OLIVER SMITHIES

CURRICULUM VITAE AND PUBLICATION LIST

1. Personal Data

Name: Oliver Smithies

Address: CB #7525 Brinkhous-Bullitt Building
Department of Pathology and Laboratory Medicine
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina 27599-7525

Date of Birth: June 23, 1925

Place of Birth: Halifax, England

Citizenship: United States

Married: Nobuyo Maeda

2. Academic and Research Career

1943-1946 Brackenbury Scholar, Balliol College, Oxford University, England

1946 B.A. with First Class Honors in Physiology

1946-1952 Graduate work at Oxford University
M.A., D. Phil. (Oxon) in Biochemistry, 1951

1951-1953 Postdoctoral fellow in Physical Chemistry,
University of Wisconsin-Madison

1953-1960 Research Assistant and Associate at Connaught Medical
Research Laboratory, University of Toronto, Toronto, Canada

1960-1961 Assistant Professor of Genetics and Medical Genetics,
University of Wisconsin-Madison

1961-1963 Associate Professor of Genetics and Medical Genetics,
University of Wisconsin-Madison

1963 Professor of Genetics and Medical Genetics,
University of Wisconsin-Madison

1971 Leon J. Cole Professor of Genetics and Medical Genetics,
University of Wisconsin-Madison

1975 President, Genetics Society of America

1980 Hilldale Professor Genetics and Medical Genetics,
University of Wisconsin-Madison

1985-1990 Member of the National Advisory Medical Sciences Council
for the National Institutes of Health, U.S.

1988 to Present	Excellence Professor of Pathology and Laboratory Medicine, University of North Carolina at Chapel Hill

3. Scientific Honours

1942	Brackenbury, State and Theodore Williams Scholarships, Balliol College, Oxford University
1946	1st Class Honours, Final Honour School of Natural Science (Animal Physiology), B.A.
1947	Christopher Welch Scholarship in Biology and College War Memorial Studentship.
1951	Commonwealth Fund Fellowship
1957	Connaught research prize "for published research of exceptional merit."
1961	Markle Scholar
1964	American Society of Human Genetics William Allen Memorial Award "for outstanding work in human genetics, in recognition of development of starch gel electrophoresis and of important work on the heredity of the haptoglobins, transferrins, and gamma globulins."
1971	Elected member of the National Academy of Sciences
1974	Vice-President, Genetics Society of America
1975	President, Genetics Society of America
1978	Elected member of the American Academy of Arts and Sciences
1984	1984 Founders Award, Electrophoresis Society "For outstanding contributions to the field of electrophoresis in the biological sciences."
1984	Karl Landsteiner Memorial Award, American Association of Blood Banks. "For the development of zone electrophoresis using starch gels, the discovery of the genetic polymorphism of haptoglobin and the insight provided on the role of chromosomal rearrangement and gene duplication in the evolution of protein structure."
1985-1990	Member, National Advisory Medical Sciences Council, N.I.H.
1986	Elected, Fellow of the American Association for the Advancement of Science
1990	Gairdner Foundation International Award. "For the discovery, development and applicaton of gel electrophoresis methods that allow the separation and identification of specific proteins and nucleic acids."
1991	Honorary Doctorate of Science Degree from the University of Chicago "conferred on Oliver Smithies innovator of concepts and technology in the fields of protein biochemistry, immunogenetics, molecular evolution and molecular biology, who has generated ideas and tools and used them to arrive at solutions to important biological problems and whose study of homologous recombination has laid the foundation for the rational use of gene therapy to correct genetic defects, representative of the highest ideal of the actively engaged scientist, the honorary degree of Doctor of Science."

1993 Gairdner Foundation International Award. "For pioneering work in the use of homologous recombination to generate targeted mutations in the mouse."

1993 North Carolina Award in Science to recognize "notable accomplishments by North Carolina citizens in the fields of scholarship, research, the fine arts and public leadership."

1994 Alfred P. Sloan Award from the General Motors Cancer Research Foundation "for the most outstanding recent basic science contributions to cancer research."

