**ALFRED L.M. BOTHWELL**

**CURRICULUM VITAE**

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**PLACE OF BIRTH:** Springfield, Missouri

**Education:**

1967-1971 Washington University, St. Louis, Missouri

A.B. cum laude in Biology, 1971

1971-1975 Yale University, New Haven, CT

Ph.D. in Biology, 1975

Mentor: Sidney Altman, Nobel laureate

**Positions Held:**

1975-1976 Postdoctoral Fellow, Cold Spring Harbor Laboratory

Cold Spring Harbor, New York

Mentor: Joe Sambrook

1976-1982 Postdoctoral Fellow, Center for Cancer Research

M. I. T., Cambridge, Massachusetts

Mentor: David Baltimore, Nobel laureate

1982-1988 Assistant Professor, Department of Pathology

1988-Date Member, Comprehensive Cancer Center

Yale Medical School, New Haven, CT

1988-2001 Associate Professor

2001-Date Professor

Dept. of Immunobiology

Yale Medical School, New Haven, CT

**HONORS AND AWARDS:**

1975-1978 Jane Coffin Childs Postdoctoral Fellowship

1978-1981 Individual National Research Service Award

1981-1982 Medical Foundation Postdoctoral Fellowship

**University SERVICE:**

Director of Graduate Studies for Immunobiology, 1986-1989; 2003 - present

President's Council on Priorities and Planning for Yale University, 1989-1990

Dean's Council on Priorities and Planning for Yale Medical School, 1989-1992

Funds and Fellowship Committee, 1989-1992; 2001-2004

Medical School Appointments and Promotions Committee, 2005-2008

Yale University Radiation Safety Committee, 2005-2011

Director of Medical Studies for Immunobiology, 1992-1997

**Teaching Experience:**

Biology of the Immune System (IBio 430a/530a)

Advanced Graduate Seminars on Molecular Immunology (IBio 536a/b)

Advanced Immunobiology (Ibio 531b)

Fundamentals of Research (Ibio 601b)

Immunobiology for medical students (Immunobiology 103)

Instructor/Organizer, Cold Spring Harbor Summer Course, 1984-1987

Molecular Cloning of Eukaryotic Genes

Peking University, Beijing, China Spring semester 2010 (Immunity & Infection MCDB 108;

Autoimmunity & Cancer MCDB 110)

**Professional Societies:**

American Association of Immunologists, AAAS, New York Academy of Sciences

American Society for Microbiology, Society of Sigma Xi

**PUBLICATIONS:**

Publications 1-19 from Undergraduate work.

Physical Electroanalytic Chemistry

1. Roy, R.N. and Bothwell, A. (1970). Thermodynamics of hydrochloric acid in 8.03, 20.76, 44.04, 70.28 and 87.71 weight % 2-propanol-water mixtures from emf. measurements at 0, 15, 25 and 35°C. J. Chem. Eng. Data 15: 548-553.

2. Roy, R.N., Vernon, W., Gibbons, J.J. and Bothwell, A.L.M. (1971). Thermodynamics of hydrochloric acid in propylene carbonate-water mixtures from emf measurements between 5 and 45°C. J. Chem. Soc. (A): 3589-3592.

3. Roy, R.N. and Bothwell, A.L.M. (1971). Thermodynamic quantities of hydrochloric acid in isopropanol, 1,2-dimethoxyethane-water and tetrahydrofuran-water mixtures. J. Chem. Eng. Data 16: 347-351.

4. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1971). Standard potentials of the silver+silver chloride electrode from 5 to 45°C and the thermodynamic properties of hydrochloric acid in 95 mass per cent isopropanol. J. Chem. Therm. 3: 769-777.

5. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1971). Thermodynamics of hydrochloric acid glycerol-water mixtures from emf. measurements between 5 to 45°C. J. Electrochem. Soc. 118:1302-1306.

6. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1971). Thermodynamics of

hydrochloric acid in 95 weight per cent glycerol from emf. measurements at 5 to 45°C. J. Electroanal. Chem. 30: 335-343.

