BIOGRAPHICAL SKETCH

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NAME: Parker, David C.

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

POSITION TITLE: 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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Haverford College, Haverford, PA	B.A.	06/1966	Cell Biology
University of California, Berkeley, CA	Ph.D.	1971	Immunology
University of California, Berkeley, CA	Postdoc	06/1973	Immunology
University College, London, UK	Postdoc	06/1976	Immunology

A. Personal Statement

I have a longstanding interest in lymphocyte activation and immunological tolerance, and how lymphocytes integrate many signals from the environment to make their life or death decisions how to respond. In my laboratory, we are examining the role of the immunological synapse in the specific delivery of the membrane-bound TNF family member, CD40L (CD154), a molecule that is necessary for T cell activation of B cells in the antibody response. We are also exploring differences among T cell subsets in the structure of the synapse and the functional consequences of those differences. In a simplified model of peripheral tolerance to self, we found that a signal through the TNF family member, OX40 (CD134), blocks functional anergy in transferred T cells responding to transgenic or allogeneic antigens, drives the T cells to differentiate into cytokine-secreting effector cells, and results in fatal acute graft versus host disease in unirradiated recipient animals. We have recently shown that NIK and the noncanonical NF-κB pathway play a previously unrecognized key role in regulatory T cell stability and in T cell responses to OX40 ligation and other late co-stimulatory signals that enable T cells to survive and function as effector cells and memory cells.

B. Positions and Honors

1971-1972	Assistant Professor of Biology, Hampshire College, Amherst, MA
1976-1980	Assistant Professor, Department of Microbiology, U. of Mass. Medical School
1980-1987	Assoc. Professor, Department of Molecular Genetics and Microbiology, U. of Mass. Medical School
1986-1987	Visiting Scientist, Whitehead Institute, David Baltimore laboratory
1987-1998	Professor, Department of Molecular Genetics and Microbiology, U. of Mass. Medical School
1993-1994	Visiting Scientist, National Jewish Center, Kappler and Marrack laboratory
1994-present	Professor, Department of Molecular Microbiology and Immunology, Oregon Health & Science University.

Awards and Other Professional Activities

B.A. w/high honors	6/66
NSF Graduate Fellow	7/66-6/70
NATO Postdoctoral Fellow	8/73-8/74

NIH Postdoctoral Fellow	5/75-5/76
Member, American Association of Immunologists	1980-present
Chair, Arthritis Foundation Basic Immunology Study Section	1991-1993
Chair, Immunobiology Study Section, NIH	1996-1998
Co-Chair, 50th Midwinter Conference of Immunologists at Asilomar	2011

C. Contribution to Science

1. My early independent work explored the roles of the B cell receptor for antigen and soluble cytokines produced by T cells in the antibody response. This work also uncovered an inhibitory role for Fc receptors on B cells that explains in part the regulation of the antibody response by circulating antibody.

Parker, D.C. 1975. Stimulation of mouse lymphocytes by insoluble anti-mouse immunoglobulin. Nature. 258:361-363.

Parker, D.C., D.C. Wadsworth, and G.B. Schneider. 1980. Activation of murine B lymphocytes by anti-immunoglobulin is an inductive signal leading to immunoglobulin secretion. J. Exp. Med. 152:138-151.

Phillips, N.E., and D.C. Parker. 1983. Fc-dependent inhibition of mouse B cell activation by whole anti-μ antibodies. J. Immunol. 130:602-606.

Phillips, N.E., and D.C. Parker. 1984. Cross-linking of B lymphocyte Fcγ receptors and membrane immunoglobulin inhibits anti-immunoglobulin-induced blastogenesis. J. Immunol. 132:627-632.

2. Probably the most important contribution of my career was to show that B cells elicit help from T cells by acting as antigen-specific antigen presenting cells. Antigens bound to the antigen receptor are processed and presented by B cells on MHC class II with extraordinary efficiency, accounting for the specificity of T cell help for B cells responding to the same antigenic particle.

Tony, H.-P., and D.C. Parker. 1985. Major histocompatibility complex-restricted, polyclonal B cell responses resulting from helper T cell recognition of antiimmunoglobulin presented by small B lymphocytes. J. Exp. Med. 161:223-241.

Tony, H.-P., N.E. Phillips, and D.C. Parker. 1985. Role of membrane immunoglobulin (Ig) crosslinking in membrane Ig-mediated, major histocompatibility-restricted T cell-B cell cooperation. J. Exp. Med. 162:1695-1708.

Gosselin, E.J., H.-P. Tony, and D.C. Parker. 1988. Characterization of antigen processing and presentation by resting B lymphocytes. J. Immunol. 140:1408-1413.

Parker, D.C. 1993. T cell-dependent B cell activation. Annu. Rev. Immunol. 11:331-360.

3. I then got very interested in the role of B cells as antigen presenting cells in acquired immunological tolerance. The factors which control the decision between immunity and tolerance has remained my main focus.

Eynon, E.E., and D.C. Parker. 1992. Small B cells as antigen-presenting cells in the induction of tolerance to soluble protein antigens. J. Exp. Med. 175:131-138.

