

# Banbury Center

COLD SPRING HARBOR LABORATORY

1989

# BANBURY CENTER DIRECTOR'S REPORT

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The Banbury Center continues to be used throughout almost the entire year, with the exception of an all-too-brief respite during the winter! Seventeen meetings were held here, in addition to four advanced lecture courses on neurobiology and one on mapping human diseases. More than 500 people participated at these meetings. The majority came from the United States, but many were visitors from Europe and as far afield as Japan and Australia. Bea Toliver and Ellie Sidorenko in the Center's office and Katya Davey at Robertson House did a wonderful job looking after all aspects of the meetings. These meetings seem to cover an increasingly diverse range of topics, a continuing testimony to the power of molecular biology and genetics.

## Topics in Basic Research

Although it is increasingly difficult to maintain a distinction between "basic" and "applied" research, in 1989, there were two meetings that perhaps qualify as basic research. One meeting was called **Molecular Clocks of Evolution**. A considerable amount of data has been produced using differences in DNA between different species to measure the relatedness of species. Some of the data obtained using DNA as a molecular clock have required radical revision of previously accepted taxonomic relationships, and the purpose of our meeting was to examine whether the assumptions underlying the use of molecular clocks are justified. It was intriguing to see data with time scales measured in millions of years rather than the minutes or hours of conventional molecular biological data!

Evolution was also the underlying theme of the meeting **Molecular Genetics of Early *Drosophila* and Mouse Development**. Homology between related genes of



Banbury Meeting House, rear view

different species is a very powerful tool for studying gene function, as the research on *Drosophila* homeo box genes and their mouse equivalents has shown. In addition, new advances such as homologous recombination offer the possibility of directly manipulating the genomes of organisms like the mouse, which were previously restricted to classic breeding experiments. This meeting brought together the world's leading scientists working on mouse and *Drosophila* development with a view to determining whether there are common themes to studies of the molecular development of these two very different organisms. As *Science* reported (244: 652–654 [1989]), the two groups did find common ground, and we hope that the meeting has stimulated continuing interactions in this field.

### **Molecular Genetics and Human Inherited Diseases**

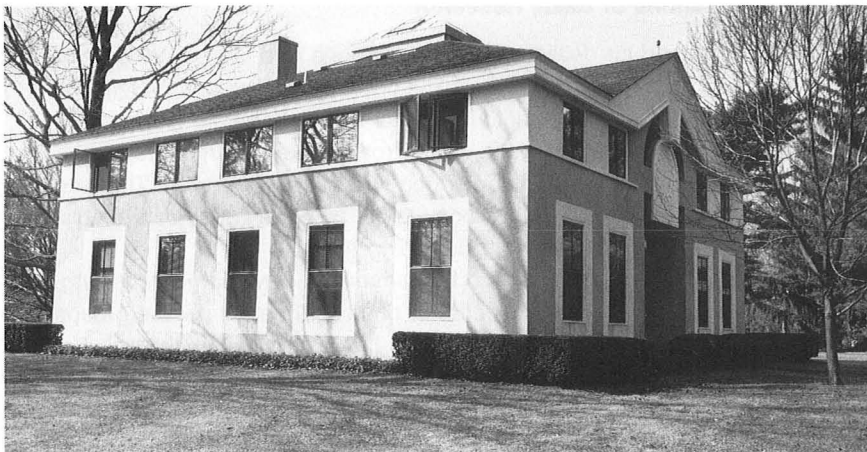
Extraordinary advances continue to be made in the exploitation of recombinant DNA techniques for studying human inherited diseases, as shown by four meetings held here this year. One of the great hopes of molecular genetics is that it will provide an understanding of the genetics of human cancer, a promise that comes closer to fulfillment each year. Some of the most important recent advances in cancer research concern anti-oncogenes or tumor suppressor genes and their interactions with oncogenes. This was the topic of the Banbury meeting,

**Recessive Oncogenes and Tumor Suppression**, held in March. It would be invidious to pick out individual contributions, for the whole meeting was remarkably stimulating and encouraging. The field seems to be at one of those rare and exciting moments in research when a series of apparently unconnected observations and findings are about to be unified.