1996 Ciba Award for Hypertension Research "for his groundbreaking work in the use of homologous recombination to insert altered genes into specified positions in the DNA of living cells and the application of this technique to transfer 'designer mutations' to living animals and to the study of high blood pressure and cardiovascular diseases."

1997 Bristol-Myers Squibb Award "for Distinguished Achievement in Cardiovascular/Metabolic Disease Research."

1998 Foreign Member of the Royal Society of London "for his contributions to advancing the knowledge of recombination events in humans, and for applying this knowledge to innovate gene targeting in mammalian cells."

1998 Association of American Medical Colleges Award for Distinguished Research in the Biomedical Sciences for "the landmark work that has made possible the only technology for directed mutagenesis in mammals."

1998 Research Achievement Award of the American Heart Association "for his extraordinary scientific accomplishments including innovative approaches in the modification of genes that have expanded the horizons of cardiovascular science and opened the door to improved treatments for heart and blood vessel diseases."

2000 Okamoto International Award of the Japanese Vascular Disease Research Foundation

2001 Albert Lasker Basic Medical Research Award “For the development of a powerful technology for manipulating the mouse genome with exquisite precision, which allows the creation of animal models of human disease.”

2002 Oliver Max Gardner Award

2002 Massry Prize for “Outstanding Contributions to Biomedical Sciences and the Advancement of Human Health.”

2003 Wolf Prize in Medicine

2003 National Institute of Medicine

2004 Honorary Doctorate of Science Degree from Duke University

2005 March of Dimes Prize

Dr. Smithies' recent work has been directed towards the targeted modification of specific genes in living animals. He and his collaborators have successfully used targeted modification to alter many genes in the mouse germ-line and to make models in the mouse of human cystic fibrosis, beta thalassemia and essential hypertension.

4. Publications

1. Ogston, A. G. and O. Smithies. Some Thermodynamic and Kinetic Aspects of Metabolic Phosphorylation. Physiol. Revs. 28:283-303 (1948).

2. Smithies, O. A Dynamic Osmometer for Accurate Measurements on Small Quantities of Material: Osmotic Pressures of Isoelectric ß-lactoglobulin Solutions. Biochem. J. 55:57-67 (1953).

3. Smithies, O. The Application of Four Methods for Assessing Protein Homogeneity to Crystalline ß-lactoglobulin: An Anomaly in Phase Rule Solubility Tests. Biochem. J. 58:31-38 (1954).

4. Smithies, O. Grouped Variations in the Occurrence of New Protein Components in Normal Human Serum. Nature 175:307 (1955).

5. Smithies, O. Zone Electrophoresis in Starch Gels: Group Variations in the Serum Proteins of Normal Human Adults. Biochem. J. 61:629-641 (1955).

6. Smithies, O. and N. F. Walker. Genetic Control of Some Serum Proteins in Normal Humans. Nature 176:1265-1266 (1955).

7. Smithies, O. and M. D. Poulik. Two-dimensional Electrophoresis of Serum Proteins. Nature 177:1033 (1956).

8. Smithies, O. and N. F. Walker. Notation for Serum-Protein Groups and the Genes Controlling their Inheritance. Nature 178:694-695 (1956).

9. Dixon, G. H. and O. Smithies. Zone Electrophoresis of Cabbage Enzymes in Starch Gels. Biochem. Biophys. Acta. 23:198-199 (1957).

10. Hickman, G. and O. Smithies. Evidence for Inherited Variations in the Serum Proteins of Cattle. Proc. Genetics Soc. Canada. 2:39 (1957).

11. Smithies, O. Variations in Human Serum ß-globulins. Nature 180:1482-1483 (1957).

12. Smithies, O. and C. G. Hickman. Inherited Variations in the Serum Proteins of Cattle. Genetics 43:374-385 (1958).

13. Poulik, M. D. and O. Smithies. Comparison and Combination of the Starch-Gel and Filter-Paper Electrophoretic Methods Applied to Human Serum: Two-Dimensional Electrophoresis. Biochem. J. 68:636-640 (1958).

