Autoimmunity, Transplantation & Inflammatory Disease

For eight percent of the population, their bodies are their own worst enemies. Diagnosed with an autoimmune or autoinflammatory disease, these patients are victims of their own in-built defense system which has, for some reason, switched allegiance and is now mistakenly attacking healthy tissue and organs.

Most often, these diseases are treated with drugs such as steroids that broadly suppress immunity. However, these medicines are often only partially effective and can make patients more susceptible to infection.

But advances in the understanding of the immune system are offering fresh hope. Our Autoimmunity, Transplantation & Inflammation (ATI) disease team is at the forefront of translational science revealing how and why the immune system malfunctions. Thanks to our insights into the causes of autoimmune diseases, we are now able to identify the specific elements of the immune system that have gone awry so we can develop highly targeted therapies and, ultimately, aim for cure.
ATI leadership

Novartis blazed a trail in the field of immunotherapy in the 1980s by originating the immunosuppressant cyclosporine that helped make organ transplantation an everyday occurrence.

Since then, we have developed breakthrough treatments for a variety of diseases caused by disorders in the immune system. For instance, we pioneered a novel first-line multiple sclerosis (MS) treatment, the first in a new class of drugs called sphingosine 1-phosphate receptor modulators, shown to significantly reduce relapses and delay disability progression. In MS, the immune system damages the covering that protects nerve fibers in the central nervous system. It is believed that this drug works by reducing the immune system’s attack on the nervous system.

We are also pioneering new research for the treatment of rheumatic diseases including rheumatoid arthritis, ankylosing spondylitis, Sjoegren’s syndrome and systemic lupus erythematosus, and are making headway on dermatological diseases, too. In 2015, we launched a targeted treatment for plaque psoriasis, a common autoimmune condition. It is not just a cosmetic problem, but a persistent, often distressing disease that affects many aspects of daily life. This treatment also shows effects in symptoms of psoriatic arthritis, a frequent complication.

We are now exploring potential treatments for other poorly understood long-term skin conditions such as atopic dermatitis, hidradenitis suppurativa, chronic urticaria and vitiligo.

Tolerance therapy: the next frontier?

One of the most promising areas of ATI research is the induction of immune tolerance. Tolerance therapies target only the immune cells that react to the specific self-antigen causing the autoimmune disease. The aim is to activate those immune cells with regulatory properties, thus counterbalancing the unwanted self-immune response. Because these therapies do not cause general immune suppression, they can treat the immune disorder without making patients more vulnerable to infection.

We currently have a range of tolerance projects in the pipeline, including through our collaboration with Parvus Therapeutics, a Canadian biotech firm, on the induction of tolerance in type 1 diabetes.

Immune dysfunction taking center stage

Increasingly, we are uncovering common biological pathways uniting different immune disorders around the body. In time, this may prompt changes to the way inflammatory diseases are defined and classified. More importantly, it has already enabled us to expand the application of some of our drugs to treat multiple inflammatory diseases. Many of our current clinical trials are following this paradigm.

Our research is pointing to the central role of immune dysfunction in diseases not usually viewed as immune-mediated or driven by an inflammatory process. These include
neurodegenerative, cardiovascular and renal diseases. Today, for example, colleagues in
Novartis are exploring the possibility that one of our most successful treatments for a range of
inflammatory disorders could also be used in fighting atherosclerosis. In the coming years, it
may be that our work in ATI transforms how medicine deals with some of the world’s most
urgent health challenges.

Footnotes:

Selected Publications

A Novel, Blocking Anti-CD40 Monoclonal Antibody Prolongs Non-Human Primate Renal
Allograft Survival in the Absence of B-Cell Depletion Or Thromboembolic Events [2]
Cordoba F, Wieczorek G, Audet M, Roth L, Schneider MA, Kunkler A, Stuber N, Erard M,

Deficiency of MALT1 Paracaspase Activity Results in Unbalanced Regulatory and Effector T
and B Cell Responses Leading to Multiorgan Inflammation [3]
N, McCoy KD, Rolink A, Régnier CH, Mak TW, Ohashi PS, Patel DD, Calzascia T

Translating nucleic acid-sensing pathways into therapies [4]
Junt T, Barchet W

GPR91 senses extracellular succinate released from inflammatory macrophages and
exacerbates rheumatoid arthritis [5]

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