The gene for Duchenne muscular dystrophy (DMD) was the first gene responsible for a human inherited disease to be cloned without any prior knowledge of the protein involved. Research on DMD has moved rapidly from analysis of DNA to studies of the function of the protein, named dystrophin, in muscle, brain, and other tissues. **Dystrophin**, a very exciting meeting in March, drew together research workers from all over the world to discuss, and in some cases to attempt to reconcile, the latest results. It is a remarkable comment on the rapid progress made possible by recombinant DNA techniques that a session could be devoted to discussing therapeutic strategies for affected boys.

A major question is whether the strategies used to clone the DMD and cystic fibrosis genes are applicable to other disorders, and whether other, more rapid and efficient methods can be devised. The meeting, **Molecular Cytogenetics: Bridging the Resolution Gap**, examined new strategies for handling and analyzing DNA intermediate in size between the DNAs studied by cytogenetics and by cloning techniques. It seems that although one can optimize techniques and strategies, a considerable element of luck is involved in finding a sought-after gene in kilobases of DNA.

Although cloning is laborious and time-consuming, the successes with the DMD and cystic fibrosis genes demonstrate that it is possible to clone the genes for human diseases caused by single genes. Most common disorders, however, while showing strong familial tendencies, do not have a simple pattern of inheritance and probably result from interactions between the environment and one or more of a number of genes. Alcoholism is a classic example of such a complex disease, and the **Molecular Genetics and Biology of Alcoholism** meeting reviewed the data on the inheritance of alcoholism and attempted to evaluate future strategies. As in the meeting held last year on schizophrenia, very few firm



Sammis Hall, guest house

conclusions could be reached, except that there is a genetic component in alcoholism. It seems unlikely that a real effort can begin on cloning the genes involved in alcoholism without many more studies of families, a project about to begin under the auspices of the National Institute on Alcohol Abuse and Alcoholism.

### Neurobiology of Vision

For 2 weeks in the middle of the summer, the Conference Center comes to resemble mission control as it is inundated by computers used for the Computational Neuroscience course. Advantage was taken of their presence to hold a Banbury Center meeting on **Computational Models of Visual Processing**. The meeting covered such topics as spatial sampling, object recognition, and scene analysis and involved hands-on computer modeling as well as more usual presentations and discussions. There is no doubt that this kind of integrated workshop/lecture format contributed enormously to the success of the meeting.

### HIV and AIDS

Two meetings on HIV and AIDS dealt with quite different aspects of the problem. The November meeting, **Control of HIV Gene Expression**, was a follow-up to a similar meeting held in February of 1988. There were some concerns that the gap between the two meetings was too long, but in the event it seemed just right. Research has continued to demonstrate the complexities of the HIV genome and of the interactions between the regulatory systems of the virus and the host cell. It is still proving to be a highly controversial field despite (or because of) the intense research activities. It was a particular pleasure to welcome Harold Varmus, newly anointed Nobel Laureate and longtime associate of Banbury Center, to the meeting.

The **Immunological Aspects of AIDS** meeting provided an opportunity for researchers to determine what progress has been made in this field and what topics require special attention. The primary target of HIV is the immune system, and it might be expected that by now there would be a clear understanding of how the virus produces an immunodeficient state. Such an understanding may be a prerequisite for designing efficient and safe vaccines. However, the difficulties of working with complex cell-culture systems or with animals make progress in this vital area of research frustratingly slow.





