

Stanford



Hugh McDevitt

Professor of Microbiology and Immunology and of Medicine, Emeritus

Microbiology & Immunology

 Curriculum Vitae available Online

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ACADEMIC APPOINTMENTS

- Emeritus Faculty, Acad Council, Microbiology & Immunology

LINKS

- Microbiology and Immunology: <http://cmgm.stanford.edu/micro/>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

I. The laboratory's research program focuses on the molecular mechanisms by which particular major histocompatibility molecules mediate the presentation of self antigens to induce autoimmunity. One of the principle disease models is the non-obese diabetic (NOD) mouse, a strain which spontaneously develops type 1 diabetes; and which is similar to the same disease in man. Current experiments focus on identifying the peptide fragments of proteins from the insulin producing beta cells which induce a T cell response leading to inflammation and destruction of the islet beta cells. Specific sequence polymorphisms in the class II MHC molecule, I-Ag7, result in the development of diabetes in individuals expressing this sequence polymorphism (as well as other susceptibility genes for type 1 diabetes). We have produced T cell hybridomas recognizing many of the peptide fragments of an important islet cell protein, glutamic acid decarboxylase 65. These T cell hybridomas have been used to produce transgenic mice, and we are currently analyzing these transgenic mice as well as their T cell receptors, which recognize GAD65 peptides bound by I-Ag7, to understand how this MHC class II molecule presents peptides in such a way as to induce an inflammatory response resulting in the destruction of the islets.

II. Other genes in the major histocompatibility complex encode the structural genes for tumor necrosis factor alpha and lymphotoxin alpha/beta. These molecules are critical in both the development of the immune system, and in the function of the immune system in the adult animal. Current studies focus on the effect of TNF alpha on signaling through the T cell receptor; on the development of CD4+, CD25+ regulatory T cells which are capable of suppressing normal immune responses, as well as autoimmune responses, and on the role of lymphotoxin in driving selective expression of chemokines which result in the development of autoreactive T cells in the spleen and lymph nodes.

Publications

PUBLICATIONS

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- **Ir genes - forty years on** *CLINICAL AND INVESTIGATIVE MEDICINE*
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- **Severe anaphylactic reactions to glutamic acid decarboxylase (GAD) self peptides in NOD mice that spontaneously develop autoimmune type 1 diabetes mellitus.** *BMC immunology*
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- **The T cell response to glutamic acid decarboxylase 65 in T cell receptor transgenic NOD mice** *6th International Congress of the Immunology-of-Diabetes-Society and American-Diabetes-Association Research Symposium*
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- **Tumor necrosis factor- α regulation of CD4(+)C25(+) T cell levels in NOD mice** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
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- **CD4(+) T cells from glutamic acid decarboxylase (GAD)65-specific T cell receptor transgenic mice are not diabetogenic and can delay diabetes transfer** *JOURNAL OF EXPERIMENTAL MEDICINE*
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- **The discovery of linkage between the MHC and genetic control of the immune response** *IMMUNOLOGICAL REVIEWS*
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- **Multiple roles for tumor necrosis factor-alpha and lymphotoxin alpha/beta in immunity and autoimmunity.** *Arthritis research*
McDevitt, H., Munson, S., Ettinger, R., Wu, A.
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- **A Critical role of Lymphotoxin-b Receptor in the Development of Diabetes in Non-obese Diabetic Mice** *J Exp. Med.*

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- **Disrupted splenic architecture, but normal lymph node development in mice expressing a soluble lymphotoxin-beta receptor-IgG1 fusion protein** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Ettinger, R., Browning, J. L., Michie, S. A., VANEWIJK, W., McDevitt, H. O.
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