7. Roy, R.N., Vernon, W., Gibbons, J.J. and Bothwell, A.L.M. (1971).

Thermodynamics of hydrochloric acid in 1-propanol from emf measurements at 5 to 45°C. J. Chem. Therm. 3: 883-889.

8. Roy, R.N., Vernon, W., Gibbons, J.J. and Bothwell, A.L.M. (1971). Standard potentials of the silver-silver chloride electrode in t-butyl alcohol-water mixtures and the thermodynamics of solutions of hydrochloric acid at different temperatures. J. Chem. Soc. (A): 1242-1246.

9. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1971). Thermodynamic properties of hydrochloric acid in dimethylformamide-water mixtures at different temperatures. J. Chem. Soc. (B): 2320-2322.

10. Roy, R.N., Vernon, W., Bothwell, A.L.M. and Gibbons, J.J. (1972). Standard potentials of Ag-AgCl electrode and related thermodynamic quantities in dimethyl sulfoxide-water mixtures from 5 to 45°C. J. Electrochem Soc. 119: 694-698.

11. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1972). Thermodynamic studies of hydrochloric acid in propan-2-ol from electromotive force measurements between 5 and 45°C. J. Chem. Soc. Faraday Trans. I 68: 2047-2052.

12. Roy, R.N., Vernon, W., Gibbons, J.J. and Bothwell, A.L.M. (1972). Standard potential of the silver-silver chloride electrode and related thermodynamic quantities in glycerol at 5 to 45°C. J. Electroanal. Chem. 34: 101-107.

13. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1972). Standard potentials of the silver-silver chloride electrode in 95 wt-% 1-propanol and related thermodynamic functions. Electrochimica Acta 17: 5-14.

14. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1972). Standard electromotive force of silver-silver chloride electrode and related thermodynamic quantities in tert-butyl alcohol-water mixtures (2, 6, and 8 wt %) between 5-45°C. J. Chem. Eng. Data 17: 79-81.

15. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1972). The activity coefficient and related thermodynamic quantities of HCl in 5 wt-% 1-butanol. Electrochimica Acta 17: 1057-1063.

16. Roy, R.N., Bothwell, A.L.M., Gibbons, J.J. and Vernon, W. (1972). Standard potential of the Ag-AgCl electrode and related thermodynamic quantities in butan-1-ol at different temperatures. J. Chem. Soc. Dalton Trans. 530-533.

17. Roy, R.N., Vernon, W., Gibbons, J.J. and Bothwell, A.L.M. (1972). Medium effects and other thermodynamic quantities in 5 wt-% 2-methyl-1-propanol between 5 and 45°C. J. Electroanal. Chem. 34: 345-350.

18. Roy, R.N., Vernon, W. and Bothwell, A.L.M. (1973). Thermodynamics of hydrochloric acid in 1-propanol-water mixtures from emf measurements at different temperatures. Electrochimica Acta 18: 81-85.

Publication 20-25 from PhD work.

Biologic Studies: RNA Metabolism and Virology

19. Bothwell, A.L.M. and Apirion, D. (1971). Is RNase V a manifestation of RNase II? Biochem. Biophys. Res. Commun. 44: 844-851.

20. Altman, S., Bothwell, A.L.M. and Stark, B.C. (1974). Processing of E. coli tRNATyr precursor RNA in vitro. Brookhaven Symposium in Biology 26: 12-25.

21. Bothwell, A.L.M. and Altman, S. (1975). Partial purification of an endoribonuclease isolated from human KB cells. J. Biol. Chem. 250: 1451-1459.

22. Bothwell, A.L.M. and Altman, S. (1975). Characterization of ribonuclease NU cleavage sites in a bacteriophage 80-induced RNA. J. Biol. Chem. 250: 1460-1463.

23. Bothwell, A.L.M., Stark, B.C. and Altman, S. (1976). Ribonuclease P substrate specificity: cleavage of a bacteriophage 80-induced RNA. Proc. Nat. Acad. Sci. USA 73: 1912-1916.

24. Bothwell, A.L.M., Garber, R.L. and Altman, S. (1976). Nucleotide sequence and *in vitro* processing of a precursor molecule to *E. coli* 4.5S RNA J. Biol. Chem. 251: 7709-7716.

