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125 years of immunology: from the 2025 Nobel Prize to research prospects in Chad

Vittorio Colizzi[1,2]*, Giulia Cappelli[3], Franck J.D. Mennechet[2,4], Ali Mahamat Moussa[2,5], Agnes Tariam Djibangar[2]

[1]*Faculty of Medicine, University Hospital Complex "Le Bon Samaritain", N'Djamena, Chad*

[2]*Laboratoire des Grandes Épidémies Tropicales, University Hospital Complex "Le Bon Samaritain", N'Djamena, Chad*

[3]*Institute for Biological Systems, National Research Council, Rome, Italy*

[4]*Pathogenesis and Control of Chronic and Emerging Infections, University of Montpellier, France*

[5]*Chad National Institute of Public Health, Chad*

***Corresponding author:** Vittorio Colizzi. Email: colizzi@uniroma2.it

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Abstract

The long list of Nobel Prize laureates in immunology from 1901 to 2025 presents some generally little-known characteristics. Beyond the obvious association of immunology with vaccination or transplantation, the Nobel Prize selection committee of the Royal Swedish Academy of Sciences has awarded Nobel Prizes in immunology to researchers whose work redefines fundamental principles of functional biology that govern physiology and pathology, as well as health and disease.

Introduction

The long list of Nobel Prize laureates in immunology from 1901 to 2025 presents some generally little-known characteristics. Beyond the obvious association of immunology with vaccination or transplantation, the Nobel Prize selection committee of the Royal Swedish Academy of Sciences has awarded Nobel Prizes in immunology to researchers whose work redefines fundamental principles of functional biology that govern physiology and pathology, as well as health and disease (Table 1).

The history of immunology can be divided into three distinct periods.

The first period predates the establishment of the Nobel Prize by the Swedish industrialist Alfred Nobel. The story of the Nobel Prizes begins in 1850, in the Paris laboratory of the Italian chemist Ascanio Sobrero, where a young Alfred Nobel first encountered nitroglycerine. Eventually, after causing an accidental explosion that killed his younger brother, Nobel developed a stable, solid compound of nitroglycerine that he called dynamite. His invention revolutionized mining and engineering, making possible feats of construction that would have been unimaginable without such explosive power, while also finding application in military contexts. Not wanting to be remembered as a war profiteer, he chose to use his wealth for the greater good and thus established the Nobel Prizes to honor "those who have conferred the greatest benefit to humankind". Nobel died in 1896 at his residence in Sanremo, Italy.

The last 50 years of the 19th century were marked by the pioneering work of foundational figures in immunology, including Louis Pasteur, Robert Koch, Paul Ehrlich, and Élie Metchnikoff. However, Edward Jenner is widely regarded as the "Father of Immunology" for his groundbreaking work in developing the first vaccine. Jenner was born in Gloucestershire, England, in 1749, a time when smallpox still claimed the lives of millions of people in periodic epidemics and left millions more with characteristic scars, or pockmarks.

The second period began with Emil von Behring (1901) and continued with Paul Ehrlich and Elie Metchnikoff (1908), winners of the first two Nobel Prizes in Physiology or Medicine, an era marked by major scientific advances from the early 20th century up to the Second World War. Following the discoveries of Pasteur, Koch, Ehrlich, and Metchnikoff in infectious diseases, vaccination, and cellular

immunopathology, the first 50 years of the 20th century saw the development of an essentially immunochemical immunology. At that time, scientific publications were often difficult for clinicians to understand. They typically consisted of long series of experiments, primarily using electrophoresis and other quantitative techniques aimed at characterizing the physicochemical properties of antibodies and antigens, particularly their affinity and the binding forces that hold them together. Antigen recognition by antibodies was considered a purely physicochemical phenomenon, and the most widely accepted models describing the dynamics of this interaction were those proposed by Linus Pauling, who won two Nobel Prizes in Chemistry for applying quantum mechanics to chemical problems and the Nobel Peace Prize for his efforts to curb nuclear proliferation between the West and the East.

