Publications

1. **Mac Nair CE**, Fernandes KA, Schlamp CL, Libby RT, Nickells RW. (2014). Tumor necrosis factor alpha has an early protective effect on retinal ganglion cells after optic nerve crush. *Accepted Journal of Neuroinflammation*.

2. Janssen KT, **Mac Nair CE**, Dietz JA, Schlamp CL, Nickells RW. (2013). Nuclear atrophy of retinal ganglion cells precedes the bax-dependent stage of apoptosis. IOVS, 54(3):1805-15. PMCID: PMC3626519

3. Schlamp CL, Montgomery AD, **Mac Nair CE**, Schuart C, Willmer DJ, Nickells RW. (2013). Evaluation of the percentage of ganglion cells in the ganglion cell layer of the rodent retina. Mol Vis. 2013;19:1387-96.
PMCID: PMC3695759

4. Greene JM, Lhost JJ, Hines PJ, Scarlotta M, Harris M, Burwitz BJ, Budde ML, Dudley DM, Pham N, Cain B, **Mac Nair CE**, Weiker MK, O'Connor SL, Friedrich TC, O'Connor DH. (2013). Adoptive transfer of lymphocytes isolated from SIVmac239Δnef-vaccinated macaques does not affect acute phase viral loads but may reduce chronic phase viral loads in MHC-matched recipients. J Virol, 87(13):7382-92. PMCID: PMC3700297

5. Weinfurter JT, May GE, Soma T, Hessell AJ, León EJ, **MacNair CE**, Piaskowski SM, Weisgrau K, Furlott J, Maness NJ, Reed J, Wilson NA, Rakasz EG, Burton DR, Friedrich TC. (2011). Macaque long-term
nonprogressors resistant superinfection with multiple CD8+ T cell escape variants of simian immunodeficiency virus. J Virol, 85(1):530-41. PMCID: PMC3014170

6. Friedrich TC, Piaskowski SM, León EJ, Furlott JR, Maness NJ, Weisgrau KL, **Mac Nair CE**, Weiler AM, Loffredo JT, Reynolds MR, Williams KY, Klimentidis YC, Wilson NA, Allison DB, Rakasz EG. (2010). High viremia is associated with high levels of in vivo MHC-I downregulation in rhesus macaques infected with SIVmac239. J Virol, 84(10):5443-7. PMCID: PMC2863841

7. O'Connor SL, Lhost JJ, Becker EA, Detmer AM, Johnson RC, **MacNair CE**, Wiseman RW, Karl JA, Greene JM, Burwitz BJ, Bimber BN, Lank SM, Tuscher JJ, Mee ET, Rose NJ, Desrosiers RC, Friedrich TC, Carrington M, O'Connor DH. (2010). MHC heterozygote advantage in simian immunodeficiency virus-infected Mauritian cynomolgus macaques. Sci Transl Med, 2(22):22ra18. PMCID: PMC2865159

8. Greene JM, Lhost JJ, Burwtiz BJ, Budde ML, **MacNair CE**, Weiker MK, Gostick E, Friedrich TC, Broman KW, Price DA, O'Connor S, O'Connor DH. (2010). Extra-lymphoid tissue-resident CD8+ T cells from
SIVmac239Δnef-vaccinated macaques suppress SIVmac239 replication ex vivo. J Virol, 84(7):3362-72. PMCID: PMC2838091

9. Valentine LE, Loffredo JT, Bean AT, León EJ, **MacNair CE**, Beal DR, Piaskowski SM, Klimentidis YC, Simon M. LanK SM, Wiseman RW, Weinfurter JT, May GE, Rakasz EG, Wilson NA, Friedrich TC, O'Connor DH, Allison DB, Watkins DI. (2009). Infection with "escaped" virus variants impairs control of SIVmac239 replication in Mamu-B*08+ macaques. J Virol, 83(22):11514-27. PMCID: PMC2772717

10. Wilson NA, Keele BF, Reed JS, Piaskowski SM, **MacNair CE**, Bett AJ, Liang X, Wang F, Thoryk E, Heidecker GJ, Citron MP, Huang L, Lin J, Vitelli S, Ahn CD, Kaizu M, Maness NJ, Reynolds MR, Friedrich TC, Loffredo JT, Rakasz EG, Erickson S, Allison DB, Piatak M Jr, Lifson JD, Shiver JW, Casimiro DR, Shaw GM, Hahn BH, Watkins DI. (2009). Vaccine-induced Cellular Immune Responses Control Acute Phase Simian AIDS Virus Replication After Heterologous Low-Dose Mucosal Challenge. J Virol, 83(13):6508-21. PMCID: PMC2698536