25. Koski, R.A., Bothwell, A.L.M. and Altman, S. (1976). Partial purification and characterization of a ribonuclease P-like activity from human KB cells. Cell 9: 101-116.

26. Fey, G., Lewis, J.B., Grodzicker, T. and Bothwell, A.L.M. (1979). Characterization of a fused protein specified by the Adenovirus Type 2-Simian Virus 40 hybrid Ad 2+ ND1dp2. J. Virol. 30: 201-217.

27. Jornvall, H., Akusjarvi, G., Alestrom, P. Petterson, U., Bahr-Lindstrom, H., Apella, E., Fowler, A.V., Bothwell, A.L.M. and Philipson, L. (1980). Correlation between protein and DNA analysis: Structure of the Adenovirus hexon protein. In: Methods in Peptide and Protein Sequence Analysis Chr. Birr, ed., Elsevier/North-Holland Biomedical Press, pp. 237-246.

Biologic Studies: Immunology

28. Alt, F.W., Enea, V., Bothwell, A.L.M. and Baltimore, D. (1979). Probes for specific mRNAs by subtractive hybridization: anomalous expression of immunoglobulin genes. In: Eukaryotic Gene Regulation, vol 14, ICN-UCLA Symposia on Molecular and Cell Biology, T. Maniatis, R. Axel and C.F. Fox (eds.), Academic Press, New York, pp. 407-419.

29. Alt, F.W., Enea, V., Bothwell, A.L.M. and Baltimore, D. (1980). Activity of multiple light chain genes in murine myeloma cells producing a single, functional light chain. Cell 21: 1-12.

30. Alt, F.W., Bothwell, A.L.M., Knapp, M., Siden, E., Mather, E., Koshland, M. and Baltimore, D. (1980). Synthesis of secreted and membrane-bound immunoglobulin Mu heavy chains is directed by mRNAs that differ at their 3' ends. Cell 20: 293-301. PMID 6771018.

31. Mather, E.L., Alt, F.W., Bothwell, A.L.M., Baltimore, D. and Koshland, M.E. (1981). Evidence that B cell differentiation to pentamer IgM secretion requires a signal for J chain gene transcription. Cell 23: 369-378. PMID 6781757.

32. Bothwell, A.L.M., Paskind, M., Reth, M., Imanishi-Kari, T., Rajewsky, K. and Baltimore, D. (1981). Heavy chain variable region contribution to the NPb family of antibodies: Somatic mutation evident in a 2a variable region. Cell 24: 625-637. PMID 6788376.

33. Bothwell, A.L.M., Paskind, M., Schwartz, R.C., Sonenshein, G.E., Gefter, M. and Baltimore, D. (1981). Dual expression of l genes in the MOPC-315 plasmacytoma. Nature 290: 65-67.

34. Schwartz, R.C., Sonenshein, G.E., Bothwell, A. and Gefter, M. (1981). Multiple expression of Ig  chain encoding RNA species in murine plasmacytoma cells. J. Immunol. 126: 2104-2108.

35. D'Eustachio, P., Bothwell, A.L.M., Takaro, T.K., Baltimore, D. and Ruddle, F.H. (1981). Chromosomal location of the structural genes encoding murine immunoglobulin  light chains. J. Exp. Med. 153: 793-800.

36. Miller, J., Bothwell, A.L.M. and Storb, U. (1981). Physical linkage of the constant region genes for immunoglobulins I and lIII. Proc. Nat. Acad. Sci. USA 78: 3829-3833.

37. Schreier, P.H., Bothwell, A.L.M., Mueller-Hill, B. and Baltimore, D. (1981). Multiple differences between the nucleic acid sequences of the IgG2aa and IgG2ab alleles of the mouse. Proc. Nat. Acad. Sci. USA 78: 4495-4499.

38. Zeelon, E., Bothwell, A.L.M., Kantor, F. and Schechter, I. (1981). An experimental approach to enumerate the genes coding for immunoglobulin variable regions. Nucl. Acids Res. 9: 3809-3820.