The third period extends from the end of the Second World War to the present day. We belong to the third generation of immunologists. Vittorio Colizzi had Sir Peter Medawar, the 1960 Nobel laureate (awarded jointly with Frank Macfarlane Burnet), as supervisor of his doctoral thesis at the Clinical Research Centre in London (Harrow). After the end of the Second World War, Peter Medawar, a young Royal Navy doctor who had treated many sailors burned on ships, began to study skin grafting, transferring skin from white mice to genetically different black mice, which systematically rejected it. Only when the mice were made "tolerant" at birth by the injection of allogeneic cells were they able to accept a graft of genetically different skin. This discovery marked a decisive turning point in modern immunology. With Burnet and Medawar, many immunologists focused their research on the biological phenomena of memory and immune tolerance, marking the repositioning of immunity studies within the theoretical and experimental framework of the life sciences. The new theory of adaptive immunity was defined as "Darwinian" because it envisioned clonal selection processes within a cellular repertoire, where each cell expressed a unique antibody with a very precise specificity. When these cells encountered their corresponding antigen, those capable of recognizing it with sufficient affinity were stimulated and multiplied (positive selection), while those likely to react against the body's own tissues were eliminated (negative selection), thus preventing autoimmunity. Hence arises the almost mystical concept of the God of Diversity, according to which our immune system would be capable of recognizing any antigen, even those found on a planet millions of light-years away from Earth. This concept was further elucidated in later years by Nobel laureate Susumu Tonegawa (1987), who, through his characterization of the diversity of antibody chains and the underlying genetic rearrangements, challenged the prevailing notion in early genetics that one gene corresponds to a single protein. Around the same time, Köhler and Milstein fused mouse B lymphocytes with myeloma cells to produce monoclonal antibodies capable of binding a specific antigen with high precision. This breakthrough, which earned them the Nobel Prize in 1984, laid the foundation for decades of clinical development leading to today's monoclonal antibody-based therapies. This discovery, along with the identification of immune response genes and T lymphocyte subpopulations that orchestrate immune responses based on receptor markers on their surface, marked the true beginning of modern immunology.

As Professor Corbellini, the Italian historian of science, aptly observed, the clarification of uncertainties and the uncovering of mechanisms underlying immunological phenomena – often seemingly at odds with prevailing models – have unfolded through historical conflicts between competing theoretical and conceptual frameworks. These include debates such as innate vs. acquired immunity; cellular vs. humoral defense (Metchnikoff vs. Ehrlich, the latter awarded the Solomon Prize in 1908); and education vs. selection of the immunological repertoire – was the genetic diversity of antibodies germinal or somatic? Other questions followed: How is genetic control exerted over immune responses and transplant rejection? Does innate immunity feature specific genetic and recognition mechanisms comparable to those of adaptive immunity? Are there cells capable of suppressing immune responses, and do regulatory T cells (Tregs) truly exist?

Medawar, in his 1960 Nobel lecture, wrote: “Tolerance is not the absence of reaction; it is the positive result of an active process of self-recognition”. Today, Shimon Sakaguchi has reiterated this concept, illustrated by his study of Tregs, according to which “tolerance is not weakness, but the active maintenance of harmony”. Additionally, the other two 2025 Nobel laureates, Mary Brunkow and Fred Ramsdell, identified the genetic marker FOXP3 and elucidated its molecular role in the function of Tregs.

Professor Corbellini also noted that the unique nature of the Nobel Prizes in Immunology stems from the evolution of the metaphors used in this field, each period reflecting a different philosophical approach to biological life. These metaphors also apply to the social sciences: they suggest protection and defense above all, but also notions of identity, tolerance, balance, and the regulation of "power". Although the immune system is commonly imagined as an army defending the body against microbial invaders, this metaphor, widely used in microbiology between 1890 and 1940, had been theoretically superseded by the mid-1950s. The immune system is on its way to becoming a "cognitive" system, endowed with memory and capable of learning to defend itself against non-self. Burnet was among the first to conceive of the immune system as a "cognitive" system, analogous to the nervous system: it acquires and processes information on the scale of the biological microcosm, while the brain categorizes the phenomena of the macrocosm.

The three 2025 Nobel Prize winners discovered, in the early 2000s, Tregs and their role in maintaining peripheral tolerance and regulating the immune system to prevent autoimmune diseases (Figure 1).

Tregs are characterized by: i) expression of the transcription factor Foxp3, which is essential for their regulatory function; ii) high levels of CD25 (the α-chain of the interleukin [IL-2] receptor); and iii) low expression of CD127, a marker inversely correlated with Foxp3.

They ensure: i) maintaining self-tolerance; ii) regulation of inflammation following an immune response; iii) prevention of autoimmunity; and iv) control of the activation and proliferation of effector lymphocytes.

