
BIOGRAPHICAL SKETCH

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| NAME Michael J. Lenardo | POSITION TITLE Chief, Molecular Development of the Immune System Section, LI, DIR, NIAID |
| eRA COMMONS USER NAME | |

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

| INSTITUTION AND LOCATION | DEGREE (if applicable) | YEAR(s) | FIELD OF STUDY |
|---|---------------------------|-----------|-------------------|
| The Johns Hopkins University, Baltimore, MD | B.A. | 1973-1977 | National Sciences |
| Washington Univ. School of Med., St. Louis, MO | M.D. | 1977-1981 | Medicine |
| MIT-Whitehead Institute, Boston, MA (post-doc) mentor: Dr. David Baltimore | | 1985-1989 | Immunology |

A. Positions and Honors.

Positions

- 1985 - 1989: Postdoctoral Fellow MIT-Whitehead Institute, Advisor Dr. David Baltimore
- 1986 - 1988: Affiliate Staff-Dana Farber Cancer Inst., Harvard Med. School, Boston, MA
- 1989 - 1994: Investigator, Laboratory of Immunology, LI, DIR, NIAID
- 1995 - present: Senior Investigator (Tenured), Chief, Mol. Dev. of the Immune Sys Sect., LI, DIR, NIAID

Honors

• Awards

- 1982-1985: National Research Service Award
- 1985-1989: National Cancer Institute Clinical Investigator Award
- 1989-1993: Investigator Award in Immunology, Cancer Research Institute, New York, N.Y.
- 1993, 2009, 2011: U.S. Public Health Service, NIH Director's Award
- 1994: NIAID Recognition Plaque
- 1998: Merit Award for Research
- 1999: SanBio Lecture, Dutch Society of Immunology
- 2002: Pfizer Lecture, Institute for Clinical Research of Montreal
- 2002: Evans Lecture, Boston University
- 2003: Distinguished Immunologist Award, University of Iowa
- 2004: Life Visiting Fellow, Clare Hall College, University of Cambridge, UK
- 2005: Charles Gould Easton Lecture, University of Toronto
- 2006: Officer of the Most Excellent Order of the British Empire (O.B.E.)
Conferred by Queen Elizabeth II,
- 2007: Honorary Professor, Southwestern Medical University, Chongqing, China
- 2009: Fellow, American Association for the Advancement of Science
- 2011: Distinguished Alumni Award, Washington University School of Medicine

• Editorial Boards

- 1989-1995: Molecular and Cellular Biology
- 1994-present: Journal of Experimental Medicine
- 1998-2005: Executive Committee, European Journal of Immunology
- 2003-present: Board of Reviewing Editors, Science magazine

• Professional Societies

- 1981: Member, American Association for the Advancement of Science
- 1990: Member, American Society for Microbiology
- 1993: Member, American Association of Immunologists
- 1994: Member, Clinical Immunology Society
- 1995: Fellow, Molecular Medicine Society
- 2000: Member, British Society of Immunology
- 2005: Member, American Association of Physicians

B. Selected peer-reviewed publications (in chronological order).

Lenardo, M.J., Pierce, J.W., and Baltimore, D.: Protein-binding motifs in immunoglobulin enhancers determine transcriptional activity and inducibility. **Science** 236: 1573-1577, 1987.

Lenardo, M.J., Staudt, L., Robbins, P., Kuang, A., Mulligan, R., and Baltimore, D.: Repression of the immunoglobulin heavy chain enhancer in mouse teratocarcinoma cells is associated with the presence of a novel octamer binding factor. **Science** 243: 544-546, 1989.

(NOTE: This paper reports the discovery of the Oct 3/4 stem cell transcription factor used for iPS production).

Lenardo, M.J., Fan, C.-M., Maniatis, T., and Baltimore, D.: Involvement of the transcription factor NF- κ B in 8-interferon gene regulation reveals its role as a widely inducible mediator of signal transduction. **Cell** 57: 287-294, 1989

Lenardo, M.J., and Baltimore, D.: NF- κ B - a paradigm for inducible and tissue-specific gene expression. **Cell** 58: 227-229, 1989.