## Practical Applications of Basic Research

One strategy proposed for dealing with viral infections is to target viral proteins that are of critical importance to the life cycle of the virus. The viral proteinases that cleave polyprotein precursors into individual viral proteins are one group of such proteins. A very exciting meeting, **Viral Proteinases as Targets for Chemotherapy**, examined what has been done in this research area. This was one of the largest meetings of 1989, a testimony to the potential importance of this approach for controlling viral infections, including AIDS.

The **Applications of Basic Research in Mammalian Development** meeting exemplified the Banbury Center's objective of bringing together diverse groups of people. The topics at this meeting ranged from sex determination, through cryopreservation of embryos and gene transfer in domestic animals, to preimplantation diagnosis of human diseases!

## Environmental Hazards

The **Mutation Induction and Heritability in Mammalian Germ Cells** meeting dealt with such important topics as How do mutations arise in germ-line cells? Can these mutations be repaired? How can they be detected? In particular, participants reviewed the ways in which new technical developments such as polymerase chain reaction can be used to get estimates of germ cell mutation rates.

## Sloan Foundation Workshops for Congressional Staff and Science Journalists

The workshop for Congressional staff dealt not with a research topic, but with an issue of public policy, the question of scientific misconduct. The meeting was entitled **The Ethos of Scientific Research** because it was intended to examine the set of beliefs held by scientists that maintains the integrity of the way in which research is done. There have been many other meetings on this topic, but we believe that ours was unique. The participants included those directly involved with the issue in Washington and a group of distinguished scientists. For the first time, these two groups had the opportunity to interact directly with each other in an informal setting. Whatever the outcome in terms of legislation, there is no doubt that the two groups—scientists and staff—left the meeting with a clear appreciation, if not understanding, of the intense feelings that this issue generates on both sides.

**Applications of the New Molecular Genetics** was the theme of the science journalists' workshop in May. The meeting covered topics that were united in being amenable to new analysis because of new experimental techniques like homologous recombination for gene targeting in mice. For the first time, we made use of the facilities of the DNA Learning Center to give the journalists an opportunity to experience a little of what they write about! This was a great success, and similar laboratory experiments will be featured in the new series of workshops supported by the Sloan Foundation.

## The Baring Brothers-CSHL Meeting

For the second year, the London merchant bankers Baring Brothers and Cold Spring Harbor Laboratory hosted a meeting for senior executives of companies with strong links to biotechnology. As in previous years, the topic of the meeting was chosen to involve fascinating research that has potential applications in biotechnology. Stanley Cohen introduced **Growth Factors in Development**, a



H. Wendt and B. Dovey  
at Baring Brothers  
Meeting

meeting intended to introduce participants to the research being done on growth factors and morphogens and to point to the therapeutic potential of these biologically active substances. Once again, the practical experience in the laboratory at the DNA Learning Center was a tremendous success. On this occasion, DNA samples were analyzed for the sickle cell anemia mutation using polymerase chain reaction, restriction enzyme digest, and gel electrophoresis.

### Other Meetings

The Center has been made available on occasion to other groups. The Deans of the Associated Medical Schools of New York, the Board of Trustees of Huntington Hospital, and Cold Spring Harbor School District held meetings here. In view of the Center's increasing interest in science policy and human genetics, we were particularly pleased to be able to host a joint meeting of the National Institutes of Health and the Department of Energy human genome initiatives at Banbury.

### Funding

The Corporate Sponsor Program provided the funding for five of the Banbury Center meetings in 1989 and, in so doing, provided the bedrock on which the Center's meeting program is built. The five meetings were **Applications of Basic Research in Mammalian Development; Viral Proteinases as Targets for Chemotherapy; Recessive Oncogenes; Molecular Cytogenetics; and The Molecular Genetics of Early *Drosophila* and Mouse Development.** The importance of the contributions from the Laboratory's Corporate Sponsors cannot be overemphasized, especially in a period of declining Federal support for meetings.

