

**David H. Wagner, Jr., Ph.D.**

*Investigator and Head Section of Immunology  
Webb-Waring Center*

*Associate Professor*

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Webb-Waring Center  
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**Education:**

- 1984 B.S. (Magna cum Laude), Chemistry/Biology  
King College, Bristol, TN/VA
- 1987 M.S. Biological Sciences  
East Tennessee State University, Johnson City, TN
- 1994 Ph.D. Biomedical Sciences  
East Tennessee State University, Quillen College of Medicine  
Johnson City, TN  
*Dissertation: "T cell activation of macrophage IL-1 production in  
rheumatoid arthritis."*
- 1995 Postdoctoral Fellowship, Immunology  
Division of Immunology, National Jewish Medical and Research Center  
1400 Jackson St, Denver, CO
- 1999 Senior Postdoctoral Fellowship, Diabetes/Immunology  
University of Colorado Denver and Health Sciences

**Professional Experience:**

- 2001-Present Investigator, Webb-Waring Institute for Cancer, Aging and  
Antioxidant Research
- 2001- 2008 Assistant Professor, Division of Pulmonary Medicine and Critical  
Care, Department of Medicine, University of Colorado Denver and  
Health Sciences Center
- 2008-present Associate Professor, Div of Pulmonary Medicine, Dept of  
Medicine, University of Colorado Denver

Head, Section of Immunology Webb-Waring Center, University of Colorado Denver

**Professional Memberships:**

American Association of Immunologists

American Diabetes Association

Society for Leukocyte Biology

Immunology of Diabetes Society (IDS) of the Federation of Clinical Immunological Societies (FOCIS)

**Professional Activities:**

***Invited Talks***

- 2009 4<sup>th</sup> Aegean Conference, Mechanisms and Treatment of Autoimmunity. Plenary Speaker "Common Mechanisms in T1D and MS: A Role for Th40 cells." Crete, Greece, October, 2009.
- 2008 12<sup>th</sup> International Conference on TNF-Superfamily Members, San Lorenzo, Spain. Plenary Speaker "CD40 expression Identifies Pathogenic T cells in Autoimmunity". March, 2009  
Invited Speaker, Society for Leukocyte Biology "Th40 cells in type 1 diabetes and multiple sclerosis", Denver, CO
- 2007 Federation of Clinical Immunology Societies, San Diego, CA. *Immuno-Modulatory Mechanisms*, Title: "CD40 Isoform Differences and Micro-domain Localization Explain Preferential Survival of CD4<sup>+</sup>CD40<sup>+</sup> T Cells in Autoimmunity"
- 2006 Keystone Symposium **Tolerance and Autoimmunity**  
*Plenary Session, Translating Tolerance to the Clinic*, Title: "Of Mice and Man: Translation of Autoaggressive T cells from NOD mice to Human type 1 diabetes"
- Federation of the American Societies for Experimental Biology, American Association of Immunologists, Boston MA.  
1) *Mechanisms of T cell Activation*, Title: "CD40 Promotes Homeostatic Disruption of the autoaggressive to regulatory T cell ratio in NOD mice"
- 2) ***Session Chair and Presenter***

*Auto-aggressive T cells* “Translating the NOD mice model to human type 1 diabetes, Title: Identification of autoaggressive T cell.”

Federation of Clinical Immunology Societies, San Francisco, CA. *T cells and Autoimmunity*, Title: “Identification of autoaggressor T cells in human Type 1 diabetes”

2005

Aegean Conferences, Santorini Greece: Mechanisms and Treatment of Autoimmunity, Session Chair and presenter, Plenary Session: Mechanisms of T cells in Autoimmunity, Title: “CD40<sup>+</sup>T cells in human and mouse type 1 diabetes”

Federation of the American Societies for Experimental Biology, American Association of Immunologists, San Diego, CA

**1) Session Co-chair:** “Pathogenesis of Type 1 Diabetes”, Title: “Identification of Auto-Aggressive T cells in IDDM”

**2) “Pathogenesis of Autoimmunity”** Title: CD40 Induces TRC Revision and Cell Survival: A Mechanism for Breach of T cell Tolerance”

