

Timeline of Immunology

Sources: Wikipedia, http://en.wikipedia.org/wiki/Timeline_of_immunology; Immunology History IV, <http://www.keratin.com/am/am004.shtml>; Stewart Sell and Scott L. Rodkey, A short history of Immunopathology.

- 3000 B.C.E. - Fever (Mesopotamia)
- 2000 B.C.E. - Recognition of "adaptive" protection against disease (Egypt, China)
- 400 B.C.E. - Anatomic identification of organs (Hippocrates)
- 80 B.C.E. - Acquired resistance to poisons (Mithridate Eupator, King of Pontus)
- 25 - Four cardinal signs of inflammation (Celsus)
- 1000 - "Snuff" variolation for smallpox (Sung Dynasty, China)
- 1590 - Bursa of birds described (Fabricius)
- 1690 - Lymphoid tissue identified in small intestine (Peyer)
- 1718 - [Lady Mary Wortley Montagu](#), the wife of the British ambassador to Constantinople, observed the positive effects of [variolation](#) on the native population and had the technique performed on her own children.
- 1798 - First demonstration of vaccination [smallpox vaccination](#) ([Edward Jenner](#))
- 1837 - First description of the role of microbes in putrefaction and fermentation ([Theodore Schwann](#))
- 1838 - Confirmation of the role of yeast in fermentation of sugar to alcohol ([Charles Cagniard-Latour](#))
- 1840 - First "modern" proposal of the germ theory of disease ([Jakob Henle](#))
- 1850 - Demonstration of the contagious nature of puerperal fever (childbed fever) ([Ignaz Semmelweis](#))
- 1855 - Tuberculous granulomas identified (Rokitansky)
- 1868 - Langhans Giant Cells identified (Langhans)
- 1857-1870 - Confirmation of the role of microbes in fermentation ([Louis Pasteur](#))
- 1862 - [phagocytosis](#) ([Ernst Haeckel](#))
- 1867 - First aseptic practice in surgery using carbolic acid ([Joseph Lister](#))
- 1876 - First demonstration that microbes can cause disease-anthrax ([Robert Koch](#))
- 1877 - [Mast cells](#) ([Paul Ehrlich](#))
- 1878 - Confirmation and popularization of the germ theory of disease ([Louis Pasteur](#))
- 1880 - Birth of Cellular Pathology (Virchow)
- 1880 - 1881 - Theory that bacterial virulence could be attenuated by culture in vitro and used as vaccines. Proposed that live attenuated microbes produced immunity by depleting host of vital trace nutrients. Used to make chicken cholera and anthrax "vaccines" ([Louis Pasteur](#))
- 1883 - 1905 - Cellular theory of immunity via phagocytosis by macrophages and microphages (polymorhonuclear leukocytes) ([Elie Metchnikoff](#))
- 1885 - Introduction of concept of a "therapeutic vaccination". First report of a live "attenuated" vaccine for rabies ([Louis Pasteur](#))
- 1887 - Anti-rattlesnake venom discovered (Sewall)
- 1888 - Identification of bacterial toxins (diphtheria bacillus) ([Pierre Roux](#) and [Alexandre Yersin](#))

