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 pharmacogenomics, 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.