**3) Regulation of Autoimmunity**, Title: “TCR revision in regulatory T cells” Nathan Pennock in the Wagner laboratory.

2004

Federation of the American Societies for Experimental Biology, American Association of Immunologists, Washington, D.C. Symposium: Mechanisms of Tolerance, Title: “CD40 Induces Breach of Tolerance in A Unique T cell Subset

The Aegean Conferences: Autoimmunity Mechanisms and Treatments, Mykonos, Greece. Title: “The Role of CD40 in Autoimmune type 1 diabetes”

2003

Federation of the American Societies for Experimental Biology, American Association of Immunologists New Orleans, LA, “Mechanisms of T cell control”, Title: “Identification of Auto-Aggressive T cells in IDDM”

2000

Gordon Conference Immunobiology and Immunochemistry Barga, Italy

***Grant Reviews/Study Sections:***

- 2010 Ad Hoc National Institutes of Health, Center for Scientific Review  
Study Section, Hypersensitivity, Autoimmunity and Immune-  
Related Diseases (HAI)
- Regular Member, American Diabetes Association Grant Review  
Panel
- 2009 Ad Hoc, HAI Study Section  
Regular Member, ADA Grant Review Panel
- 2008 Ad Hoc Reviewer, Susan Komen Breast Cancer Research
- American Institute for Biological Sciences (Department of  
Defense, Congressionally Directed Medical Research Programs)  
Ad Hoc Reviewer
- 2005 Ad Hoc reviewer National Institutes of  
Health HAI-Study Section
- 2004 Ad Hoc reviewer National Institutes of  
Health HAI-Study Section

***Professional Awards:***

- 2007 Federation of Clinical Immunology Societies, San Diego,  
CA., Travel Award
- 2006 Federation of Clinical Immunology Societies, San  
Francisco, CA, Travel Award
- 2005 Junior Faculty Award, American Association of  
Immunologists, San Diego, CA
- 2003 Pfizer-Showell National Junior Faculty Award, American  
Association of Immunologists, New Orleans, LA
- 1999 Gitzen Fellowship, National Jewish Medical and Research  
Center, Denver, CO, Excellence in Immunology

***Journal Reviewer:***

Trends in Immunology  
Journal of Immunology

Journal of Endocrinology  
 Journal of Leukocyte Biology  
 Clinical and Experimental Immunology  
 Journal of Experimental Medicine  
 Clinical Immunology  
 Expert Review of Clinical Immunology  
 Diabetologia  
 Diabetes

**Directed Studies:**

2007	Daniel Craig, 2 <sup>nd</sup> year medical student, UCDHSC Caitlin Broe, Pomona College, Pomona, CA Luke Domaleski, Regis High School, Denver, CO
2006	Michael Ross, Notre Dame University Luke Domaleski, Regis High School
2004	Elizabeth Callaway, Stanford Univ., Alex Gart Kent High School; Jessica Moore Tulane University
2003	Elizabeth Callaway, Stanford Univ.
2001	Sarah Bowman, Univ. Colo. at Denver

**Teaching:**

Co-Course Director	2008-2010	Biology/ General Immunology	
		University of Colorado Colorado Springs	
Co-Course Director	2006-2007	Methods in Immunology	Univ. Colo at Colorado Springs
Co-Course Director	2006-2007	Biology/ General Immunology	
		UCCS	
Co-Course Director	2003 /2005	Biology/ General Immunology	UCCS
Instructor	2005	Advanced Immunology	UCCS
Instructor	1998-2003	Immunology	UCCS
Lecturer	2001	Micro/Immuno.	UCHSC-Nursing
Lecturer	2001	Micro/Immuno.	UCHSC-Dentistry

**University Service:**

2008 – 2010	Institutional Animal Care and Use Committee, Assistant Chair
2004 – 2007	IACUC

**Peer Reviewed Publications:**

Vaitaitis, GM, Waid, DM and **Wagner, Jr., DH**. 2010. "The expanding role of TNF-Receptor Super Family member CD40 (tnfrsf5) in Autoimmune Disease: Focus on Th40 cells." *Current Immunology Reviews*, *In Press*.

**Wagner, D. H., Jr.** 2009. The co-evolution of our understanding of CD40 and inflammation. *Diabetologia* 52:997-999.

Vaitaitis, G. M., and **D. H. Wagner, Jr.** 2008. High distribution of CD40 and TRAF2 in Th40 T cell rafts leads to preferential survival of this auto-aggressive population in autoimmunity. *PLoS ONE* 3:e2076.