- [1888](#) - Bactericidal action of blood ([George Nuttall](#))
- [1890](#) - Demonstration of antibody activity against diphtheria and tetanus toxins. Beginning of humoral theory of immunity. ([Emil von Behring](#)) and ([Shibasaburo Kitasato](#)). Attempt to cure tetanus with passive immunotherapy (Behring)
- [1891](#) - Demonstration of cutaneous (delayed type) hypersensitivity ([Robert Koch](#))
- [1893](#) - Use of live bacteria and bacterial lysates to treat tumors-"Coley's Toxins" ([William B. Coley](#))
- [1894](#) - Bacteriolysis ([Richard Pfeiffer](#))
- [1896](#) - An antibacterial, heat-labile serum component ([complement](#)) is described ([Jules Bordet](#))
- [1900](#) - [Antibody](#) formation theory "side chain theory" "horror autotoxicus" ([Paul Ehrlich](#))
- [1901](#) - [blood groups](#) ([Karl Landsteiner](#))
- 1901-8 Carl Jensen & Leo Loeb, Transplantable tumors
- [1902](#) - Immediate hypersensitivity [anaphylaxis](#) ([Paul Portier](#)) and ([Charles Richet](#))
- 1902 Paul Portier & Charles Richet, Anaphylaxis
- [1903](#) - Intermediate hypersensitivity, the "Arthus reaction" ([Maurice Arthus](#))
- [1903](#) - [Opsonization](#) (Almroth Wright & Stewart Douglas)
- [1905](#) - "Serum sickness" [allergy](#) ([Clemens von Pirquet](#) and ([Bela Schick](#))
- 1905 - successful organ transplantation (Correl and Guthrie)
- 1906 - Clemens von Pirquet, coined word "allergy"
- 1907 - Svante Arrhenius, coined the term immunochemistry
- 1910 - Emil von Dungern, & Ludwik Hirszfeld, Inheritance of ABO blood groups
- 1910 - Peyton Rous, Viral immunology theory
- [1911](#) - 2nd demonstration of filterable agent that caused tumors ([Peyton Rous](#))
- 1914 - Clarence Little, Genetics theory of tumor transplantation
- 1915-20 - Leonell Strong & Clarence Little, Inbred mouse strains
- [1917](#) - [hapten](#) ([Karl Landsteiner](#))
- [1921](#) - Cutaneous allergic reactions ([Carl Prausnitz](#) and [Heinz Küstner](#))
- 1922 - Fleming found lysozyme and penicillin
- [1924](#) - [Reticuloendothelial system](#) (Aschoff)
- 1925 - Chemical mediators of inflammation (Lewis)
- 1926 - Lloyd Felton & GH Bailey, Isolation of pure antibody preparation
- 1935 Quantitative precipitin reaction (Heidelberger)
- 1936 - Peter Gorer, Identification of the H-2 antigen in mice
- 1938 - Gammaglobulin identified (Tiselius and Kabat)
- [1938](#) - [Antigen](#)-Antibody binding hypothesis ([John Marrack](#))
- [1940](#) - Identification of the [Rh antigens](#) ([Karl Landsteiner](#) and [Alexander Weiner](#))
- 1941 - Hemolytic disease of the newborn (Rh antigens) (Levine)
- 1941 - Albert Coons, Immunofluorescence technique
- [1942](#) - [Anaphylaxis](#) ([Karl Landsteiner](#) and [Merill Chase](#))
- [1942](#) - [Adjuvants](#) ([Jules Freund](#) and [Katherine McDermott](#))
- [1944](#) - hypothesis of [allograft](#) rejection (Peter Medawar)
- 1945 - Passive transfer of cell mediated immunity (Chase)
- [1946](#) - identification of mouse [MHC](#) (H2) by [George Snell](#) and [Peter A. Gorer](#)
- 1947 - Twins do not demonstrate transplant rejection (Owen)
- [1948](#) - antibody production in plasma [B cells](#) (Astrid Fagraeus)

- [1949](#) - growth of polio virus in tissue culture, neutralization with immune sera, and demonstration of attenuation of neurovirulence with repetitive passage ([John Enders](#)) and ([Thomas Weller](#)) and ([Frederick Robbins](#))
- [1949](#) - immunological tolerance hypothesis (Macfarlane Burnet & Frank Fenner)
- 1950 - Richard Gershon and K Kondo, Discovery of suppressor T cells
- 1952 - Ogden and Bruton, discovery of agammaglobulinemia (antibody immunodeficiency)
- [1951](#) - vaccine against [yellow fever](#)
- [1953](#) - [Graft-versus-host disease](#) (Morton Simonsen and WJ Dempster)
- [1953](#) - [immunological tolerance](#) hypothesis (Rupert Billingham, Leslie Brent, Peter Medwar, & Milan Hasek)
- 1953 - James Riley & Geoffrey West, Discovery of histamine in mast cells
- 1955-1959 - Niels Jerne, David Talmage, Macfarlane Burnet, Clonal selection theory
- [1957](#) - [Clonal selection theory](#) ([Frank Macfarlane Burnet](#))
- [1957](#) - Discovery of [interferon](#) (Alick Isaacs & Jean Lindermann)
- 1957 Ernest Witebsky et al., Induction of autoimmunity in animals
- [1958-1962](#) - Discovery of human leukocyte antigens ([Jean Dausset](#) and Snell)
- [1959-1962](#) - Discovery of antibody structure (independently elucidated by [Gerald Edelman](#) and [Rodney Porter](#))
- [1959](#) - Discovery of [lymphocyte](#) circulation ([James Gowans](#))
- [1960](#) - Discovery of lymphocyte "blastogenic transformation" and proliferation in response to mitogenic lectins-phytohemagglutinin (PHA) ([Peter Nowell](#))
- [1961-1962](#) Discovery of [thymus](#) involvement in [cellular immunity](#) ([Jacques Miller](#))
- [1961](#)- Demonstration that glucocorticoids inhibit PHA-induced lymphocyte proliferation ([Peter Nowell](#))
- 1962 - Classification of immune mechanisms (Gell and Coombs)
- [1963](#) - Development of the plaque assay for the enumeration of antibody-forming cells in vitro ([Niels Jerne](#)) ([Albert Nordin](#))
- 1963 - Jaques Oudin et al., antibody idiotypes [1964-1968](#) T and B cell cooperation in immune response (Anthony Davis)
- 1964 - Mixed lymphocyte reaction (Bain, Vas, et al.)
- [1965](#) - Discovery of the first lymphocyte mitogenic activity, "blastogenic factor" ([Shinpei Kamakura](#)) and ([Louis Lowenstein](#)) ([J. Gordon](#)) and ([L.D. MacLean](#))
- [1965](#) - Discovery of "immune interferon" (gamma interferon) ([E.F. Wheelock](#))
- [1965](#) - Secretory [immunoglobulins](#) (Thomas Tomasi et al.)
- 1966 - Identification of T and B cells (Claman)
- [1967](#) - Identification of [IgE](#) as the reaginic antibody ([Kimishige Ishizaka](#))
- [1968](#) - Passenger leukocytes identified as significant immunogens in allograft rejection ([William L. Elkins](#) and [Ronald D. Guttman](#))
- 1968 - Accessory cell role in immune response (Mosier)
- [1969](#) - The lymphocyte cytotoxicity Cr51 release assay ([Theodore Brunner](#)) and ([Jean-Charles Cerottini](#))
- 1969 - Immune response genes (Benacerraf and McDevitt)
- 1971 - Donald Bailey, Recombinant inbred mouse strains
- [1971](#) - Peter Perlmann and [Eva Engvall](#) at [Stockholm University](#) invented [ELISA](#)
- [1972](#) - Structure of the antibody molecule
- 1974 - Network theory for antibody control on immune response (Niels K. Jerne)