Corporations and private foundations seem to be taking on this role increasingly. The Alfred P. Sloan Foundation has already undertaken to support the **Congressional Staff and Science Journalist's Workshops** for a further 3 years,



NIH-DOE Human Genome Meeting

beginning in 1990. The Sloan Foundation also helped to underwrite the costs of the **Molecular Clocks of Evolution** meeting as part of the Foundation's continuing interest in promoting research on molecular evolution. The Muscular Dystrophy Association funded the meeting on **Dystrophin**, and the Christopher D. Smithers Foundation gave very generously to support the meeting on the **Molecular Genetics and Biology of Alcoholism**. The book of this meeting will reach a wider audience than is usually the case because of the generosity of an anonymous donor who has underwritten the production costs of the book. Given the Center's interest in human molecular genetics, I hope to persuade other disease-specific foundations to consider holding workshops here.

Partial support for three meetings was obtained from Federal sources. The Environmental Protection Agency underwrote the costs of the **Mutation Induction and Heritability in Mammalian Germ Cells** meeting, and the National Institute for Allergy and Infectious Diseases supported the meetings on HIV and AIDS.

### **Banbury Center Publications**

Two books published in 1989 deserve special mention. *Polymerase Chain Reaction*, part of the *Current Communications in Molecular Biology* series, was based on the meeting sponsored by Perkin-Elmer Cetus, and it seems set to become a best seller as applications of PCR increase day by day. The second important publication was *Banbury Report 32: DNA Technology and Forensic Science*. This could not have come at a more opportune moment as controversy continues unabated about the standards to be applied in this real-life application of molecular genetics. The papers and especially the discussions in this book should make a very valuable contribution to this debate.

### **Banbury Center Publicity**

Publicity for Banbury Center meetings can be a two-edged sword. On the one hand, it provides a means of informing people about what goes on at our meetings, but, on the other hand, it may cause administrative difficulties given the



Robertson House provides housing and dining accommodations at Banbury Center



restricted numbers that can attend meetings here. On balance, the advantages are likely to outweigh the disadvantages, and journalists and writers attended some meetings in 1989 either for background or to write reports. The report in *Science* on **The Molecular Genetics of Early *Drosophila* and Mouse Development** meeting was an excellent example of how we can achieve a wider audience for the information presented at our meetings. The **DNA Technology and Forensic Science** meeting also received wide publicity, as did the Congressional Workshop, **The Ethos of Scientific Research**, although not all of the latter was favorable.

### Looking Forward to 1990

The Center will continue to hold meetings on topics in five main areas: (1) basic research and technical developments in molecular biology and genetics; (2) advances in the applications of molecular genetics to human inherited disorders, especially complex disorders like alcoholism; (3) environmental issues; (4) the increasing impact of molecular biology and genetics on the public; and (5) issues of scientific policy that are of special importance to the research scientist, e.g., animal experimentation and granting mechanisms. These latter topics will become increasingly important as public oversight of what scientists do continues to increase. We have to lead, and not simply respond, in matters where there is legitimate public interest in our activities. The Center will continue to play a unique role in furthering all aspects of research in molecular biology and encouraging thoughtful and thought-provoking examination of its relationships with society.