39. Reth, M., Bothwell, A.L.M. and Rajewsky, K. (1981). Structural properties of the hapten binding site and of idiotopes in the NPb antibody family. In: Immunoglobulin Idiotypes and their Expression, ICN-UCLA Symposia on Molecular and Cellular Biology, vol. XX C. Janeway, E.E. Sercarz, H. Wigzell and C.F. Fox (eds.) Academic Press, New York, pp 169-178.

40. Bothwell, A.L.M., Paskind, M., Reth, M., Imanishi-Kari, T., Rajewsky, K. and Baltimore, D. (1981). The origin of the NPb antibody family: Somatic mutation evident in a heavy chain variable region. In: Immunoglobulin Idiotypes and their Expression, ICN-UCLA Symposia on Molecular and Cellular Biology, vol. XX C. Janeway, E.E. Sercarz, H. Wigzell and C.F. Fox (eds.) Academic Press, New York, pp 111-121.

41. Bothwell, A.L.M., Paskind, M., Reth, M., Imanishi-Kari, T., Rajewsky, K. and Baltimore, D. (1982). Somatic variants of murine light chains. Nature 298: 380-382.

42. Loh, D.Y., Bothwell, A.L.M., White-Scharf. M.E., Imanishi-Kari, T. and Baltimore, D. (1983). Molecular basis of a mouse strain-specific anti-hapten response. Cell 33: 85-93.

43. Bothwell, A.L.M. (1983). Immunoglobulin structure and genetics. Enhancement, translocation, and behaviour of V genes. Immunol. Today 4: 315-316.

44. Bothwell, A.L.M. (1984). The genes encoding anti-NP antibodies in inbred strains of mice. In: The Biology of Idiotypes, M.I. Greene and A. Nisonoff (eds.) Plenum Publishing Corp., New York, pp 19-34.

45. Bothwell, A.L.M. (1984). Idiotypic Inheritance: Allelic relationships between immunoglobulin genes. Annales of Immunology, (Inst. Pasteur), Paris, 135C: 51-55.

46. Beaman, K.D., Ruddle, N.H., Bothwell, A.L.M. and Cone, R.E. (1984). Messenger RNA for an antigen-specific binding molecule from an antigen specific T cell Hybrid. Proc. Nat. Acad. Sci. USA 81: 1524-1528.

47. Maizels, N. and Bothwell, A. (1985). The T cell independent immune response to the hapten NP uses a large repertoire of heavy chain genes. Cell 43: 715-720.

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49. Dzierzak, E.A., Janeway, Jr., C.A., Richard, N. and Bothwell, A. (1986). Molecular characterization of antibodies bearing Id-460. I. The structure of two highly homologous VH genes used to produce idiotype positive immunoglobulins. J. Immunol. 136: 1864-1870.

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51. Krawinkel, U., Zoebelein, R. and Bothwell, A.L.M. (1986). Palindromic sequences are associated with sites of DNA breakage during gene conversion. Nucl. Acids Res. 9: 3871-3882.

52. LeClair, K.P., Palfree, R.G.E., Flood, P.M., Hammerling, U. and Bothwell, A. (1986). Isolation of a murine Ly-6 cDNA reveals a new multigene family. EMBO J. 5: 3227-3234.

53. Ballard, D.W. and Bothwell, A. (1986). Mutational analysis of the immunoglobulin heavy chain promoter region. Proc. Nat. Acad. Sci. USA 83: 9626-9630.

54. LeClair, K.P., Rabin, M., Nesbitt, M., Pratcheva, D., Ruddle, F.H., Palfree, R.G.E. and Bothwell, A. (1987). Murine Ly-6 multigene family is located on chromosome 15. Proc. Nat. Acad. Sci. USA 84: 1638-1642.

55. Palfree, R.G.E., LeClair, K.P., Bothwell, A. and Hammerling, U. (1987). cDNA characterization of an Ly-6.2 gene expressed in BW5147 tumor cells. Immunogenetics 26: 389-391.

56. Blier, P.R. and Bothwell, A. (1987). A limited number of B cell lineages generates the heterogeneity of a secondary immune response. J. Immunol. 139: 3996-4006.