14. Horsfall, W. R. and O. Smithies. Genetic Control of Some Human Serum ß-globulins. Science 128:35 (1958).

15. Smithies, O. Third Allele at the Serum ß-globulin Locus in Humans. Nature 181:1203-1204 (1958).

16. Smithies, O. The Serum ß-globulin System in Humans. Proc. X International Congress of Genetics 2:266 (1958).

17. Smithies, O. and O. Hiller. The Genetic Control of Transferrins in Humans. Biochem. J. 72:121-126 (1959).

18. Giblett, E. R., C. G. Hickman and O. Smithies. Serum Transferrins. Nature 183:1589-1590 (1959).

19. Smithies, O. An Improved Procedure for Starch-Gel Electrophoresis: Further Variations in the Serum Proteins of Normal Individuals. Biochem. J. 71:5858-587 (1959).

20. Connell, G. E. and O. Smithies. Human Haptoglobins: Estimation and Purification. Biochem. J. 72:115-121 (1959).

21. Smithies, O. Zone Electrophoresis in Starch-Gels and its Application to Studies of Serum Proteins. Adv. Protein Chem. 14:65-113 (1959).

22. Smithies, O. and G. E. Connell. Biochemical Aspects of the Inherited Variations in Human Serum Haptoglobins and Transferrins. In: Biochemistry of Human Genetics. Ciba Symposium, Churchill (London) pp. 178-189 (1959).

23. Harris, H., S. D. Lawler, E. B. Robson, and O. Smithies. The Occurrence of Two Unusual Serum Protein Phenotypes in a Single Pedigree. Ann. Human Genet. 24:63-69 (1960).

24. Smithies, O. Haptoglobins. In: Transactions of Macy Foundation Conference on Genetics. pp. 129-136 (1960).

25. Connell, G. E., G. H. Dixon and O. Smithies. Subdivision of the Three Common Haptoglobin Types Based on "Hidden" Differences. Nature 505-506 (1961).

26. Connell, G. E., O. Smithies, and G. H. Dixon. Inheritance of Haptoglobin Subtypes. Amer. J. Human Genet. 14:14-21 (1962).

27. Smithies, O., G. E. Connell and G. H. Dixon. Chromosomal Rearrangements and the Evolution of Haptoglobin Genes. Nature 196:232-236 (1962).

28. Smithies, O. Molecular Size and Starch-Gel Electrophoresis. Arch. Biochem. Biophys. Supplement 1:125-131 (1962).

29. Mueller, J. O., O. Smithies, and M. R. Irwin. Transferrin in Variants in Columbidae. Genetics 47:1385-1392 (1962).

30. Nance, W. E. and O. Smithies. New Haptoglobin Alleles: A Prediction Confirmed. Nature 198:869-870 (1963).

31. Smithies, O. Gamma-globulin Variability: A Genetic Hypothesis. Nature 198:1231-1236 (1963).

32. Smithies, O. Protein Variations in Man. In: Proc. XI International Congress of Genetics. Pergamon Press pp. 897-901 (1963).

33. Nance, W. E., A. Claflin and O. Smithies. Genetic Control of Lactic Dehydrogenase in Man. Science 142:1075-1077 (1963).

34. Smithies, O. Starch-gel Electrophoresis. Proc. Brook Lodge Conf. Proteins and Polypeptides. Metabolism 13:974-984 (1964).

35. Smithies, O. Chromosomal Rearrangements and Protein Structure. Cold Spring Harbor Symp. Quant. Biol. 29:309-319 (1964).

36. Azen, E. A., S. Orr and O. Smithies. Starch-gel Electrophoresis of Erythrocyte Stroma. J. Lab. and Clin. Med. 65(3):440, March (1965).

37. Smithies, O. Somatic Mutations and Proteins. Proc. Royal Soc. London (B) 164:320-327 (1965).

38. Smithies, O. Antibody Induction and Tolerance. Science 149:151-156 (1965).

39. Smithies, O. Characterization of Genetic Variants of Blood Proteins. In: Proc. of the X Cong. of the Int. Soc. of blood Transf. S. Karger, ed. pp. 1175-1177.