Baker, R. L., **D. H. Wagner, Jr.**, and K. Haskins. 2008. CD40 on NOD CD4 T cells contributes to their activation and pathogenicity. *J Autoimmun* 31:385-392.

Waid, D. M., G. M. Vaitaitis, N. D. Pennock, and **D. H. Wagner, Jr.** 2008. Disruption of the homeostatic balance between autoaggressive (CD4+CD40+) and regulatory (CD4+CD25+FoxP3+) T cells promotes diabetes. *J Leukoc Biol* 84:431-439.

Siebert, J. C., M. Inokuma, D. M. Waid, N. D. Pennock, G. M. Vaitaitis, M. L. Disis, J. F. Dunne, **D. H. Wagner, Jr.**, and H. T. Maecker. 2008. An analytical workflow for investigating cytokine profiles. *Cytometry A* 73:289-298.

Waid, DM, Wagner, BA, Putnam, Vaitaitis, GM, Pennock, ND, Calverley, DC, Gottlieb, PA, **Wagner Jr., DH**. 2007 "A unique T cell subset described as CD4<sup>lo</sup>CD40<sup>+</sup> (T<sub>CD40</sub>) in human type 1 diabetes" *Aug; 124(2):138-148. Epub June 8, 2007*

**Wagner, Jr., D. H.** 2007. "Reshaping the T cell repertoire: TCR editing and TCR revision for Good and for Bad." *Clin. Immunol Apr* 123 (1): 1-6.

Waid, DM, Vaitaitis, GM, and **Wagner Jr., D.H.** 2004. Peripheral CD4<sup>lo</sup>CD40<sup>+</sup> Auto-Aggressive T Cell Expansion During Insulin-Dependent Diabetes Mellitus. *Eur. J. Immunol* 34:1488-1497.

Vaitaitis, GM, Poullin, M., Sanderson, RJ, Haskins, KJ, and **Wagner, Jr., DH**. 2003. CD40 Induced Expression of Recombinase Activating Gene (RAG) 1 and RAG 2: A Mechanism for The Generation of Autoaggressive T Cells in The Periphery. *Cutting Edge, J. Immunol.* 170:3455-3459.

**Wagner, DH, Jr.**, G. Vaitaitis, R. Sanderson, M. Poulin, C. Dobbs, and K. Haskins. 2002. Expression of CD40 identifies a unique pathogenic T cell population in type 1 diabetes. *Proc Natl Acad Sci U S A* 99:3782-3788.

**Wagner, Jr., DH**, E. Newell, R. Sanderson, J.H. Freed, and M.K. Newell. "Increased expression of CD40 on thymocytes and peripheral T cells in autoimmunity: A mechanism for acquiring changes in the peripheral T cell repertoire." 1999. *Intr. J. Mol. Med.* 4:231-242.

Huber SA., **DH, Wagner Jr.**, J.E. Stone, J. Kupperman, L. Pfeiffer, C. David, R L. O'Brein, G. S. Davis, and M.K. Newell. 1998. CD40<sup>+</sup> T cells regulate MHC class II (IA and IE)-dependent susceptibility to coxsackievirus B3-induced autoimmune ocarditis." *J. Virol.* 73:5630-5636.

Poe J.C., **Wagner Jr., DH**, Miller, R.W., Stout, R.D., and Suttles, J. 1997. " Role of protein tyrosine kinase activity in CD40 signaling of NF- $\kappa$ B activation and interleukin-1B synthesis in monocytes: modulation by interleukin-4 and interleukin-10." *J. Immunol.* 159 (2):846-852.

**Wagner Jr, DH**, J. Hagman, P.S. Linsley, W.H. Hodsdon, J.H. Freed, and M.K. Newell. 1996. "Rescue of thymocytes from glucocorticoid-induced cell death mediated by CD28/CTLA-4 costimulatory interactions with B7-1/B7-2." *J. Exp. Med.* 184:1631-1638.

**Wagner Jr., DH**, R.D. Stout, and J. Suttles. 1994. "Role of the CD40-CD40 ligand interaction in CD4<sup>+</sup> T cell contact-dependent activation of monocyte interleukin-1 synthesis. *Eur. J. Immunol.* 24:3148-3154-3164.