57. Bothwell, A., Pace, P.E. and LeClair, K.P. (1988). Isolation and expression of an interferon responsive Ly-6C chromosomal gene. J. Immunol. 140: 2815-2820.

58. Maizels, N., Lau, J.C., Blier, P.R. and Bothwell, A. (1988). The T cell independent antigen, NP-ficoll, primes for a high affinity IgM anti-NP response. Mol. Immunol. 25:1277-1282.

59. Ballard, D.W., Philbrick, W.P. and Bothwell, A.L.M. (1988). Identification of a novel 9-kDa polypeptide from nuclear extracts: DNA-binding properties, primary structure and *in vitro* expression. J. Biol. Chem. 263: 8450-8457.

60. Blier, P.R. and Bothwell, A.L.M. (1988). The immune response to the hapten NP in C57BL/6 mice: Insights into the structure of the B cell repertoire. Immunol. Rev. 105: 27-43.

61. Marion, T.N., Bothwell, A.L.M., Briles, D.E. and Janeway, C.A., Jr. (1989). IgG anti-DNA autoantibodies within an individual autoimmune mouse are the products of clonal selection. J. Immunol. 142: 4269-4274.

62. Su, B. and Bothwell, A.L.M. (1989). Biosynthesis of a phosphatidylinositol-glycan linked membrane protein: signals for posttranslational processing of the Ly-6E antigen. Mol. Cell. Biol. 9: 3369-3376.

63. LeClair, K.P., Bridgett, M.M., Dumont, F.J. Palfree, R.G.E., Hammerling, U. and Bothwell, A.L.M. (1989). Kinetic analysis of Ly-6 gene induction in a T lymphoma by interferons and interleukin-1, and demonstration of Ly-6 inducibility in diverse cell types. Eur. J. Immunol. 19: 1233-1239.

64. Smith, R.G., Ballard, D.W., Blier, P.R., Pace, P.E., Bothwell, A.L.M., Herron, J.N., Edmundson, A.B. and Voss, Jr., E.W. (1989). Structural features of a murine monoclonal anti-ssDNA autoantibody. J. Indian. Inst. Sci. 69: 25-46.

65. Philbrick, W.M., Palfree, R.G.E., Maher, S., Bridgett, M.M., Sirlin, S. and Bothwell, A.L.M. (1990). The CD59 antigen is a structural homologue of murine Ly-6 antigens but lacks interferon inducibility. Eur. J. Immunol. 20: 87-92.

66. Bothwell, A.L.M., Yancopoulos, G.D. and Alt, F.W. (1990). Methods for cloning and analysis of eukaryotic genes. Jones and Bartlett Publishers, Boston, 324 pp.

67. Philbrick, W.M., Maher, S., Bridgett, M.M. and Bothwell, A.L.M. (1990). A recombination event in the 5' flanking region of the Ly-6C gene correlates with impaired expression in the NOD, NZB and ST strains of mice. EMBO J. 9: 2485-2492.

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69. Tao, W. and Bothwell, A.L.M. (1990). Formation and development of B cell lineages during a primary anti-hapten immune response. J. Immunol. 145:3216-3222.

70. Bothwell, A.L.M., Tao, W. and Blier, P.R. (1991). A model for the development of somatic variants in memory B cells. In: Somatic Hypermutation in V-regions. E.J. Steele, ed., CRC Press, Boca Raton, pp 55-67.

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81. Tao, W., Hardardottir, F. and Bothwell, A.L.M. (1993). Extensive somatic mutation in Ig heavy chain V genes in a late primary anti-hapten immune response. Mol. Immunol.30:593-602. PMID 8487778.

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84. Murray, A., Khodadoust, M.M., Maher, S.E., Pober, J.S. and Bothwell, A.L.M. (1994). Porcine aortic endothelial cells activate human T cells: Direct presentation of MHC antigens and costimulation by ligands for human CD2 and CD28. Immunity 1:57-63.

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98. Khodadoust, M.M., Khan, K.D., Park, E.-H. and Bothwell, A.L.M. (1998). Distinct regulatory mechanisms for interferon- (IFN-)and IFN- mediated induction of Ly-6E gene in B cells. Blood 92:2399-2409.

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**Patents:**

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