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GUEST EDITORIAL

Introduction to the special issue on Stanford Immunology

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Dedication

Leonard A. Herzenberg (© Leonore A. Herzenberg, 2011. Used with permission)

This special issue is dedicated to the memory of Leonard A. Herzenberg, innovative scientist, colleague, mentor, and friend, who passed away on October 27, 2013 at age 81.

A key founder of Stanford Immunology, Len leaves a lasting legacy of creativity, generosity, and caring. He will be missed by the local and global immunology communities.

Special issue on Stanford Immunology

It is a pleasure to introduce this special issue of *Immunologic Research* on Stanford Immunology. Stanford has been a leading center of research in immunology for more than 50 years. From Stanford immunologists have come pioneering contributions to both basic and clinical immunology, including technological advances that have revolutionized the field—most notably the invention of the fluorescence-activated cell sorter. Currently, the Stanford Immunology community includes approximately 75 faculty in many departments and divisions across the School of Medicine. This issue highlights the research being done in many of these laboratories. Articles are organized thematically; in most cases, the lead article for a set is a historical perspective by a senior immunologist.

The first article, by Pat Jones and Lee Herzenberg, is a special one, in that it recounts the early history of Stanford Immunology beginning with the move of the Stanford School of Medicine from San Francisco to the Stanford campus in 1959. The article describes the vibrant early immunology community established by Joshua Lederberg, the Nobel Prize-winning chairman of the new Genetics Department, highlighted by the recruitment of Len and Lee Herzenberg. While the interests of that early group were centered largely on antibodies, the article describes another early focus—originating with Rose Payne and Walter and Julia Bodmer and expanded by Hugh McDevitt—on leukocyte antigens (later called HLA antigens) and their roles in transplantation and in controlling immune responses and

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disease susceptibility. These early immunologists and the cohort that followed in the late 1960's and 70's—Irv Weissman, Sam Strober, and Ron Levy—established the tradition of innovative, interactive, and collaborative research and the sense of community that characterize Stanford Immunology today. The article ends with the rapid expansion of immunology in the late 1970's and early 80's, ~25 years after the milestone move of the Medical School to Stanford.

The first seven articles that follow describe research in basic mechanisms and processes of the immune system; several introduce new methods and applications that should facilitate immunologic research. Shoshana Levy reviews the functions of the tetraspanin molecule CD81 in B and T cells. The article by Ruppert et al. from Paul Bollyky's laboratory describes immunoregulatory roles of high molecular weight hyaluronan in extracellular matrices. In a thorough and fascinating review, Firdaus Dhabhar discusses his and others' recent novel and important findings that stress can have beneficial—as well as harmful—effects on the immune system. An exciting new approach for investigating the triggering of cells, using physical force from atomic force microscopy, is described in the Hu et al. manuscript from Manish Butte's laboratory. The next article, by Meehan et al., introduces the latest innovation in software for flow cytometry from the Herzenberg laboratory; it describes AutoGate, which makes gating and analysis of flow data more automated and should greatly facilitate the identification of cell subsets. Holden Maecker's group in the Human Immune Monitoring Core describes the differential effects of serum versus plasma on multiplex immunoassays (e.g., for levels cytokines), with some cautionary notes, in the article by Rosenberg-Hasson et al. Finally, the article by Bhattacharya et al. describes the valuable ImmPort online data resource developed by Atul Butte's group. ImmPort is the archival data repository and dissemination system for molecular and clinical data sets developed by research consortia supported by NIAID; it has as its goal promoting new hypothesis- and data-driven research and facilitating transparency and reproducibility in immunology research.

The next set of articles focuses on transplantation. The lead article, by Sam Strober, tells the story of his introduction to problems of transplantation as a medical student and his subsequent long pursuit of the Holy Grail of being able to induce tolerance to allogeneic tissue to prevent organ transplantation rejection and graft vs. host disease. The article closes with promising recent results in tolerance induction that have emerged from this decades-long journey. The next article, by Popli et al., is a review from David Miklos' group on the clinical impact of H-Y alloimmunity in bone marrow and organ transplants. Sheri Krams and colleagues (Hadad et al.) review the controversial roles of NK cells—helpful and/or harmful?—after transplantation. The last article in this group, by Hatton et al. from Olivia Martinez' laboratory, presents a thorough review of the complex interactions between Epstein Barr Virus and B cells, including EBV-associated B-cell lymphomas that arise in immunosuppressed and immunocompromised populations, such as following organ transplantation.