Lenardo, M.J.: Interleukin-2 programs mature alpha beta T cells for apoptosis. **Nature** 353: 858-861, 1991.

Zuniga-Pflucker, J.C., Schwartz, H., and Lenardo, M.J.: Gene transcription in differentiating immature TCR^{neg} thymocytes resembles antigen-activated mature T cells. **J. Exp. Med.** 178: 1139-1150, 1993.

Critchfield, J.M., Racke, M.K., Zuniga-Pflucker, J.C., Cannella, B., Raine, C.S., Goverman, J., and Lenardo, M.J.: T cell deletion in high antigen dose therapy of autoimmune encephalomyelitis. **Science** 263: 1139-1143, 1994.

Zuniga-Pflucker, J.C., Jiang, D., Schwartzberg, P., and Lenardo, M.J.: Sublethal γ -radiation induces differentiation of CD4⁻/CD8⁻ into CD4⁺/CD8⁺ thymocytes without TCR- α rearrangement in RAG-2^{-/-} mice. **J. Exp. Med.** 180: 1517-1522, 1994.

Zuniga-Pflucker, J.C., Jiang, D., and Lenardo, M.J.: Requirement of TNF α and IL-1 α in mouse thymocyte commitment and differentiation. **Science** 268: 1906-1909, 1995.

Zheng, L., Fisher, G., Miller, R.E., Peschon, J., Lynch, D.H., and Lenardo, M.J.: Induction of apoptosis in mature T cells by tumor necrosis factor. **Nature** 377: 348-351, 1995.

Combadiere, B., Freedman, M., Chen, L., Shores, E.W., Love, P., and Lenardo, M.J.: Qualitative and quantitative contributions of the T cell receptor ζ chain to mature T cell apoptosis. **J. Exp. Med.** 183: 2109-2117, 1996.

Jiang, D., Lenardo, M.J., and Zuniga-Pflucker, J.C.: p53 prevents maturation of the CD4⁺/CD8⁺ stage of thymocyte differentiation in the absence of TCR rearrangement. **J. Exp. Med.** 183: 1923-1928, 1996.

Lenardo, M.J.: Fas and the art of lymphocyte maintenance. **J. Exp. Med.** 183: 721-724, 1996.

Wang, J. and Lenardo, M.J.: Essential lymphocyte function associated 1 (LFA-1): Intercellular adhesion molecule interactions for T cell-mediated B cell apoptosis by Fas/APO-1/CD95. **J. Exp. Med.** 186: 1171-1176, 1997.

Combadiere, B., Reis e Sousa, C., Trageser, C., Kim, C.R., and Lenardo, M.J.: Differential TCR signaling regulates apoptosis and immunopathology during antigen responses in vivo. **Immunity** 9: 305-313, 1998.

Siegel, R.M., Martin, D.A., Zheng, L., Ng, S.Y., Bertin, J., Cohen, J., and Lenardo, M.J.: The death-effector filament: a novel cytoplasmic protein assembly that recruits caspases and triggers apoptosis. **J. Cell Biol.** 141: 1243-1253, 1998.

Eberstadt, M., Huang, B., Chen, Z., Meadows, R.P., Ng, S-C., Zheng, L., Lenardo, M.J., and Fesik, S.W.: NMR structure and mutagenesis of the FADD (MORT1) death effector domain. **Nature** 392: 941-945, 1998.

Lenardo, M., Chan, F.K-M., Hornung, F., McFarland, H., Siegel, R., Wang, J., and Zheng, L.: Mature T lymphocyte apoptosis – Immune regulation in a dynamic and unpredictable antigenic environment. **Ann. Rev. Immunol.** 17:221-253, 1999.