11. Reynolds MR, Weiler AM, Weisgrau KL, Piaskowski SM, Furlott JR, Weinfurter JT, Kaizu M, Soma T, León EJ, **MacNair CE**, Leaman DP, Zwick MB, Gostick E, Musani SK, Price DA, Friedrich TC, Rakasz EG, Wilson NA, McDermott AB, Boyle R, Allison DB, Burton DR, Koff WC, Watkins DI. (2008). Macaques

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CMP Cellular and Molecular Pathology

Caitlin MacNair

Program of the Dissertation Defense Seminar
for the Degree of Doctor of Philosophy
in Cellular and Molecular Pathology

"Characterizing the mechanisms of secondary degeneration in a mouse model of optic nerve crush"

SERVICE MEMORIAL INSTITUTE

Friday, June 21, 2015

1:00pm Room 516

Research conducted in the lab of
Robert W. Nickells, PhD
Department of Ophthalmology and Visual Sciences

UNIVERSITY OF WISCONSIN – MADISON

Caitlin MacNair

Education

University of Wisconsin-Madison
PhD in Cellular and Molecular Pathology

University of Wisconsin-Madison, 2007
BS, Biochemistry, Minor: Criminal Justice

Research Experience

University of Wisconsin – Madison (Ophthalmology and Visual Sciences)
September 2009 – present
Graduate Research Assistant (Advisor: Robert Nickells, PhD)

- Studied glaucoma and the role of the retinal immune response in a mouse model of neuronal injury
- Major findings
  - Found that injured neurons may release a danger signal to activate retinal immune cells
  - Explored the less understood protective potential of the inflammatory cytokine TNFα
  - Investigated a mechanism by which ATP may auto-regulate the activation of macroglial cells

University of Wisconsin – Madison (Biomolecular Chemistry)
September – December 2013
Teaching Assistant (Intro to Human Biochemistry)

- Taught 40 undergraduate students
- Prepared 2 discussion sections per week, graded exams and homework

University of Wisconsin – Madison (AIDS Vaccine Research Lab)
July 2007 – August 2009
Associate Research Specialist

- Performed Quantitative PCR (QPCR) on non-human primate plasma samples
- Cultured SIV stocks in a BL3+ laboratory to be used by researchers for *in vitro* and *in vivo* studies

DISSERTATION ABSTRACT

Blinding optic neuropathies such as glaucoma are characterized by the degeneration and death of retinal ganglion cells (RGCs). Although RGC pathology is initiated following trauma to the optic nerve, the innate immune response is thought to contribute to secondary RGC degeneration through the production of inflammatory cytokines. The innate immune response in the retina is regulated by a population of cells termed glia, which become activated during the course of glaucomatous neurodegeneration. It is unclear, however, how the glial cells in the retina recognize damage that originates distantly in the optic nerve. Additionally the consequence of cytokine signaling by the glia continues to be debated, as inflammatory cytokines have been linked to both detrimental and protective signaling networks.

Although optic nerve injury has an impact on many retinal cell types, the only cells systematically sacrificed in the retina are the RGCs. This suggests that these neurons may release a danger signal that initiates the activation of the retinal glia. It was subsequently found that when RGC death was blocked, both microglial and macroglial activation in the retina were significantly attenuated following optic nerve injury, supporting that complete neuronal death is a pre-requisite for glial activation. Additionally, purinergic signaling through the P2X7 receptor modulated macroglial activation in the absence of RGC death, while antagonizing the receptor suppressed macroglial activation following optic nerve trauma. This implied that purines, such as ATP, may be the signal released by dying RGCs to trigger macroglial activation. Alternatively, microglia did not respond to exogenous purines, suggesting that this glial population is activated by a different signaling pathway. While the pannexin 1 (PANX1) hemichannel appeared to be a good candidate mediating ATP release from dying RGCs, ablating this receptor selectively in RGCs enhanced macroglial activation rather than attenuating it.

Once the glia become activated, they have been shown to release a number of cytokines, including the pro-inflammatory cytokine tumor necrosis factor alpha (TNFα). While a plethora of studies support that long-term exposure to this cytokine mediates RGC injury, TNFα appeared to have an early protective effect on the RGCs. It was found that when Tnfα was genetically ablated in mice, the RGCs were more susceptible to crush injury, while pre-treating with TNFα prior to crush promoted RGC survival. This response may be mediated by the retinal macroglia, in particular the Müller cell population, through the activation of the transcription factors nuclear factor kappa B (NFκB) and JUN.

Many of these observations are consistent with a model of sequential responses of cell types during periods of damage in the central nervous system. In this model, damaged neurons signal to microglia by non-purinergic signaling mechanisms such as Toll-like receptor activation. Microglia, in turn, communicate with macroglial cells, principally through the production of inflammatory cytokines. Macroglial activation in response to these cytokines is then amplified by purinergic signaling pathways, likely through an autocrine pathway involving the P2X7 receptor. Evidence from these studies suggests that in the retina, the early activation of macroglia is protective to RGCs after optic nerve damage.