Jan A. Witkowski

### Publications

- Ballantyne, J., G. Sensabaugh, and J.A. Witkowski, eds. 1989. *DNA Technology and Forensic Science. Banbury Rep.* **32**.
- McCabe, E.R.B., J. Towbin, J. Chamberlain, L. Baumbach, J.A. Witkowski, G.J.B. van Ommen, M. Koenig, L.M. Kunkel, and W.K. Seltzer. 1989. cDNA for the Duchenne muscular dystrophy locus demonstrates a previously undetectable deletion in a patient with dystrophic myopathy, glycerol kinase deficiency and congenital adrenal hypoplasia. *J. Clin. Invest.* **83**: 95–99.
- Ward, P.A., J.F. Hejtmancik, J.A. Witkowski, L. Baumbach, S. Gunnel, J. Speer, P. Hawley, U. Tantravahi, C.T. Caskey, and S. Latt. 1989. Prenatal diagnosis of Duchenne muscular dystrophy: Prospective linkage analysis and retrospective dystrophin cDNA analysis. *Am. J. Hum. Genet.* **44**: 270–281.
- Witkowski, J.A. 1989. Dystrophin-related muscular dystrophies. *J. Child Neurol.* **4**: 251–271.
- Witkowski, J.A. 1989. *The NEB Transcript* **2**: 1–7.
- Witkowski, J.A. 1989 [correspondence]. Reprint requests and *Current Contents*. *Nature* **337**: 684.
- Witkowski, J.A. 1989 [book review]. *Is Science Necessary?* by Max Perutz. *Trends Genet.* **5**: 387.
- Witkowski, J.A. 1989 [book review] *Science as a Process* by David Hull. *Trends Biochem. Sci.* **14**: 420–421.
- Witkowski, J.A. 1990. *Milestones in the development of DNA technology*. American Chemical Society. (In press.)
- Witkowski, J.A. 1990. Julian Huxley in the laboratory: Embracing inquisitiveness and widespread curiosity. In *Julian Huxley, Biologist and Statesman of Science* (ed. A. Van Helden and K. Waters). Cambridge, Cambridge University Press. (In press.)





# MEETINGS

## Sloan Foundation Congressional Workshop on the Ethos of Scientific Research

January 26 - January 28

ARRANGED BY

**J.A. Witkowski**, Banbury Center, Cold Spring Harbor Laboratory, New York

### SESSION 1

- P. Woolf, Princeton University, New Jersey: Some characteristics of publicly reported cases.
- D. Rennie, Journal of the American Medical Association, Mill Valley, California: The editor, the journal, and scientific misconduct.
- B. Mishkin, Hogan & Hartson, Washington, D.C.: Need for institutional policies and procedures.

### SESSION 2

- D. Zuckerman, House Subcommittee on Human Resources & Intergovernmental Relations, Washington, D.C.: Role of Congress in helping prevent and investigate scientific fraud.
- B. Chafin, House Subcommittee on Oversight & Investigations, Washington, D.C.: Collapse of self-regulation in the absence of oversight.
- W. Stewart, National Institutes of Health, Bethesda, Maryland: Keeping Congress out of science.



D. Zuckerman, D. Nathans

### SESSION 3

- H. Wortis, Tufts University, Boston, Massachusetts: Science investigation.
- D. Korn, Stanford University Medical School, California: Institutional policy and process.
- J. Newburgh, National Institutes of Health, Bethesda, Maryland: Response and role of NIH.
- C. Scheman, Association of American Universities, Washington, D.C.: Issues relating to the development of institutional policies.



G. Booth, N. Zinder, H. Varmus



M. Mathews, M. Ptashne, R. Axel

## Recessive Oncogenes and Tumor Suppression

March 29 - April 1

ARRANGED BY

**W. Cavanee**, Ludwig Institute for Cancer Research, Montreal, Canada

**N. Hastie**, Western General Hospital, Edinburgh, Scotland

**E.J. Stanbridge**, University of California, Irvine

## SESSION 1: Somatic Cell Genetics

**Chairperson: E.J. Stanbridge**, University of California, Irvine

H. Harris, University of Oxford, England: Role of differentiation in the suppression of malignancy.

I. Herskowitz, University of California, San Francisco: Response and resistance to negative growth factors in yeast: Function and control of synthesis of peptide receptors.

J.C. Barrett, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina: Tumor suppressor genes as negative regulators of cell growth.

C. Harris, National Cancer Institute, Bethesda, Maryland: Tumor suppression studies of human lung cancer.

N. Bouck, Northwestern University, Chicago, Illinois: Suppressor control of an inhibitor of angiogenesis.

H. Zarbl, Massachusetts Institute of Technology, Cambridge: Genetic analysis of transformation effector and suppressor genes.