Tregs exert their effects through: i) secretion of immunosuppressive cytokines (IL-10, transforming growth factor [TGF]β, IL-35); ii) expression of inhibitory molecules (CTLA4, PD1); iii) competitive consumption of IL-2; and iv) direct cell-to-cell contact inhibiting effector cells (monocytes and lymphocytes).

An imbalance of Tregs is implicated in: i) autoimmune diseases (e.g., type 1 diabetes or multiple sclerosis); ii) cancers, where excessive activity can inhibit the antitumor response; iii) transplants, by promoting graft tolerance; and iv) chronic infectious diseases, where Tregs modulate viral persistence.

Overall, Treg cells play a crucial role in maintaining self-tolerance and preventing autoimmunity, safeguarding the fetus during pregnancy, controlling chronic inflammation and cancer, and modulating immune responses in infectious diseases and transplantation to prevent excessive, potentially harmful activity.

Today, the metaphor driving research is that of ecology: the immune system is an ecosystem actively regulated internally to achieve an adaptive equilibrium in response to changes in context (including microbiological). In 2006, Franck Mennechet demonstrated that the activation of immature dendritic cells by type III interferons generates dendritic cells exhibiting a semi-mature tolerogenic phenotype capable of inducing Treg production in vitro. In Cameroon, the Centre International de Référence Chantal Biya (CIRCB) identified the role of Tregs in the immune response of patients with AIDS. In Côte d’Ivoire, Agnes Tariam thoroughly characterized the cytotoxic lymphocyte profile of children with malaria. The adaptability and memory of the immune system of Chadian populations were characterized by young Chadian researchers from the Laboratoire des Grandes Épidémies Tropicales (LAGET) at the University Hospital Complex “Le Bon Samaritain” (N’Djamena) in 2022, whose results, published in several scientific journals, showed that antibodies against the SARS-CoV-2 virus, responsible for the COVID-19 epidemic, were already present in the immunological repertoire of the Chadian population, testifying to cross-immunity and remarkable resilience of the African immune system.

These results mark the beginning of a new era in immunological research in Chad, where LAGET is establishing itself as a key player in understanding the interactions between immunity, the environment, and public health. In a context of climate change and the close interconnectedness of human, animal, and environmental health (the One Health approach), the study of immune adaptation mechanisms is becoming a major challenge for national biomedical research. To meet this challenge, it is now necessary to establish a national immunology platform integrating cell culture, molecular biology, advanced serology, flow cytometry, sequencing, and bioinformatics technologies. Such an infrastructure (located at the National Institute of Public Health of Chad) will enable in-depth analysis of the diversity and memory of the immune system, strengthen the country’s immune surveillance research capacity, and train a new generation of Chadian researchers at the forefront of immunological science.

Table 1. Nobel Prizes in immunology (1901-2025).

Year	Laureates	Immunology-related work/reason for the price
1901	Emil Adolf von Behring	Serum therapy against diphtheria (passive immunity)
1908	Eli Metchnikoff and Paul Ehrlich	Phagocytosis antibodies (adaptive immunity)
1913	Charles Robert Richet	Anaphylaxis
1919	Jules Bordet	Complement proteins and complement fixation tests
1930	Karl Landsteiner	Human blood groups
1960	Peter B. Medawar and Frank Macfarlane Burnet	Acquired immunological tolerance
1972	Gerald Maurice Edelman and Rodney Robert Porter	Chemical structure of antibodies
1980	Baruj Benacerraf, Jean Dausset and George Davis Snell	Structures of immune response genes
1984	Niels Jerne, Georges J. F. Köhler and César Milstein	Monoclonal antibodies
1987	Susumu Tonegawa	Antibody diversity
1996	Peter C. Doherty and Rolf M. Zinkernagel	Antigen-complex recognition by T lymphocytes
2011	Bruce Beutler, Jules A. Hoffmann, and Ralph Marvin Steinman	Dendritic cells and the triggering of the adaptive immune response
2018	James P. Allison and Tasuku Honjo	Cancer therapies through the inhibition of negative immune checkpoints
2025	Mary Brunkow, Fred Ramsdell and Shimon Sakaguchi	Peripheral immune tolerance

Figure 1. Nobel Prize winners of 2025.

Conflict of interest

The authors have no conflict of interest to declare. We thank Professor Gilberto Corbellini, full professor of History of Medicine at Sapienza University of Rome, for inspiring this reflective article on the history of immunology.onflict of interest:

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1. None (n.d.). .