Honor & Awards

American Heart Association Predoctoral Fellowship 2012 – 2014
NIH Biotechnology Training Program Predoctoral Fellowship 2008 – 2011
Outstanding Senior in Biochemistry, Wartburg College 2008
Wartburg College Regents Scholarship 2004 – 2008

Presentations

Clarkson, B. D. S., A. Rayasam, A. Walker, M. Harris, M. Sandor, Z. Fabry
CCR2-dependent dendritic cell recruitment to CNS tissues during EAE promotes disease progression and inflammatory cytokine production by CNS T cells
AAI Annual Meeting, Pittsburgh, PA May 5, 2014
Clarkson, B. D.S., A. Rayasam, A. Walker, M. Harris, M. Sandor, Z. Fabry
Migration of i.c. injected BMDCs from brain to deep cervical lymph nodes is CCR7 dependent but does not promote EAE disease progression
AAI Annual Meeting, Pittsburgh, PA May 5, 2014
Clarkson B.D. S., S.J. Ollar, A. Walker and Z. Fabry
Interleukin-21 promotes neuronal autophagy following cerebral ischemia
International Stroke Conference, Honolulu Hawaii Feb 6, 2013
Clarkson B.D., C. Ling, Y. Shi, D. Sun, M. Sandor, and Z. Fabry
Role of Interleukin 21 in Focal Cerebral Ischemia / Reperfusion Injury
Michael N. Hart Pathology Research Day (Winner best poster 2013) Aug, 2011-13
Biotechnology Training Program Winter Banquet Mar, 2011-13
Clarkson B.D. Interleukin 21 in ischemic stroke reperfusion injury
Cell and Molecular Pathology Program Student Seminar Series Nov 2, 2011
Biotechnology Training Program Seminar Series Nov 10, 2010
Clarkson B.D. Dendritic cell migration in MS and EAE
Biotechnology Training Program Seminar Series Apr 28, 2010
Cell and Molecular Pathology Program Student Seminar Series Apr 7, 2010
Clarkson B.D. Dendritic cells in CNS autoimmune disease
Cell and Molecular Pathology Program Student Seminar Series May 7, 2009
Clarkson B.D., S. Huey, W. Fangman, S. Ellerbroek, and J.K. McClung
Inhibition of microglial TNFa secretion by co-cultured neuronal cells
Wartburg College Spring Poster session Apr 2008
Clarkson B.D. and B. Bousquet
Axial segregation patterns in granular media
Wartburg College Spring Poster session Apr 2007

WISCONSIN
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The University of Wisconsin - Madison
CMP
Cellular and Molecular Pathology

Ben Clarkson

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

"Migration and Function of Dendritic Cells in CNS Autoimmunity"

Wednesday, April 2, 2014
2:00 p.m.
Room 5001A Wisconsin Institutes for Medical Research

Research conducted in the lab of
Zsuzsanna Fabry, PhD
Department of Pathology & Laboratory Medicine

Ben Clarkson's Thesis Abstract

Migration and Function of Dendritic Cells in CNS Autoimmunity

Ben Clarkson
Under the supervision of
Professor Zsuzsanna Fabry, PhD
at the University of Wisconsin-Madison

Due to the essential function and delicate nature of neuronal cells, immune responses within the CNS are highly regulated. In terms of understanding the development of autoimmunity to CNS antigen as seen in multiple sclerosis (MS), two prevailing hypotheses have emerged: that primary aberrant activation of CNS-specific peripheral immune cells causes these cells to enter the CNS where they initiate injury (the "outside in" hypothesis) or that primary CNS tissue injury disrupts self-tolerance activating CNS-specific adaptive immune cells (the "inside out" hypothesis). To further discern these possibilities, we need a better understanding of how immune cell entry into the CNS is regulated, how tolerance to CNS tissue antigens is maintained, and how CNS injury affects peripheral CNS-directed adaptive immune responses.

Capable of sensing danger signals associated with tissue injury and priming adaptive immune responses, dendritic cells (DCs) function at the epicenter of these questions. Yet, due to the blood brain barrier and limited lymphatic drainage in the CNS, how these cells contribute to the development of CNS autoimmunity is not completely understood. In particular, how these cells are recruited to the CNS, how they contribute to retention and activation of co-infiltrating immune cells, and whether CNS DCs contribute to cell-mediated antigen drainage is unknown. Therefore, we sought to determine the level of DC recruitment to and identify key chemokine receptors involved in DC migration to and from CNS during CNS autoimmune disease.

Using a mouse model of MS, experimental autoimmune encephalomyelitis (EAE), we systematically describe the time course and distribution of CNS DCs and their interaction with co-infiltrating myelin specific T cells. We further report that 1) DC recruitment to the CNS is dependent upon CCR2, 2) DC recruitment to the CNS promotes retention of and inflammatory cytokine production by myelin-specific CD4+ T cells in an MHC class II-dependent fashion, and 3) DC migration from brain to cervical lymph nodes is CCR7-dependent but does not promote EAE disease progression. These findings suggest that CNS DCs may be key targets for modifying disease course in MS patients and that selective inhibition of DC recruitment to CNS may be therapeutic.

Publications

1. Isaak, A., J. Prechl, **B.D.S. Clarkson**, A. Nelson, M.G. Harris, D. Stewart, M. Sandor, and Z. Fabry (2014). Selective targeting of encephalitogenic MOG peptide to complement receptor type 2 ameliorates EAE. PLoS ONE (submitted).

2. Peng, Y., M. Li, **B. Clarkson**, M. Pehar, P.J. Lao, A.T. Hillmer, T.E. Barhart, B.T. Christain, H.A. Mitchell, B.B. Bendlin, M. Sandor, and L. Puglielli (2014). Deficient import of acetyl-coA into the ER lumen causes neurodegeneration as well as propensity to infections, inflammation and cancer. *Journal of Neuroscience* (in review).

3. Harris M.G., P. Hulseberg,, C. Ling, J. Karman, **B.D.S. Clarkson**, J.S. Harding, M. Zhang, A. Sandor, K. Christensen, A. Nagy, M. Sandor, and Z. Fabry (2014). Immune privilege of the CNS is not the consequence of limited antigen sampling. *Scientific Reports* (4: 4422).

4. **Clarkson, B.D.S.,** M.G. Harris A. Rayasam, an Z. Fabry (2014). The Blood-Brain Barrier and the Immune Privilege of the Central Nervous System. In K. Dorovini-Zis (Ed.), The Blood Brain Barrier in Health and Disease. Enfield, New Hampshire: Science Publishers (invited book chapter review)

5. **Clarkson B.D.S.**, C. Ling, Y. Shi, M.G. Harris, A. Rayasam, D. Sun, M.S. Salamat, V. Kuchroo, J.D. Lambris, M. Sandor, and Z. Fabry (2014). T cell derived IL-21 promotes brain injury following stroke in mice. *Journal of Experimental Medicine* (doi: 10.1084/jem.20131377).

6. **Clarkson B.D.**, E. Héninge, M.G. Harris, J.E. Lee, M. Sandor, and Z. Fabry (2012). Innate-adaptive crosstalk: How dendritic cells shape immune responses in the CNS. *Adv Exp Med Biol.* 946: 309-33

7. Zozulya A., **B.D. Clarkson**, S. Ortler, Z. Fabry, H. Wiendl (2010). The role of dendritic cells in CNS autoimmunity. *Journal of Molecular Medicine.* 88(6):535-44.