demyelination and remyelination.

a. Emery B, Agalliu D, Cahoy JD, Watkins TA, Dugas JC, Mulinyawe SB, Ibrahim A, Ligon KL, Rowitch DH, Barres BA. Myelin gene regulatory factor is a critical transcriptional regulator required for CNS myelination. *Cell*. 2009 Jul 10;138(1):172-85.

b. Koenning M, Jackson S, Hay CM, Faux C, Kilpatrick TJ, Willingham M, Emery B. Myelin gene regulatory factor is required for maintenance of myelin and mature oligodendrocyte identity in the adult CNS. *J Neurosci*. 2012 Sep 5;32(36):12528-42.

c. McKenzie IA, Ohayon D, Li H, de Faria JP, Emery B, Tohyama K, Richardson WD. Motor skill learning requires active central myelination. *Science*. 2014 Oct 17;346(6207):318-22.

3. Characterization of Myrf as a novel membrane-associated transcription factor

More recently, work from my laboratory has uncovered the molecular mechanisms by which Myrf promotes CNS myelination. We demonstrated that Myrf is initially generated as a endoplasmic reticulum-bound precursor that undergoes an autoproteolytic cleavage, enabling the N-terminal cleavage product to access the nucleus. Intriguingly, we showed that this autoproteolytic cleavage occurs via a protein domain previously only described in bacteriophages, suggesting that the domain has been incorporated into an ancestral *Myrf* gene via horizontal gene transfer. This mechanism of activation distinguishes Myrf from previously identified membrane-associated transcription factors such as Notch and the SERBPs, all of which use a Regulated Intramembrane Proteolysis (RIP) mechanism requiring other proteases. We further demonstrated that the N-terminal fragment acts as a transcription factor, directly binding to target DNA via a 7bp consensus sequence and directly inducing the expression of several hundred genes that underpin the CNS myelination process. The role of the C-terminal region of the protein, both during and after the activating cleavage event, is an ongoing topic of research both in my laboratory and others. Research into this exciting protein has now spread to a number of laboratories world-wide, many of who are using mutant mice, reagents and datasets generated by my laboratory either as genetic tools to manipulate myelination or to study Myrf itself.

a. #Bujalka H, #Koenning M, Jackson S, Perreau VM, Pope B, Hay CM, Mitew S, Hill AF, Lu QR, Wegner M, Srinivasan R, Svaren J, Willingham M, Barres BA, Emery B. MYRF is a membrane-associated transcription

factor that autoproteolytically cleaves to directly activate myelin genes. *PLoS Biol*. 2013;11(8):e1001625. #Equally contributing authors.

Complete list of published work:

http://www.ncbi.nlm.nih.gov/pubmed/?term=emery+ben[author]

D. RESEARCH SUPPORT

Ongoing Research Support

Oregon Medical Research Foundation Emery (PI) 06/2015-06/2018
The goal of this project is to generate the methodology for purifying transcripts specifically from the oligodendrocyte lineage in the intact adult mouse brain, characterizing the oligodendrocyte transcriptional response to neuronal activity *in vivo*.

National Multiple Sclerosis Society Project Grant Emery (PI) 01/2015-03/2018
The goal of this project is to understand the role of the transcription factor Myrf in mediating remyelination and to assess whether the expression or activating cleavage Myrf is disrupted in Multiple Sclerosis patients (in collaboration with Dr. Ranjan Dutta, Cleveland Clinic).

Race to Erase MS Pilot Award Emery (PI) 07/2016-07/2017
This project seeks to develop the Myrf inducible conditional knockout mice we generated as a genetic tool with which to study the cellular and molecular events occurring during a primary demyelinating event and the subsequent remyelination.

Completed Research Support

Myelin Repair Foundation Emery (PI) 2011-2014
This funding (as an external investigator) supported ongoing research into understanding the molecular mechanisms regulating remyelination including the identification of novel genes with pro-myelination roles.

Multiple Sclerosis Research Australia Project Grant Emery (PI) 2013
This project involved characterization of the consensus sequence for binding of Myrf to DNA and elucidation of its direct target genes in oligodendrocytes

Multiple Sclerosis Research Australia Project Grant Young (PI) 2011-2013
This project aimed to follow the dynamics of oligodendrocyte birth and death as well as addition or pruning of myelin segments during normal aging and in the context of mild and severe demyelinating insults.
Role: Co-investigator

National Health and Medical Research Council (NHMRC) Project Grant Emery (PI) 2011-2013
This project investigated the role of the Myrf transcription factor in maintenance of myelin in the adult CNS and the mechanisms by which it is cleaved to separate the transcription factor component from the membrane.

Multiple Sclerosis Research Australia Project Grant Emery (PI) 2010-2011
This project investigated the role of the Myrf transcription factor in maintenance of myelin in the adult CNS.

Internal University of Melbourne Early Researcher Grant Emery (PI) 2010
This project characterized the phenotype of mice lacking the *Gpr62* gene, which encodes an oligodendrocyte-specific orphan G-protein coupled receptor.