The first of four articles on cancer immunology is a brief personal history from Ron Levy, describing his quest for cancer immunotherapies. From specific anti-idiotypes for treating B lymphomas to the anti-CD20 antibody that became the widely-used rituximab to more recent approaches, this is a story of persistence and adaptation in pursuit of an important clinical goal. The next article, by Casey et al., describes exciting recent findings from Dean Felsher's laboratory of essential roles of T cells in the processes by which targeted oncogene inactivation results in tumor regression. A promising strategy for screening tumor proteins for mutations that could generate T-cell epitopes that might serve as immunotherapeutic targets is described in the article by Khodadoust et al. Developed in Ash Alizadeh's laboratory, the approach combines cancer genome sequencing with computational analysis of MHC binding and high throughput approaches to measure T-cell responses to each candidate mutated antigen. The final article on cancer immunology, by Schmidt et al., is a review from Chris Contag's laboratory of the properties and prospects of new versions of cytokine-induced killer cells as potential immunotherapeutic agents against cancers.

Autoimmune diseases are the focus of the next four articles, starting with historical accounts from two faculty. Larry Steinman describes the history of his research on multiple sclerosis, much of it using the mouse model experimental autoimmune encephalomyelitis (EAE) to identify the cells and processes responsible for autoimmune pathogenesis. He describes the development of a number of therapeutic approaches to treating EAE, MS, and other autoimmune diseases, including some successes and possible promising results with the repurposing of drugs currently in use for other conditions. The next article is a fascinating history by Emmanuel Mignot of his long journey to understand narcolepsy, which eventually yielded the finding that narcolepsy is an autoimmune disease targeting brain hypocretin, which controls sleep. The story becomes even more amazing with the recent indications that a specific preparation of influenza vaccine may have caused some narcolepsy cases in recent years, providing perhaps the best example yet that molecular mimicry can lead to autoimmunity. The next two articles focus on Type 1 diabetes (T1D). Linda Yip and Garry Fathman describe their search for genes associated with spontaneously

occurring diabetes in the NOD mouse, establishing a roadmap of genes differentially expressed in susceptible versus resistant mice, including two that seem to be associated with T1D in both mice and humans. The article by Shan et al. from Sarah Michie's laboratory reports their recent finding that the chemokine receptor CCR7 on T cells and its chemokine ligand on vascular endothelial cells play essential roles in T-cell recruitment into inflamed islets during the induction of T1D in NOD mice.

The final set of articles focuses on allergy and inflammation. The first article, by Pellerin et al., is a review article from Kari Nadeau's laboratory summarizing the current understanding from their and others' work on roles of defects in regulatory T-cell populations in allergy. The second article, also from the Nadeau laboratory (Klingbeil et al.), reviews the evidence for roles of environmental polycyclic aromatic hydrocarbons (PAH) in epigenetic remodeling and in asthma. PAH are also found in tobacco smoke, and the article discusses the relationship between exposure to tobacco smoke and occurrence of asthma. The next article, by Alonso et al., describes the recent development in Ed Engleman's laboratory of a method to eliminate inflammatory tissue dendritic cells arising from infiltrating monocytes, using an antibody to a DC marker coupled to a toxin. The roles of innate and adaptive immune system cells in pancreatitis are discussed in the review from Aida Habtezion's laboratory (Xue et al.). Initially triggered by premature activation of pancreatic enzymes, acute and chronic pancreatitis can involve damage from inflammatory neutrophils, macrophages, and dendritic cells, as well as from T cells. Finally, the roles of leukotrienes in the inflammation and resulting pulmonary vascular remodeling associated with pulmonary arterial hypertension are discussed in the review by Tian et al. from Mark Nicoll's laboratory. The article concludes that pharmacologic inhibition of leukotriene pathways may be an effective treatment for this serious condition.

The articles in this issue illustrate just a portion of the breadth of immunology research at Stanford, spanning basic to translational and clinical immunology research. For a complete list of immunology faculty and Stanford Immunology program activities, see http://immunol.stanford.edu/.

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