Parker, D.C., D.L. Greiner, N.E. Phillips, M.C. Appel, A.W. Steele, F.H. Durie, R.J. Noelle, J.P. Mordes, and A.A. Rossini. 1995. Survival of mouse pancreatic islet allografts in recipients treated with allogeneic small lymphocytes and antibody to CD40 ligand. Proceedings of the National Academy of Sciences. 92:9560-9564.

Yuschenkoff, V.N., M.P. Sethna, G.J. Freeman, and D.C. Parker. 1996. Coexpression of B7-1 and antigen blocks tolerance induction to antigen presented by resting B cells. J. Immunol. 157:1987-1995.

Murray, S.E., K.G. Toren, and D.C. Parker. 2013. Peripheral CD4(+) T-cell tolerance is induced in vivo by rare antigen-bearing B cells in follicular, marginal zone, and B-1 subsets. Eur. J. Immunol. 43:1818-182.

4. After my move to OHSU, I became involved in studying the immunological synapse (the contact area between T cells and antigen presenting cells) and its functions in the immune response. I and my trainees here at OHSU showed that MHC class II molecules are transferred from the antigen presenting cell to the T cell, that CD4 T cell subsets form morphologically very different synapses, that memory and effector CD4 T cells contain pre-formed CD40L protein in a secretory compartment that comes to the cell surface with T cell antigen receptor signaling, and that motility of regulatory T cells is controlled by CD28.

Wetzel, S.A., T.W. McKeithan, and D.C. Parker. 2005. Peptide-specific intercellular transfer of MHC class II to CD4+ T cells directly from the immunological synapse upon cellular dissociation. J. Immunol. 174:80-89.

Koguchi, Y., T.J. Thauland, M.K. Slifka, and D.C. Parker. 2007. Preformed CD40 ligand exists in secretory lysosomes in effector and memory CD4+ T cells and is quickly expressed on the cell surface in an antigen-specific manner. Blood. 110:2520-2527.

Thauland, T.J., Y. Koguchi, S.A. Wetzel, M.L. Dustin, and D.C. Parker. 2008. Th1 and Th2 cells form morphologically distinct immunological synapses. J. Immunol. 181:393-399.

Thauland, T.J., Y. Koguchi, M.L. Dustin, and D.C. Parker. 2014. CD28-CD80 interactions control regulatory T cell motility and immunological synapse formation. J. Immunol. 193:5894-5903.

5. The other major focus of my research at OHSU has been costimulatory signals delivered by OX40, a TNF receptor family member expressed on activated CD4 T cells and regulatory T cells. These signals can convert a tolerogenic antigen encounter into an immunogenic encounter. This function of OX40 engagement is completely dependent on NIK, an essential kinase linking OX40 and other costimulatory TNF receptor family members to the non-canonical NFκB pathway. We showed that NIK is essential for CD4 and CD8 T cell memory formation following acute viral infection, and that slight overexpression of NIK results in fatal autoimmunity through effects on conventional T cells and destabilization of regulatory T cells.

Lathrop, S.K., C.A. Huddleston, P.A. Dullforce, M.J. Montfort, A.D. Weinberg, and D.C. Parker. 2004. A signal through OX40 (CD134) allows anergic, autoreactive T cells to acquire effector cell functions. J. Immunol. 172:6735-6743.

Williams, C.A., S.E. Murrray, A.D. Weinberg, and D.C. Parker. 2007. OX40-mediated differentiation to effector function requires IL-2 receptor signaling but not CD28, CD40, IL-12Rbeta2, or T-bet. J. Immunol. 178:7694-7702.

Murray, S.E., F. Polesso, A.M. Rowe, S. Basak, Y. Koguchi, K.G. Toren, A. Hoffmann, and D.C. Parker. 2011. NF-kappaB-inducing kinase plays an essential T cell-intrinsic role in graft-versus-host disease and lethal autoimmunity in mice. J. Clin. Invest. 121:4775-4786.

Rowe, A.M., S.E. Murray, H.P. Raue, Y. Koguchi, M.K. Slifka, and D.C. Parker. 2013. A cell-intrinsic requirement for NF-kappaB-inducing kinase in CD4 and CD8 T cell memory. J. Immunol. 191:3663-3672.5.

Complete List of Published Journal Articles on PubMed:
http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/public/1fco02p_kvBCoodrQlwSp6Q/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

R01 AI092080-02 Parker (PI) 5/01/2011 to 4/30/2016
NIH/NIAID
The non-canonical NF-κB pathway in survival and function of T lymphocytes
The major goal of this project is to test the hypothesis sustained activation of NF-κB through the non-canonical NF-κB pathway downstream of costimulatory TNFR family members is necessary to allow T cells to survive and function as differentiated effector and memory cells.
Role: PI

Completed Research Support (last three years)

R01 AI-50823-10 Parker (PI) 5/01/02 to 2/28/13
NIH/NIAID
Imaging and Function of the Immunological Synapse
This project explores the role of the immunological synapse in T cell activation and effector function.
Role: PI.