40. Smithies, O. Disulfide-Bond Cleavage and Formation in Proteins. Science 150:1595-1598 (1965).

41. Wegmann, T. and O. Smithies. A Simple Hemagglutination System Requiring Small Amounts of Red Cells and Antibodies. Transfusion 6:67 (1966).

42. Azen, E. A., O. Smithies, and R. A. Nazhat. Acidic Buffer Systems for Urea-Starch Gel Electrophoresis. J. Lab. and Clin. Med. 67(4):650-659 (1966).

43. Claflin, A., O. Smithies and R. K. Meyer. Antibody Responses in Bursa-Deficient Chickens. J. of Immunology 97:5 (1966).

44. Smithies, O., G. E. Connell and G. H. Dixon. Gene Action in the Human Haptoglobins.
    I. Dissociation into Constituent Polypeptide Chains. J. Mol. Biol. 21:213-224 (1966).
    II. Isolation and Physical Characterization of Alpha Polypeptide Chains. J. Mol. Biol. 21:225-229 (1966).

45. Claflin, A. and O. Smithies. Antibody-Producing Cells in Division. Science 157:1561-1562 (1967).

46. Smithies, O. Antibody Variability. Science 157:267-273 (1967).

47. Smithies, O. The Genetic Basis of Antibody Variability. In: Cold Spring Harbor Symposia on Quantitative Biology, Vol. XXXII pp. 161-168 (1967).

48. Smithies, O. Perspectives: Mutation and Selection in the Immune System. Regulation of Antibody Response, B. Cinader, Ed., 363-375 (1968).

49. Wegmann, T. G. and O. Smithies. Improvement of the Microtiter Hemagglutination Method. Transfusion 8:47 (1969).

50. Azen, E. and O. Smithies. Genetic Polymorphism of C 3($ß_{lc}$-Globulin) in Human Serum. Science 162:905-907 (1968).

51. Gilman, J. G. and O. Smithies. Fetal Hemoglobin Variants in Mice. Science 160:885-886 (1968).

52. Smithies, O. Genetic Aspects of the Immune System. In: Child Care in Health and Disease. Year Book Medical Publishers pp. 364-372 (1968).

53. Smithies, O. The Variability of Antibodies. Proc. XXII Intern Congress of Genetics 3:167-176 (1969).

54. Sung, M. and O. Smithies. Differential Elution of Histones from Gel-trapped Nuclei. Biopolymers 7:39-59 (1969).

55. Azen, E. A., O. Smithies and O. Hiller. High-voltage Starch-Gel Electrophoresis in the Study of Post-Albumin Proteins and C 3($ß_{lc}$-Globulin) Polymorphism. Biochemical Genetics 3:215-228 (1969).

56. Smithies, O., D. Gibson and M. Levanon. Linkage Relationships in Normal Light Chains. In: Symposium on Developmental Aspects of Antibody Formation and Structure, Prague, Czechoslovakia, Vol. I, pp. 339-345 (1969).

57. Smithies, O. Pathways Through Networks of Branched DNA. Science 169:882 (1970).

58. Sung, M. T., G. H. Dixon and O. Smithies. Phosphorylation and Synthesis of Histones in Regenerating Rat Liver. J. of Biol. Chem. 246(5):1358-1364 (1971).

59. Smithies, O., D. M. Gibson, E. M. Fanning, M. E. Percy, D. M. Parr and G. E. Connell. Deletions in Immunoglobulin Polypeptide Chains as Evidence for Breakage and Repair in DNA. Science 172:574-577 (1971).

60. Gibson, D., M. Levanon, and O. Smithies. Heterogeneity of Normal Individual Light Chains. Non-Allelic Variation in the Constant Region of Lambda Chains. Biochemistry 10:3114-3122 (1971).

61. Smithies, O., D. Gibson, E. M. Fanning, R. M. Goodfliesch, J. B. Gilman and D. L. Ballantyne. Quantitative Procedures for Use with the Edman-Begg Sequenator: Partial Sequences of Two Unusual Immunoglobulin Light Chains, Rzf and Sac. Biochemistry 10:4912-4921 (1971).

