

WILLIAM F. DOVE

Title:

Professor of Oncology and Medical Genetics, Emeritus
George Streisinger Professor of Experimental Biology
University of Wisconsin-Madison

Date of Birth:

June 20, 1936

Education:

Amherst College, Amherst, Mass.	A.B.	1958	Chemistry
Caltech, Pasadena, California	Ph.D.	1962	Chemistry
Cambridge University, England	Fellow	1962-1963	Molecular Genetics
Stanford University, California	Fellow	1964	Biochemistry

Positions held:

Assistant Professor of Oncology, University of Wisconsin-Madison	1965-1968
Associate Professor of Oncology, University of Wisconsin-Madison	1968-1973
Professor of Oncology, University of Wisconsin-Madison	1973-1977
Professor of Oncology and Medical Genetics, University of Wisconsin-Madison	1977-2011
George Streisinger Professor of Experimental Biology, University of Wisconsin-Madison	1986-present
Director, Predoctoral Training Program in Genetics, University of Wisconsin-Madison	1987-2002
Director, Cancer Genetics Program, Wisconsin Comprehensive Cancer Center	1998-2008

Professional activities:

Societies:

Genetics Society of America
Program Committee Chairman 1968, 1989
International Genetics Federation Council 1984-1993
Board of Directors, 1986-1989
Nomination Committee, 2006

Review panels:

Genetics Study Section, NIH, *ad hoc* member 1975, 1977, 1979, 1980
Pathology Study Section, NIH, *ad hoc* member 1981
Council, NIGMS, *ad hoc* member 1985
External Visiting Committee, Department of Microbiology, University of Texas-Austin, 1983-1991
Howard Hughes Predoctoral Fellowship Panel, 1989
NIH/DOE Joint Working Group on the Mouse Genome, 1991
NIH Genome Center: Second Five-year Planning Conference, May 1993
Board of Scientific Counselors, Division of Cancer Biology, Diagnosis, and Centers, National Cancer Institute, 1994-1996
Working Group, Preclinical Models for Cancer, NCI, 1996-1999
Co-Chair, NIH Priority Setting for Mouse Genomics and Genetic Resources, 1998
Scientific Advisory Board, University of Minnesota Cancer Center, 1998-2011
Mouse Models for Human Cancer Consortium from 1999: Steering Committee, Working Groups on Modifier Genetics and on Pathology and Laboratory Medicine, and GI Organ Site Committee
Association of Professors of Human and Medical Genetics, UW representative, 2001-2008
Scientific Advisory Board of Northwestern University Mouse Mutagenesis Center, 2001-2009

Professional activities: (continued)

Review panels (continued):

- External Advisory Board, Medical College of Wisconsin (Milwaukee) Mass Spectrometry Proteomics Initiative, 2002-2008
- NHGRI Knockout Mouse Working Group, 2003 and 2005
- External Review Board, Searle Leadership Fund, Northwestern University, 2005

Editorial:

- JOURNAL OF MOLECULAR BIOLOGY, 1971-1977
- GENETICS, Perspectives co-editor, 1987-2008

Courses, Workshops and Symposia:

- Phage Course, Cold Spring Harbor Laboratory, 1970, faculty
- EMBO Seminar in Biology, Tromsø, Norway, 1973, faculty
- NATO Advanced Research Workshop, The Molecular Biology of *Physarum polycephalum*, Madison, WI, July 1985, director
- NSF-Japan Bilateral Workshop on the Molecular Cell Biology of *Physarum*, Okazaki, Japan, May 1988, co-director
- NSF Western Europe Cooperative Program: Workshop on Genes and Development, France, May 1990, co-organizer
- Howard Hughes/UWCCC Symposium: The Genetic Analysis of Human Biology—Genes, Genomics, and Molecules, May 1999, co-organizer
- Workshop and Conference: The experimental analysis of intestinal cancer, The Jackson Laboratory, October 2000, organizer
- Workshop and Conference: Colon cancer in humans and murine models, NCI, AACR, and The Jackson Laboratory, October 2004, organizer
- Wisconsin Symposia on Human Biology, chair of the organizing committee: 1999, 2001, 2003, 2006
- 38th International Symposium of the Princess Takamatsu Cancer Research Fund: New Challenges and Controls for Colon Cancer, 2007, member of the organizing committee

Honors:

