Prof. David Baltimore
President Emeritus of Caltech; Judge Shirley Hufstedler Professor of Biology; Nobel laureate in Physiology or Medicine, 1975

Most important awards, prizes and academies

Awards: First recipient of the Gustave Stern Award in Virology (1970); Warren Triennial Prize from the Massachusetts General Hospital (1971); Eli Lilly and Co. Award in Microbiology and Immunology (1971); National Academy of Sciences' United States Steel Award in Molecular Biology (1974); Gairdner Foundation Annual Award (1974); Nobel Prize in Physiology or Medicine (1975); National Medal of Science (1999); Warren Alpert Foundation Prize (2000); American Medical Association Scientific Achievement Medal (2002), Einstein Medal from the Israel Academy of Sciences and Humanities (2004), Research!America Advocacy Award (2009), Gregor Mendel Award (2010), Hope Funds for Cancer Research Basic Science Award (2017). *Academies*: US National Academy of Sciences (1974); American Academy of Arts and Sciences (1974); Pontifical Academy of Sciences (1978); Chairman of the Board of Directors, American Association for the Advancement of Science (1980); Honorary Fellowship, American Medical Writers Association (1985); Foreign Member, The Royal Society, UK (1987); Honorary Membership, Alpha Omega Alpha Honor Medical Society (1987); Institute of Medicine (1988); Honorary Member, Japanese Biochemical Society (1991); Fellow, American Academy of Microbiology (1992); Member,

American Philosophical Society (1997); Foreign Associate Member, French Academy of Sciences (2000); Honorary Academician, Academia Sinica (2008); Honorary Fellow, Riken (2011); Fellow, American Association for Cancer Research (2013); Fellow, National Academy of Inventors (2014); Distinguished Fellow, American Association of Immunologists (2019).

Summary of scientific research

Our laboratory is involved in two major research thrusts. One is basic investigation of the development and functioning of the mammalian immune system. The other is Engineering Immunity: translational studies using viral vectors to carry new genes into immune cells to increase the range of pathogens effectively fought by the immune system and to make the immune system resist cancer growth more effectively.

Our basic studies have two directions: to understand the remarkable range of activity of the NF-kB transcription factor and to understand the normal and pathologic functions of microRNAS. NF-kB activates perhaps 1000 genes in response to a wide range of stimuli. It has different physiologic roles in different cells. How one factor can be so varied in its activity is the puzzle that has interested us for many years and that we have studied at many different levels.

MicroRNAs are small (~22 nucleotide) RNAs that regulate the amount of protein made by a particular messenger RNA and that therefore provide a level of fine control over gene expression. We have been interested in their role in hematopoietic cell development and function. We have recently concentrated on microRNAs that modulate myeloid cell development. Most interesting is miR-146a, which is a feedback regulator of NF-kB activation. A mouse knockout of the gene encoding miR-146a is normal at birth but slowly develops myeloid hyperproliferation and, ultimately, cancer. We have traced the earliest events to dysregulation of hematopoietic stem cells suggesting that a normal function of miR-146a is to be a guardian of hematopoietic stem cell health and longevity.

Our translational work centers on using gene transfer methods to reprogram the immune system. We first showed that we could design a retrovirus vector able to express cDNAs encoding both chains of the T cell receptor (TCR) protein. When mouse hematopoietic stem cells are transduced with the vector and then inoculated into irradiated mice, many of the resulting T cells express the TCR encoded by the vector. When the TCR is able to recognize specific peptides from a tumor antigen, the animal can reject tumors carrying the antigen. We are extending these studies to TCRs that react with human tumor antigens with the goal of developing a human therapy. We have also developed therapies based on transfer of lentiviral vectors that encode small, interfering RNAs and vectors that carry antigen genes into dendritic cells. Because we found it difficult to make lentiviral vectors that would reprogram B cells to make specific antibodies, we switched to adeno-associated virus (AAV) vectors carrying genes that encode antibodies and have used them to reprogram muscle cells in mice to make anti-HIV and anti-influenza virus antibodies. Four programs that have emerged from these laboratory efforts are presently in clinical development,

two in start-up companies and two in academic collaborations. We are also developing new programs that have clinical goals.

Main publications

Zarnegar B., He J.Q., Oganesyan G., Hoffmann A., Baltimore D., Cheng G. (2004) Unique CD40-mediated biological program in B cell activation requires both type 1 and type 2 NF-kappaB activation pathways, *Proc. Natl. Acad. Sci. USA* 101, 8108-13; Schatz D.G., Baltimore D. (2004) Uncovering the V(D)J recombinase, *Cell* 116, S103-6, 2 p following S106; Lu W., Yamamoto V., Ortega B., Baltimore D. (2004) Mammalian ryk is a wnt coreceptor required for stimulation of neurite outgrowth, *Cell* 119, 97-108; Leung T.H., Hoffmann A., Baltimore D. (2004) One nucleotide in a kappaB site can determine cofactor specificity for NF-kappaB dimers, *Cell* 118, 453-64; Baltimore D. (2004) Science and the Bush Administration. *Science* 305, 1873; Qin XF, An DS, Chen IS, Baltimore D (2003) Inhibiting HIV-1 infection in human T cells by lentiviral-mediated delivery of small interfering RNA against CCR5, *Proc. Natl. Acad. Sci. USA* 100, 183-8; Porteus M.H., Baltimore D. (2003) Chimeric nucleases stimulate gene targeting in human cells, *Science* 300, 763; Porteus M.H., Cathomen T., Weitzman M.D., Baltimore D. (2003) Efficient gene targeting mediated by adeno-associated virus and DNA double-strand breaks, *Mol. Cell. Biol.* 23, 3558-65; Meffert M.K., Chang J.M., Wiltgen B.J., Fanselow M.S., Baltimore D. (2003) NF-kappa B functions in synaptic signaling and behavior, *Nat. Neurosci.* 6, 1072-8; Klausner R.D., Fauci A.S., *et al.* (2003) Medicine. The need for a global HIV vaccine enterprise,*Science* 300, 2036-9; Hoffmann A., Leung T.H., Baltimore D. (2003) Genetic analysis of NF-kappaB/Rel transcription factors defines functional specificities, *Embo J.* 22, 5530-9; Brown E.J., Baltimore D. (2003) Essential and dispensable roles of ATR in cell cycle arrest and genome maintenance, *Genes Dev.* 17, 615-28; Antov A., Yang L., Vig M., Baltimore D., Van Parijs L. (2003) Essential role for STAT5 signaling in CD25+CD4+ regulatory T cell homeostasis and the maintenance of self-tolerance, *J. Immunol.* 171, 3435-41.