Schaeffer, E.M., Debnath, J., Yap, G., McVicar, D., Liao, X.C., Littman, D.R., Sher, A., Varmus, H.E., Lenardo, M.J., and Schwartzberg, P.L.: Requirement for tec kinases rik and itk in T cell receptor signaling and immunity. **Science** 284: 638-641, 1999.

Wang, J., Zheng, L., Lobito, A., Chan, F.K., Dale, J., Sneller, M., Yao, Y., Puck, J.M., Straus, S.E., and Lenardo, M.J.: Inherited human Caspase 10 mutations underlie defective lymphocyte and dendritic cell apoptosis in autoimmune lymphoproliferative syndrome type II. **Cell** 98: 47-58, 1999.

Chan, F. K., Chun, H. J., Zheng, L., Siegel, R. M., Bui, K. L., and Lenardo, M. J.: A domain in TNF receptors that mediates ligand-independent receptor assembly and signaling. **Science** 288: 2351-2354, 2000.

Siegel, R. M., Frederiksen, J. K., Zacharias, D. A., Chan, F. K., Johnson, M., Lynch, D., Tsien, R. Y., and Lenardo, M. J.: Fas preassociation required for apoptosis signaling and dominant inhibition by pathogenic mutations. **Science** 288: 2354-2357, 2000.

Siegel, R. M., Chan, F. K-M., Chun, H. J., and Lenardo, M. J.: The multifaceted roll of Fas signaling in immune cell homeostasis and autoimmunity. **Nature Immunol.** 1: 469-474, 2000.

Locksley, R.M., Killeen, N., and Lenardo, M.J.: The TNF and TNF-receptor superfamilies: Integrating mammalian biology. **Cell** 104: 487-501, 2001.

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Tibbetts, M., Zheng, L., and Lenardo, M. J. The death effector domain protein family: regulators of cellular homeostasis. **Nat. Immunol.** 4: 404-409, 2003.

Yu, L., Alva, A., Su, H., Dutt, P., Freundt, E., Welsh, S., Baehrecke, E. H., and Lenardo, M. J.: Regulation of an ATG7-beclin 1 program of autophagic cell death by caspase-8. **Science** 304: 1500-1502, 2004.

Su, H., Bidere, N., Zheng, L., Cubre, A., Sakai, K., Dale, J., Salmena, L., Hakem, R., Straus, S., and Lenardo, M.: Requirement for caspase-8 in NF- κ B activation by Antigen receptor. **Science** 307: 1465-1468, 2005.

Deng, G-M., Zheng, L., Chan, F. K-M., and Lenardo, M.: Amelioration of inflammatory arthritis by targeting the pre-ligand assembly domain (PLAD) of tumor necrosis factor receptors. **Nat. Med.** 11: 1066-1072, 2005.
Yang, J. K., Wang, L., Zheng, L., Wan, F. Ahmed, M., Lenardo, M. J., and Wu. H.: Crystal structure of a MC159 reveals molecular mechanism of DISC assembly and FLIP inhibition. **Mol. Cell** 20: 939-949, 2005.

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Wan F, Lenardo MJ. Specification of DNA binding activity of NF-kappaB proteins. **Cold Spring Harb Perspec Biol** 2009 Oct; 1(4): a00067.

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Yu, L., McPhee, C.K., Zheng, L., Mardones, G. A., Rong, Y., Peng, J., Mi, N., Zhao, Y., Liu, Z., Wan, F., Hailey, D. W., Oorschot, V., Klumperman, J., Baehrecke, E. H., and Lenardo, M. J.: Termination of Autophagy and reformation of lysosomes regulated by mTOR. **Nature** 465: 942-946, 2010.

Li FY, Chaigne-Delalande B., Kanellopoulou C., Davis J.C. Matthews H.F., Douek D.C., Cohen J.I., Uzel G., Su H.C., Lenardo M.J.: Second messenger role for Mg²⁺ revealed by human T-cell immunodeficiency. **Nature**, 2011 Jul 27;475(7357):471-6. doi: 10.1038/nature10246.

Total publication: 209