- Guggenheim Fellow and American Cancer Society Scholar, Institut Pasteur, Paris, 1975-1976
- George Streisinger Professor of Experimental Biology, Wisconsin, 1986
- American Cancer Society International Fellow, Oxford, UK, 1991
- Verne Chapman Memorial Lectures:
 - Roswell Park, NY, 1998;
 - Mammalian Genome Society, Washington DC, 2011
- Merit Award, National Cancer Institute, Genes Controlling Neoplasia of the Intestinal Epithelium, 1998-2007
- Member, National Academy of Sciences, from 1998
- Foreign Associate, Belgian Royal Academy of Arts, Letters, and Sciences, from 1999
- Fellow, American Academy of Arts and Sciences, from 2000
- Keynote Lecture, AACR Special Conference, Genetic Modifiers of Cancer Susceptibility: Lessons from Human Population Studies and Mouse Models, 2001
- Evelyn Spritz Lecture, University of Colorado, Denver, 2005
- J. L. Guénet Tribute Lecture, Pasteur Institute, Paris, 2005
- H. P. Rusch Award for Translational Cancer Research, 2006
- Visiting Senior Fellow, Wolfson College and Cambridge Research Institute, 2006-2007
- Nakahara Memorial Lectureship Prize, Japan, 2007
- Wisconsin Academy of Sciences, Arts and Letters Elected Fellow, 2009
- Hilldale Award for Research, Teaching and Service, Biological Sciences Division, University of Wisconsin, 2009
- Wisconsin Medical Alumni Association Basic Sciences Emeritus Faculty Award, 2013

Major research advances:

Over time, William Dove and his colleagues have contributed in five distinct areas of genetics and biology. These constitute distinct facets for understanding biological replication and its control.

- 1) Efficient mutagenesis in *Physarum polycephalum* and the laboratory mouse, leading to the first extensive university-based program of phenotype-driven genetic analysis of the biological problems special to each of these two experimental organisms (Haugli and Dove, 1972; Schedl et al., 1984; Shedlovsky et al., 1986; Moser et al., 1990; McDonald et al., 1990; and Vitaterna et al., 1994). With his McArdle colleague Michael Gould he adapted germline ENU mutagenesis to the laboratory rat, obtaining a colon cancer kindred of this second mammalian genus (Amos-Landgraf et al., 2007).
- 2) The molecular genetics of *Physarum polycephalum*, from Mendelian dissection of the gene families for the eukaryotic cytoskeleton to opening the molecular analysis of gene function in this organism by DNA transformation (Schedl and Dove, 1982 and Burland et al., 1993).
- 3) Nested sets and genetic structure:
 - The integrated lambda prophage (Franklin et al., 1965)
 - Regions of mammalian chromosomes over which strong positive interference operates (King et al., 1989).
- 4) Elements of growth control – from DNA replication of phage lambda, through nuclear cycling in *Physarum polycephalum*, to neoplasia in the intestinal epithelium of mammals:
 - *Trans*-acting positive factors and a *cis*-acting replication origin intrinsically activated by local transcription (Dove et al., 1969 and 1971; Furth et al., 1978; and Furth et al., 1979).
 - Periodic transcription for regulators of the cell cycle (Laffler et al., 1981 and Schedl et al., 1984).
 - Autonomous and non-autonomous negative regulators controlling homeostasis in the intestinal epithelium, identified by the *Min*, *Mom1*, and *Pde4b* alleles of the mouse and the *Pirc* allele of the rat (Moser et al., 1990; Su et al., 1992; Dietrich et al., 1993; Gould and Dove, 1996; Cormier et al., 1997; Pleiman et al., 2018; and Amos-Landgraf et al., 2006).
 - A general strategy for the discovery of protectors against cancer predispositions (Dove et al., 1998).
 - Strong synergy between complementary factors, each with a mild effect on the growth of a tumor (Cormier and Dove, 2000).
 - Polyclonal interactions in the establishment of intestinal neoplasms (Merritt et al., 1997; Thliveris et al., 2005).
- 5) Discovering factors fundamental to early colon cancer by conservation with the mouse and rat (Pleiman et al., 2018 and Ivancic et al., 2019).

With the closing of the Dove "wet lab", the emergent focus of Dove's effort is to synergize with collaborators to characterize further the molecular biology of the early stages of intestinal neoplasia in a mammalian triad – the mouse, the rat, and the human. The over-arching goal of these investigations is to elaborate complementary molecular discovery strategies to find ways to improve the early detection of these neoplasms in human populations. This effort has been enhanced by the abilities of Linda Clipson, a long-term McArdle researcher who also participates in the research on colon cancer in the labs of Drs. Halberg and Deming.