**Wagner Jr., DH**, and Suttles J. 1993. "Cognate T cell signaling of monocyte inflammatory cytokine production." *J. Immunol.* 150:135.

#### **Submitted:**

Vaitaitis, GM and **Wagner Jr., DH**. The signaling impact on glycosylation status - CD40 glycoforms and TNF-receptors 1 and 2 in the formation of CD40 receptor(s) on Th40 cells"

## ***Support:***

### **Active**

**NIH, ARRA funds, 2010**, PI Supplemental Funding, Total Award, \$65,000

**State of Colorado Technology Developmental Award, 2010**, PI Total Award, \$142,428 An Award for development of a small therapeutic molecule to treat type 1 diabetes.

**National Institutes of Health (NIDDK)** 1R01DK075013-01A2 PI  
08/01/07 – 07/31/12 *CD40 Induction of RAG1 and RAG2: A Mechanism for Autoimmunity* Total Award, \$922,500

The aims of this grant are to determine how CD40 T cells arise and the nature of their function in normal immunity. Further it will be determined how these T cells progress to pathogenicity. \$184,500/year for 5 yr.

**Kleberg Foundation:** *PI*. Role of CD40 in Vaccine Development: Tuberculosis Study. Total Award, \$214,250.

**Juvenile Diabetes Research Foundation:** PI 06/01/2008 – 06/01/ 2011. Total Award \$660,000/year “Common Mechanisms in Autoimmunity: A role for Th40 cells.” The aims of this grant are to determine how Th40 cells in human T1D and MS affect the disease process.

**American Diabetes Association**, Career Development Award, PI Total Award \$773,725

01/01/08 – 12/31/12 *CD40 As A Biomarker in Type 1 Diabetes*  
The aims of this grant are to understand the signaling capacity of CD40 in auto-aggressive T cells. Five different isoforms of CD40 are detected and T cells express an atypical combination. Furthermore, T cells from autoimmune mice and human subjects express different CD40 isoform combinations than cells from non-autoimmune subjects. This grant will delineate those differences and determine how different CD40 isoform configurations affect CD40 signaling in autoimmune versus non autoimmune conditions.

### **Previous Funding:**

*Kleberg Foundation: T cells and Tuberculosis* \$105,200

**American Diabetes Association** Junior Faculty Award, *PI* 01/01/03 – 01/01/06  
\$424,000

*CD40 Prevents AICD in Auto-Aggressive T cells*

This grant proposal compares the responses of auto-aggressive T cells and regulatory T cells in modes of activation induced cell death, including the role of NF- $\kappa$ B.

**Juvenile Diabetes Research Foundation**      Regular Research Grant, PI 11/01/03 – 10/31/06

#1-2003-703      \$450,000

*Development of Auto-Aggressive T Cells in IDDM:* The aims of this grant are to examine the expansion of CD40+, autoaggressive T cells specifically focusing on T cell receptor expression and altered expression using the nonobese diabetic (NOD) mouse model.

**Juvenile Diabetes Research Foundation** Transitional Award      \$100,000 “

The role of CD40 in diabetogenic T cells” The aims of this grant were to establish CD40 as a T cell molecule, describe how CD40 T cells affect diabetogenesis and attempt to control the now identified pathogenic, i.e. autoaggressive T cells.

01/01/2002 – 12/31/2002

**Juvenile Diabetes Research Foundation** Advanced Postdoctoral Fellowship      \$231,000

“The role of CD40 in diabetogenic T cells” The aims of this grant were to establish CD40 as a T cell molecule, describe how CD40 T cells affect diabetogenesis and attempt to control the now identified pathogenic, i.e. autoaggressive T cells.

01/01/2000 – 12/31/2002

**NIH, NRSA**      National Jewish Medical Research Center \$60,000

**Community Involvement:**      Board of Directors 2000-2005  
Howard Dental Center for HIV/AIDS patients

**Patents:**

1999	“USE OF CD40 ENGAGEMENT TO ALTER T CELL RECEPTOR USAGE” Patent Executed in 2001
2003	“METHODS FOR PREDICTING DEVELOPMENT OF AUTOIMMUNE AND TREATMENTS OF THE SAME” Office Action, July 2007
2009	“Peptides for modulating T cell activity and uses thereof”