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Nussenzweig's laboratory studies the molecular aspects of the immune system's innate and adaptive responses using a combination of biochemistry, molecular biology, and genetics. For work on adaptive immunity, he focuses on B lymphocytes and antibodies to HIV-1, while his studies of innate immunity focus on dendritic cells. His work is leading to new antibody-based therapies for infections by HIV and the novel SARS-CoV-2 coronavirus, among other viruses.

The immune system protects vertebrates from a multitude of pathogens. Two types of immune responses have evolved to accomplish this task: one innate and the other adaptive. Adaptive immune responses are primarily carried out by cells called lymphocytes, which produce a diverse repertoire of immune receptors that recognize almost any antigen. Most of these receptors have relatively low affinity for their antigens and must be refined by somatic hypermutation and class switch recombination, yielding high-affinity antibodies that protect against most pathogens, including HIV-1. Hypermutation and selection occur in specialized micro-anatomical compartments called germinal centers. Nussenzweig's laboratory investigates the molecular basis of such hypermutation, and the selection for high affinity antibody-producing cells in the germinal center.

Nussenzweig's research aims to understand the rules that govern hypermutation and high affinity antibody selection, with the goal of creating vaccines for pathogens such as HIV-1. As part of that effort his laboratory has devised strategies to isolate, analyze, and produce highly potent human antibodies capable of neutralizing multiple HIV strains.

Nussenzweig has isolated such broadly neutralizing antibodies from HIV-infected patients whose immune systems had an exceptional ability to neutralize HIV in the blood. In clinical trials conducted at The Rockefeller University Hospital, two of these antibodies interfered with chronic HIV infection, driving the amount of virus in the blood to below detectable levels. And unlike traditional antiretroviral therapy, which requires daily dosing, the antibodies continue to provide protection and treatment for months after they have been administered, suggesting they might lead to long-term control of the virus. This work has helped establish a new paradigm for developing vaccines and therapies for infectious diseases. This paradigm has been extended to other viruses such as hepatitis B and flaviviruses.

In response to the COVID-19 outbreak, Nussenzweig has extended this research to SARS-CoV-2 and is working to isolate and characterize highly potent neutralizing antibodies from patients who have recovered from the disease.

A second focus of Nussenzweig's lab is on dendritic cells, which elicit adaptive immune responses by taking up antigens and presenting them to lymphocytes. Current studies focus on outlining the pathway of human dendritic cell development and differentiation.

Nussenzweig's experiments are consistent with the notion that self-antigens taken up by dendritic cells induce tolerance, whereas antigens taken up in the context of activation stimuli, such as those found during inflammation or tissue destruction, induce prolonged T cell activation. During inflammation or infection, dendritic cells present self-antigens simultaneously with non-self-antigens. By establishing tolerance to self-antigens before challenge with pathogens, dendritic cells can focus the adaptive immune system entirely on the pathogen, thereby avoiding autoimmunity. The ability to target antigens to dendritic cells and control their function in vivo has significant implications for the development of vaccines and therapies for autoimmunity. Recently, the lab defined distinct progenitor lineages for classical spleen dendritic cells, plasmacytoid dendritic cells, and monocytes, a step toward antigen-specific targeting.

EDUCATION

B.A., 1975
New York University
Ph.D., 1981
The Rockefeller University
M.D., 1982
New York University School of Medicine

MEDICAL TRAINING

Internship and Residency in medicine, 1982–1985
Fellowship in infectious diseases, 1984–1985
Massachusetts General Hospital

POSTDOC

Harvard Medical School, 1986–1989

POSITIONS

Assistant Professor, 1990–1994
Associate Professor, 1994–1996
Professor, 1996–
Director, Christopher Browne Center for Immunology and Immune Diseases, 2011–
Co-director for Immunology, Stavros Niarchos Foundation Institute for Global Infectious Disease Research, 2023–
The Rockefeller University
Senior Physician, 1996–
The Rockefeller University Hospital
Assistant Investigator, 1990–1995
Associate Investigator, 1995–1999
Investigator, 1999–
Howard Hughes Medical Institute

AWARDS

Meritorious Career Award, American Association of Immunologists–Huang Foundation, 2004
Lee C. Howley Sr. Prize for Arthritis Research, 2008
Brazilian Diaspora Award, 2015
Rabbi Shai Shacknai Memorial Prize in Immunology and Cancer Research, 2016
Robert Koch Award, 2016
AAI-BioLegend Herzenberg Award, 2017
Sanofi-Institut Pasteur Award, 2017
Harrington Prize for Innovation in Medicine, 2022

HONORARY SOCIETIES

National Academy of Sciences
National Academy of Medicine
American Academy of Arts and Sciences
Brazilian Academy of Sciences

SELECTED PUBLICATIONS

MacLean, A. J. et al. Affinity maturation of antibody responses is mediated by plasma cell proliferation. *Science*, eadr6896 (2024).
Schaefer-Babajew, D. et al. Antibody feedback regulates immune memory after SARS-CoV-2 mRNA vaccination. *Nature* 613, 735–742 (2023).
Muecksch, F. et al. Increased memory B cell potency and breadth after a SARS-CoV-2 mRNA boost. *Nature* 607, 128–134 (2022).
Gaebler, C. et al. Prolonged viral suppression with anti-HIV-1 antibody therapy. *Nature* 606, 368–374 (2022).
Merkenschlager, J. et al. Dynamic regulation of TFH selection during the germinal centre reaction. *Nature* 591, 458–463 (2021).