Rebecca L. O'Brien, PhD

- *Professor*
- *Department of Biomedical Research*

Conditions Treated:

Research Areas:

- *Infectious Diseases*
- *Autoimmunity/Rheumatology*
- *Inflammation*

Research Interets

My research concerns the specificity and function of the gamma delta T lymphocytes. These cells represent a relatively rare type of T cell in mice and humans whose purpose is at this time not clear. Other lymphocytes, alpha beta T cells and B lymphocytes, by virtue of their antigen receptors, can detect and eliminate foreign micro-organisms from the body. The gamma delta T cells also carry T cell receptors (TCRs), related to but distinct from those carried by alpha beta T cells. However, instead of recognizing foreign molecules, gamma delta TCRs at least in some cases recognize molecules that are produced by our own bodies, which are induced during infection or inflammation and may be present on tumor cells.

Different gamma delta T cell subsets appear to play distinct roles. These subsets are often defined by the expression in their TCR of particular Vgammas or Vgamma/Vdelta combinations. Projects are currently underway to further define the functional roles of several distinct mouse gamma delta T cell subsets during disease, two of which we have recently shown are potent producers of IL-17, a cytokine that is critically important in clearing infectious bacteria but which also can promote autoimmune damage. In addition, we recently discovered that female mice having particular genetic background, which cannot produce gamma? delta T cells, develop a severe inflammation of the cornea with high incidence. Investigation of how gamma delta T cells normally suppress this autoimmune attack on the eye is now in progress.

Finally, we are attempting to discover the ligands for the TCRs expressed by certain gamma delta T cell subsets. This is critical not only to understanding how these cells function, but may also be key to manipulating gamma/delta T cells for use therapeutically. Here, we have generated multimeric versions of recombinant soluble gamma? delta TCRs, which can be used like monoclonal antibodies as reagents to detect their own ligands. The ligands appear to be cell surface molecules which are either themselves proteins or are protein-associated. We are now further defining which cells normally express these ligands, and what induces their expression. As well, work towards the purification and identification of natural ligands of gamma delta TCRs is underway.

Education

1979 Boise State University, BS
1982 University of Washington, MS
1986 University of Washington, PhD

Fellowship

1986 - 1989 National Jewish Health,

Affiliations with the University of Colorado Denver

Professor, Department of Immunology & Microbiology, University of Colorado Denver

Awards & Recognition

2008-Present: Member, Advisory Board, Faculty of 1000
2004-2008: NIH Study Section AITRC, regular member
2000: Harmon Award for Outstanding Research (Arthritis Foundation, Rocky Mountain Chapter)
1999: Schwartz-Weinstein Research Grant (Arthritis Foundation, Rocky Mountain Chapter)

Publications

O'Brien, R.L., Roark, C.L., Born, W.K. IL-17-producing gamma? delta T cells. Eur. J. Immunol. 39: 662-666, 2009 (ViewPoints article).

French, J.D., Roark, C.L., Born, W.K., and O'Brien, R.L. gamma delta T lymphocyte homeostasis is negatively regulated by beta 2-microglobulin. J. Immunol.182: 1892-1900, 2009 (featured in, “In this issue”).

Aydintug, M.K., Roark, C.L., Chain, J.L., Born, W.K., and O’Brien, R.L. Macrophages express several inducible ligands for gamma delta TCRs. Mol. Immunol. 45: 3253-3263, 2008.

Roark, C.L., French, J.D. , Taylor, M.A., Bendele, A.M., Born, W.K., and O’Brien, R.L. Exacerbation of collagen-induced arthritis by oligoclonal, IL-17-producing gamma delta T cells. J. Immunol. 179: 5576-5583, 2007.

French, J.D., Roark, C.L., Born, W.K., and O'Brien, R.L. gamma delta T cell homeostasis is established in competition with alpha beta T cells and NK cells. Proc. Natl. Acad. Sci. USA 102: 14741–14746, 2005.

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