Our website, <https://dove.mcardle.wisc.edu>, contains PDFs or links for these key publications and images of the Dove Lab.

Publications of W. F. Dove and his research group:

Dove, W. F., Wallace, F. A., and Davidson, N. Spectrophotometric Study of the Protonation of Undenatured DNA. *Biochem. Biophys. Res. Commun.*, 1: 312-317, 1959.

Dove, W. F., and Yamane, T. The Complete Retention of Transforming Activity After Reversal of the Interaction of DNA with Mercuric Ion. *Biochem. Biophys. Res. Commun.*, 3: 608-612, 1960. PMID: 13724114.

Dove, W. F., and Davidson, N. Cation Effects on the Denaturation of DNA. *J. Mol. Biol.*, 5: 467-478, 1962.

Dove, W. F., and Davidson, N. The Thermal Inactivation of Transforming Activity at Low Ionic Strength. *J. Mol. Biol.*, 5: 479-486, 1962.

Vinograd, J., Morris, J., Davidson, N., and Dove, W. F., Jr. The Buoyant Behavior of Viral and Bacterial DNA in Alkaline CsCl. *Proc. Natl. Acad. Sci., U.S.A.*, 49: 12-17, 1963. PMID: 13997384. Free PMC Article.

Dove, W. F., and Weigle, J. J. Intracellular State of the Chromosome of Bacteriophage Lambda. I. The Eclipse of Infectivity of the Bacteriophage DNA. *J. Mol. Biol.*, 12: 620-629, 1965. PMID: 5323478.

Franklin, N. C., Dove, W. F., and Yanofsky, C. The Linear Insertion of a Prophage into the Chromosome of *E. coli* Shown by Deletion Mapping. *Biochem. Biophys. Res. Commun.*, 18: 910-923, 1965. Available at <https://dovelab.wiscweb.wisc.edu/research-publications/>

Dove, W. F. Action of the Lambda Chromosome. I. Control of Functions Late in Bacteriophage Development. *J. Mol. Biol.*, 19: 187-201, 1966. PMID: 5967283.

Dove, W. F. The Synthesis of the λ Chromosome: the Role of the Prophage Termini. In: J. Colter and W. Paranchych (Eds.), *The Molecular Biology of Viruses*, pp. 111-123. New York: Academic Press, 1967

Dove, W. F. The Genetics of the Lambdoid Phages. *Annu. Rev. Genet.*, 2: 305-340, 1968.

Dove, W. F. The Extent of *rII* Deletions in Phage T4. *Genet. Res., Camb.*, 11: 215-219, 1968.

Dove, W. F. Strains of Phage Lambda in Current Use. *Virology*, 38: 349-351, 1969. PMID: 4891412.

Dove, W. F., Hargrove, E., Ohashi, M., Haugli, F., and Guha, A. Replicator Activation in Lambda. (Proceedings of the XIIth International Congress of Genetics, Tokyo, August, 1968). *Japan. J. Genet.*, 44: Suppl. 1, 11-22, 1969. Available at <https://dovelab.wiscweb.wisc.edu/research-publications/>

Dove, W. F., and McLeester, C. A Quantitative, Sensitive Assay for Defective Lambda Particles. *Virology*, 39: 607-609, 1969. PMID: 4902073.

Franklin, N. C., and Dove, W. F. Genetic Evidence for Restriction Targets in the DNA of Phages λ and $\phi 80$. *Genet. Res., Camb.*, 14: 151-157, 1969. PMID: 5367368.

Corbett, T. H., Heidelberger, C., and Dove, W. F. Determination of the Mutagenic Activity to Bacteriophage T4 of Carcinogenic and Noncarcinogenic Compounds. *Mol. Pharmacol.*, 6: 667-679, 1970. PMID: 5497717.

Dove, W. F. An Energy-Level Hypothesis for λ Prophage Insertion and Excision. *J. Mol. Biol.*, 47: 585-589, 1970. PMID: 4907274.

Dove, W. F. Biological Inferences. In: A. D. Hershey (Ed.), *The Bacteriophage Lambda*, Chap. 15, pp. 297-312. Cold Spring Harbor: Cold Spring Harbor Laboratory, 1971.