- [1974](#) - T-cell restriction to [major histocompatibility complex](#) ([Rolf Zinkernagel](#) and [Peter Doherty](#))
- [1975](#) - Generation of the first [monoclonal antibodies](#) ([Georges Köhler](#)) and ([César Milstein](#))
- 1975 - Identification of natural killer cells (Kieśling, et al.)
- [1976](#) - Identification of somatic recombination of [immunoglobulin](#) genes ([Susumu Tonegawa](#))
- [1979](#) - Generation of the first monoclonal T cells ([Kendall A. Smith](#))
- 1980 - Immunoglobulin structure (Kabat)
- [1980-1983](#) - Discovery and characterization of the first interleukins, 1 and 2 [IL-1](#) [IL-2](#) ([Kendall A. Smith](#))
- [1981](#) - Discovery of the IL-2 receptor [IL2R](#) ([Kendall A. Smith](#))
- 1981 - Appearance of AIDS on a global scale
- [1983](#) - Discovery of the T cell antigen receptor [TCR](#) ([Ellis Reinherz](#)) ([Philippa Marrack](#)) and ([John Kappler](#)) ([James Allison](#))
- [1983](#) - Discovery of [HIV](#) ([Luc Montagnier](#))
- [1984](#) - The first single cell analysis of lymphocyte proliferation ([Doreen Cantrell](#)) and ([Kendall A. Smith](#))
- 1984 - Robert Good, Failed treatment of severe combined immunodeficiency (SCID, David the bubble boy) by bone marrow grafting
- 1984-1987 - Identification of genes for the T cell receptor (Leroy Hood, et al.; Hedrick Davis, Mak)
- 1985 Tonegawa, Hood et al., Identification of immunoglobulin genes, somatic generation of Ig variable regions
- 1985-onwards - Rapid identification of genes for immune cells, antibodies, cytokines and other immunological structures
- 1987- Structure of MHC I defined (Wiley and Strominger)
- [1986](#) - [Hepatitis B](#) vaccine produced by [genetic engineering](#)
- [1986](#) - Th1 vs Th2 model of [T helper cell](#) function ([Timothy Mosmann](#))
- [1988](#) - Discovery of biochemical initiators of T-cell activation: CD4- and CD8-p56lck complexes ([Christopher E. Rudd](#))
- 1989 - Catalytic antibody cleavage of peptide bonds (Sudhir Paul)
- 1990 - Yamamoto et al., Molecular differences between the genes for blood groups O and A and between those for A and B
- [1990](#) - [Gene therapy](#) for [SCID](#) using cultured T cells
- 1991- Role of peptide for MHC Class II structure (Sadegh-Nasseri & Germain)
- 1992 - Hepatitis A vaccine developed
- 1993 - NIH team, Treatment of SCID using genetically altered umbilical cord cells
- [1994](#) - 'Danger' model of [immunological tolerance](#) ([Polly Matzinger](#))
- [1995](#) - Regulatory T cells ([Shimon Sakaguchi](#))
- [1996-1998](#) - Identification of [Toll-like receptors](#)
- [2001](#) - Discovery of [FOXP3](#) - the gene directing [regulatory T cell](#) development
- [2005](#) - Development of [human papillomavirus](#) vaccine ([Ian Frazer](#))
- 2011 - Nobel Prize awarded to Bruce A. Beutler, Jules A. Hoffmann, and Ralph M. Steinman for landmark discoveries indicating TLRs are gatekeepers of innate immunity