James G. Krueger, M.D., Ph.D.

SENIOR ATTENDING PHYSICIAN • CO-DIRECTOR, CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE • D. MARTIN CARTER PROFESSOR IN CLINICAL INVESTIGATION, LABORATORY FOR INVESTIGATIVE DERMATOLOGY

Caused when the immune system attacks the skin, psoriasis is one of the most accessible human diseases in which to examine how the activation of white blood cells called T cells leads to autoimmune disorders. Krueger uses psoriasis as a model to study inflammatory diseases that involve Th17 cells, a set of T cells. His work has implications for other common inflammatory diseases, such as rheumatoid arthritis and inflammatory bowel disease.

Krueger's group focuses on cutaneous inflammation and autoimmune mechanisms in human skin. Their research is fundamentally rooted in "bench-to-bedside" science, combining the clinical study of new medical therapeutics with laboratory research on relevant immunopathogenic mechanisms in human cells and tissues. The laboratory conducts clinical research on patients with psoriasis vulgaris at The Rockefeller University Hospital. They treat patients with a wide variety of engineered immune molecules in order to restore normal immune responses. By combining novel immune-directed therapeutics with large-scale study of gene expression, an approach called pharmacogenetics, the researchers seek to uncover the molecular pathways that cause pathogenic inflammation and regulate normal human immune responses.

More experimental immunotherapeutics have been tested for psoriasis than for any other human inflammatory disease. Krueger's group has pioneered a number of successful treatments, including some that act on T cells. One of these therapies counteracts specific inflammatory cytokines; another involves a type of ultraviolet light with immunomodulatory properties.

The lab-based research accompanying Krueger's clinical trials includes the study of T cell, dendritic cell, and keratinocyte activation responses using techniques such as cell culture, flow cytometry, and biochemical analysis. His group also studies the expression of a defined set of proinflammatory genes using real-time PCR, and that of all other genes by broader methods (gene array or sequencing). The lab defined the first disease classification set for psoriasis using chip-based approaches, and recently determined a specific genetic and immunological signature that differentiates psoriasis from atopic eczema, a closely related skin disorder.

Krueger's research in healthy skin has shown that a previously unknown population of dendritic cells exists alongside macrophages in the skin. Other recent work by members of the lab has shown that a newly discovered immune cell, Th17, plays a central role in psoriasis and could serve as a target for future therapies. This T cell subset is regulated by IL-23, a protein shown by the group to be upregulated in psoriasis. IL-23 antagonism has produced major improvements in psoriasis, suggesting a new class of therapeutics. And by investigating the contribution of activated T lymphocytes, Krueger has found that psoriasis may be induced by tissue-infiltrating T lymphocytes, which trigger keratinocytes into a physiologically regulated wound repair pathway of hyperplasia and altered differentiation.

In order to place inflammatory pathways discovered in psoriasis in the context of other T cell mediated diseases and tissue rejection responses, the team is collaborating with investigators of other inflammatory cutaneous diseases. They are attempting to define molecular pathways that control cellular immune responses in order to broaden our understanding of organ-specific autoimmune diseases.

EDUCATION

A.B. in biochemistry, 1979
Princeton University

Ph.D., 1984
The Rockefeller University

M.D., 1985
Cornell University Medical College

MEDICAL TRAINING

Residency in internal medicine, 1985–1986
Residency in dermatology, 1986–1990
Cornell University Medical College

POSTDOC

The Rockefeller University, 1988–1989

POSITIONS

Assistant Professor, 1990–1995
Associate Professor, 1995–2003
Professor, 2003–
The Rockefeller University

Associate Physician, 1989–1995
Physician, 1995–2003
Senior Physician, 2003–
Medical Director, 1996–2008
Program Director, General Clinical Research Center, 1996–2006
Co-director, Center for Clinical and Translational Science, 2006–
Chief Executive Officer, July 2008–
The Rockefeller University Hospital

AWARDS

Distinguished Achievement Award, American Skin Association, 2001

Psoriasis Research Achievement Award, American Skin Association, 2001

E.H. Ahrens Jr. Award, Association for Patient-Oriented Research, 2006

Astellas Award, American Academy of Dermatology, 2010

Farber Award, Society of Investigative Dermatology, 2010

Van Scott Award for Innovative Therapy of the Skin, 2015

SELECTED PUBLICATIONS

Kim, J. and Krueger, J.G. Highly effective new treatments for psoriasis target the IL-23/Type 17 T cell autoimmune axis. *Annu. Rev. Med.* 68, 255–269 (2017).

Krueger, J.G. et al. Anti-IL-23A mAb BI 655066 for treatment of moderate-to-severe psoriasis: Safety, efficacy, pharmacokinetics, and biomarker results of a single-rising-dose, randomized, double-blind, placebo-controlled trial. *J. Allergy Clin. Immunol.* 136, 116–124 (2015).

Lowes, M.A., et al. Immunology of psoriasis. *Annu. Rev. Immunol.* 32, 227–255 (2014).

Krueger, J.G. et al. IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis. *J. Allergy Clin. Immunol.* 130, 145–154 (2012).

Papp, K.A. et al. Brodalumab, an anti-interleukin-17-receptor antibody for psoriasis. *N. Engl. J. Med.* 366, 1181–1189 (2012).