Dove, W. F., Inokuchi, H., and Stevens, W. F. Replication Control in Phage Lambda. In: A. D. Hershey (Ed.), *The Bacteriophage Lambda*, pp. 747-771. Cold Spring Harbor: Cold Spring Harbor Laboratory, 1971. Peer-reviewed by E. Siguer and I. Herskowitz. Available at <https://dovelab.wiscweb.wisc.edu/research-publications/>

Hershey, A. D., and Dove, W. F. Introduction to Lambda. In: A. D. Hershey (Ed.), *The Bacteriophage Lambda*, Chap. 1, pp. 3-11. Cold Spring Harbor: Cold Spring Harbor Laboratory, 1971.

Nijkamp, H. J. J., Szybalski, W., Ohashi, M., and Dove, W. F. Gene Expression by Constitutive Mutants of Coliphage Lambda. *Mol. Gen. Genet.*, 114: 80-88, 1972. PMID: 5015426.

Shedlovsky, A., and Dove, W. F. The Study of Protein Synthesis. In: *Topics in the Study of Life -- The BIO Source Book*, pp. 273-281. New York: Harper and Row, 1971.

Davies, R. W., Dove, W. F., Inokuchi, H., Lehman, J. F., and Roehrdanz, R. L. Regulation of λ Prophage Excision by the Transcriptional State of DNA. *Nature New Biol.*, 238: 43-45, 1972. PMID: 18663851.

Haugli, F. B., and Dove, W. F. Mutagenesis and Mutant Selection in *Physarum polycephalum*. *Mol. Gen. Genet.*, 118: 109-124, 1972. PMID: 4673170. PMID: 4673170

Haugli, F. B., Dove, W. F., and Jimenez, A. Genetics and Biochemistry of Cycloheximide Resistance in *Physarum polycephalum*. *Mol. Gen. Genet.*, 118: 97-107, 1972. PMID: 4562869.

Jones, T. C., and Dove, W. F. Photosensitization of Transcription by Bromodeoxyuridine Substitution. *J. Mol. Biol.*, 64: 409-416, 1972. PMID: 4554019.

Dove, W. F., Lehman, J. F., Roehrdanz, R. L., and Wyatt, W. M. Currents and Cross-Currents of Information Flow in the Growth of Temperate Phages. In: C. F. Fox and W. S. Robinson (Eds.), *Virus Research, 2nd ICN-UCLA Symposium on Molecular Biology*, pp. 171-180. New York: Academic Press, 1973.

Inokuchi, H., Dove, W. F., and Freifelder, D. Physical Studies of RNA Involvement in Bacteriophage λ DNA Replication and Prophage Excision. *J. Mol. Biol.*, 74: 721-727, 1973. PMID: 4580911.

Lehman, J. F., Gleason, M. K., Ahlgren, S. K., and Metzenberg, R. L. Regulation of Phosphate Metabolism in *Neurospora crassa*. Characterization of Regulatory Mutants. *Genetics*, 75: 61-73, 1973. PMID: 137163. Free PMC Article

Barrett, K., Barclay, S., Calendar, R., Lindqvist, B., and Six, E. Reciprocal *transactivation* in a Two Chromosome Phage System. In: W. S. Robinson and C. F. Fox (Eds.), *Mechanisms of Virus Disease*, pp. 385-401. Menlo Park, CA: W. A. Benjamin Inc., 1974.

Gorman, J. A., and Dove, W. F. A Method of Indirect Mutant Selection in *Physarum polycephalum* Using the Antibiotic Netropsin. *Mol. Gen. Genet.*, 133: 345-351, 1974. PMID: 4474585

Lehman, J. F. λ Site-specific Recombination: Local Transcription and an Inhibitor Specified by the *b2* Region. *Mol. Gen. Genet.*, 130: 333-344, 1974. PMID: 4852640.

Wyatt, W. M., and Inokuchi, H. Stability of Lambda *O* and *P* Replication Functions. *Virology*, 58: 313-315, 1974. PMID: 4821702.

Jacobson, D. N., and Dove, W. F. The Amoebal Cell of *Physarum polycephalum*: Colony Formation and Growth. *Dev. Biol.*, 47: 97-105, 1975. PMID: 239390.