62. Smithies, O. and M. D. Poulik. Initiation of Protein Synthesis at an Unusual Position in an Immunoglobulin Gene? Science 175:187-189 (1972).

63. Kornguth, S. E., L. R. Kozel and O. Smithies. Probable Identity of Tissue Specific Histone with Encephalitogenic Protein. Nature New Biology 237:49-50 (1972).

64. Smithies, O. and M. D. Poulik. Dog Homologue of Human $ß_2$-Microglobulin. Proc. Natl. Acad. of Sci. USA 69(190):2914-2917 (1972).

65. Fett, J. W., H. F. Deutsch and O. Smithies. Hinge-Region Deletion Localized in the IgG_1-globulin Mcg. Immunochemistry 10:115-118 (1973).

66. Smithies, O. Immunoglobulin Genes: Arranged in Tandem or in Parallel? Cold Spring Harbor Symposium on Quantitative Biology, Volume XXVII, 725-737 (1973).

67. Finlayson, J. S., M. Potter, C. S. Shinnick and O. Smithies. Components of the Major Urinary Protein Complex of Inbred Mice: Determination of NH_2-Terminal Sequences and Comparison with Homologous Components from Wild Mice. Biochemical Genetics 11(4):325-335 (1974).

68. McKean, D. J., E. H. Peters, J. I. Waldby and O. Smithies. Amino Acid Sequence Determination with Radioactive Proteins. Biochemistry 13(15):3048-3051 (1974).

69. Poulik, M. D., D. Farrah, G. H. Malek, C. J. Shinnick and O. Smithies. Low Molecular Weight Urinary Proteins. I. Partial Amino Acid Sequences of the Retinol-binding Poteins of Man and Dog. Biochemica et Biophysica Acta 412:326-334 (1975).

70. Shinnick, T. M., E. Lund, O. Smithies and F. R. Blattner. Hybridization of Labelled RNA to DNA in Agarose Gels. Nucleic Acids Research 2(10):1911-1929 (1975).

71. Faber, H. E., R. S. Kucherlapati, M. D. Poulik, F. H. Ruddle and O. Smithies. Beta-2-microglobulin Locus on Human Chromosome 15. Somatic Cell Genetics 2(2):141-153 (1976).

72. Ballou, B., D. J. McKean, E. F. Freedlender and O. Smithies. HLA Membrane Antigens: Sequencing by Intrinsic Radioactivity. Proc. Natl. Acad. Sci. USA 73(12):4487-4491 (1976).

73. Ballou, B. and O. Smithies. A Simplified Chloral Hydrate Electrophoresis System for Analysis of Biological Membranes. Analytical Biochemistry 80:616-623 (1977).

74. Freedlender, E. F., L. Taichman and O. Smithies. Nonrandom Distribution of Chromosomal Proteins During Cell Replication. Biochemistry 16(9):1802-1808 (1977).

75. Blattner, F. R., B. G. Williams, A. E. Blechl, K. Denniston-Thompson, H. E. Faber, L. A. Furlong, D. J. Grunwald, D. O. Kiefer, D. D. Moore, J. W. Schumm, E. L. Sheldon and O. Smithies. Charon Phages for Cloning DNA: Characterization and Safety Tests. Science 196:161-169 (1977).

76. Walker, I. D., O. Smithies, B. Ballou, E. F. Freedlender and C. J. Shinnick. Protein Sequencing with Radioisotopes. Trends in Biochemical Sciences 2(8):179-184 (1977).

77. Frangione, G., E. F. Franklin and O. Smithies. Unusual Genes at the Aminoterminus of Human Immunoglobulin Variants. Nature 273:400-401 (1978).

78. Freedlender, E. F., L. Taichman and O. Smithies. Segregation of Some Chromosomal Proteins during Cell Replication. Cold Spring Harbor Symp. on Quant. Biol., Vol. XLII, pp. 417-420 (1978).

79. Wessels, B. W., D. J. McKean, N. C. Lien, C. Shinnick, P. M. Deluca and O. Smithies. Amino Acid Sequence Determination of Proteins Labelled in Tritium Gas by Microwave Discharge. Radiation Research 74:35-50 (1978).