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- Young, J. D., Gorman, J. W., Gorman, J. A., and Bock, R. M. Indirect Selection for Auxotrophic Mutants of *Saccharomyces cerevisiae* Using the Antibiotic Netropsin. *Mutat. Res.*, 35: 423-428, 1976. PMID: 778604.
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- Laffler, T. G., and Dove, W. F. Viability of *Physarum polycephalum* Spores and Ploidy of Plasmodial Nuclei. *J. Bacteriol.*, 131: 473-476, 1977. PMID: 560366. Free PMC Article.
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- Roehrdanz, R. L., and Dove, W. F. Studies of the Stimulation by Helper of λ Site-specific Recombination in Lytic Crosses. *Virology*, 79: 32-39, 1977. PMID: 867821.
- Roehrdanz, R. L., and Dove, W. F. A Factor in the *b2* Region Affecting Site-specific Recombinations in Lambda. *Virology*, 79: 40-49, 1977. PMID: 867822.
- Yates, J. L., Gette, W. R., Furth, M. E., and Nomura, M. Effects of Ribosomal Mutations on the Read-Through of a Chain Termination Signal: Studies on the Synthesis of Bacteriophage λ *O* Gene Protein *in Vitro*. *Proc. Natl. Acad. Sci., U.S.A.*, 74: 689-693, 1977. PMID: 322139.
- Avner, P. R., Dove, W. F., Dubois, P., Gaillard, J. A., Guénet, J.-L., Jacob, F., Jakob, H., and Shedlovsky, A. The Genetics of Teratocarcinoma Transplantation: Tumor Formation in Allogeneic Hosts by the Embryonal Carcinoma Cell Lines F9 and PCC3. *Immunogenetics*, 7: 103-115, 1978. PMID: 21302063.
- Barclay, S. L., and Dove, W. F. Mutations of Bacteriophage P2 Which Prevent Activation of P2 Late Genes by Satellite Phage P4. *Virology*, 91: 321-335, 1978. PMID: 741656.
- Barclay, S. L., and Dove, W. F. Mutants of *E. coli* in Which Bacteriophage P4 Cannot Activate the Late Genes of Its Helper, Bacteriophage P2. *Virology*, 91: 336-344, 1978. PMID: 369115.
- Furth, M. E., McLeester, C., and Dove, W. F. Specificity Determinants for Bacteriophage Lambda Replication. I. a Chain of Interactions that Controls the Initiation of Replication. *J. Mol. Biol.*, 126: 195-225, 1978. PMID: 739547. Available at <https://dovelab.wiscweb.wisc.edu/research-publications/>

- Furth, M. E., and Yates, J. L. Specificity Determinants for Bacteriophage Lambda DNA Replication. II. Structure of O Proteins of λ - ϕ 80 and λ -82 Hybrid Phages and of a λ Mutant Defective in the Origin of Replication. *J. Mol. Biol.*, 126: 227-240, 1978. PMID: 739548. Available at <https://dovelab.wiscweb.wisc.edu/research-publications/>
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- Gorman, J. A., Dove, W. F., and Shaibe, E. Mutations Affecting the Initiation of Plasmodial Development in *Physarum polycephalum*. *Dev. Genet.*, 1: 47-60, 1979.
- Laffler, T. G., Wilkins, A., Selvig, S., Warren, N., Kleinschmidt, A., and Dove, W. F. Temperature-sensitive Mutants of *Physarum polycephalum*: Viability, Growth, and Nuclear Replication. *J. Bacteriol.*, 138: 499-504, 1979. PMID: 438137. Free PMC Article.
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- Gorman, J. A., and Wilkins, A. S. Developmental Phases in the Life Cycle of *Physarum* and Related Myxomycetes. In: W. F. Dove and H. P. Rusch (Eds.), *Growth and Differentiation in Physarum polycephalum*, Chap. 6, pp. 157-202. Princeton: Princeton University Press, 1980.
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- Furth, M. E., Dove, W. F., and Meyer, B. J. Specificity Determinants for Bacteriophage λ DNA Replication. III. Activation of Replication in λr_i^c Mutants by Transcription Outside of *ori*. *J. Mol. Biol.*, 154: 65-83, 1982. PMID: 6210781.
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- Johnson, L. L., Clipson, L. J., Dove, W. F., Feilbach, J., Maher, L. J., and Shedlovsky, A. Teratocarcinoma Transplantation Antigens Are Encoded in the *H-2* Region. *Immunogenetics*, 18: 137-145, 1983. PMID: 6350173.
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