80. Blattner, F. R., A. E. Blechl, K. Denniston-Thompson, H. E. Faber, J. E. Richards, J. L. Slightom, P. W. Tucker and O. Smithies. Cloning Human Fetal γ Globin and Mouse α-Type Globin DNA: Preparation and Screening of Shotgun Collections. Science 202:1279-1284 (1978).

81. Smithies, O., A. E. Blechl, K. Denniston-Thompson, N. Newell, J. E. Richards, J. L. Slightom, P. W. Tucker and F. R. Blattner. Cloning Human Fetal γ Globin and Mouse α-Type Globin DNA: Characterization and Partial Sequencing. Science 202:1284-1289 (1978).

82. Smithies, O., J. L. Slightom, P. W. Tucker and F. R. Blattner. Genomic Clones and Unfractionated DNA. From Gene to Protein: Information Transfer in Normal and Abnormal Cells. The Eleventh Miami Winter Symposium, pp. 167-186 (1979).

83. Poulik, M. D. and O. Smithies. Partial Amino Acid Sequences of Rabbit and Rat $ß_2$-Microglobulins. Molecular Immunology 16:731-734 (1979).

84. Slightom, J. L., A. E. Blechl and O. Smithies. Human Fetal G_γ and A_γ Globin Genes: Complete Nucleotide Sequences Suggest that DNA can be Exchanged Between These Duplicated Genes. Cell. 21:627-638 (1980).

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86. Efstratiadis, A., J. W. Posakony, T. Maniatis, R. M. Lawn, C. O'Connell, R. A. Spritz, J. K. DeRiel, B. G. Forget, S. M. Weissman, J. L. Slightom, A. E. Blechl, O. Smithies, F. E. Baralle, C. C. Shoulders and N. J. Proudfoot. The Structure and Evolution of the Human ß-Globin Gene Family. Cell 21:653-668 (1980).

87. Smithies, O., A. E. Blechl, S. Shen, J. L. Slightom and E. F. Vanin. Co-Evolution and Control of Globin Genes. In Organization and Expression of Globin Genes. G. Stamatoyannopoulos and A. W. Nienhuis, Editors. Alan R. Liss, New York. Pp. 101-116 (1981).

88. Smithies, O., A. E. Blechl, S. Shen. J. L. Slightom and E. F. Vanin. Co-Evolution and Control of Globin Genes. 39th Symposium for the Society for Developmental Biology. In Levels of Genetic Control in Development. S. Subtlelny and U. K. Abbot, editors. Alan R. Liss, New York. Pp. 185-200 (1981).

89. Shen, S., J. L. Slightom and O. Smithies. A History of the Human Fetal Globin Gene Duplication. Cell 26:191-203 (1981).

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92. Hsiung, N., R. S. Roginski, P. Henthorn, O. Smithies, R. Kucherlapati and Skoultchi, A. I. Introduction and Expression of a Fetal Human Globin Gene in Mouse Fibroblasts. Molecular and Cellular Biology 2:401-411 (1982).

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95. Vanin, E. F., P. S. Henthorn, D. Kioussis, F. Grosveld and O. Smithies. Unexpected Relationships Between Four Large Deletions in the Human ß Globin Gene Cluster. Cell 35:701-709 (1983).

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98. Maeda, N., F. Yang, D. R. Barnett, B. H. Bowman and O. Smithies. Duplication Within the Haptoglobin Hp^2 Gene. Nature 309:131-135 (1984).

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101. Smithies, O., M. A. Koralewski, K. Y. Song, and R. S. Kucherlapati. Homologous Recombination with DNA Introduced into Mammalian Cells. Cold Spring Harbor Symp. on Quant. Biology, Vol. XLIX, 161-170 (1984).

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108. Smithies, O., R. G. Gregg, S. S. Boggs, M. A. Koralewski and R. S. Kucherlapati. Insertion of DNA Sequences into the Human Chromosomal ß Globin Locus via Homologous Recombination. Nature 317:230-234 (1985).

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