B.E. Weissman, University of North Carolina, Chapel Hill: Tumor suppressor genes in pediatric cancers.

## SESSION 2: Deletions and Cancer

**Chairperson: N. Hastie**, Western General Hospital, Edinburgh, Scotland

W.K. Cavenee, Ludwig Institute for Cancer Research, Montreal, Canada: Loss of genetic information in cancer predisposition and progression.

R.L. White, Howard Hughes Medical Institute, Salt Lake City, Utah: High-resolution mapping of inherited tumor genes.

B. Vogelstein, John Hopkins Oncology Center, Baltimore,

Maryland: Genetic alterations in colorectal tumors.

N. Hastie, Western General Hospital, Edinburgh, Scotland: Wilms' tumor locus at 11p13.

B.A.J. Ponder, Institute of Cancer Research, Surrey, England: Genetics of multiple endocrine neoplasia type 2.

## SESSION 3: Retinoblastoma

**Chairperson: W.K. Cavenee**, Ludwig Institute for Cancer Research, Montreal, Canada

M.F. Hansen, M.D. Anderson Cancer Center, University of Texas, Houston: Molecular genetics of familial mixed cancer.

W.-H. Lee, University of California at San Diego, La Jolla: Molecular basis of tumor suppression by the retinoblastoma gene.

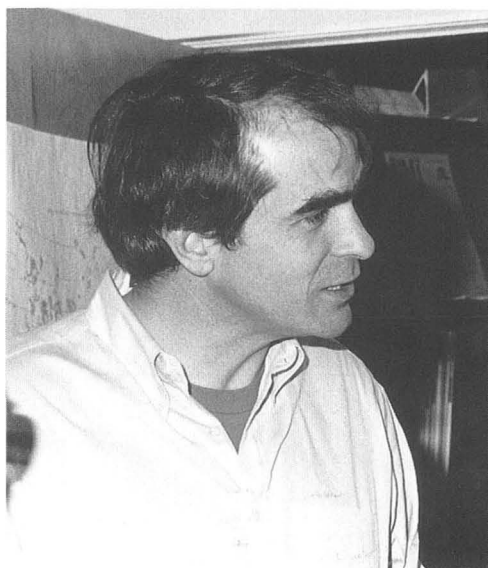
B. Phillips, Hospital for Sick Children, Toronto, Canada:

Characterization of mutations in the retinoblastoma gene.

W. Benedict, The Woodlands, Texas: The retinoblastoma gene and its product.

D. Livingston, Dana-Farber Cancer Institute, Cambridge, Massachusetts: SV40 T antigen-RB interactions.

R.A. Weinberg, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: The retinoblastoma gene.



R. White



F. McCormick, R. Sager

#### **SESSION 4: Other Candidate Tumor Suppressor Genes**

**Chairperson: R.A. Weinberg**, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts

- B.M. Mechler, Johannes Gutenberg University, Mainz,  
Federal Republic of Germany: Molecular basis for tumor  
suppression in *Drosophila*.  
M. Noda, The Institute of Physical and Chemical Research,  
Ibaraki, Japan: Biological activities of the transformation  
suppressor gene Krev-1 and its mutants.  
R. Schaefer, University of Zurich, Switzerland: Molecular and

functional analysis of tumor suppressor genes by  
transfection.

- L.A. Liotta, National Cancer Institute, Bethesda, Maryland:  
Metastasis suppressor gene.  
R. Sager, Dana-Farber Cancer Institute, Cambridge,  
Massachusetts: The *gro* gene as putative cytokine and  
tumor suppressor.

#### **SESSION 5: Strategies for Cloning Tumor Suppressor Genes**

**Chairperson: R.L. White**, Howard Hughes Medical Institute, Salt Lake City, Utah

- J.D. Minna, National Cancer Institute, Bethesda, Maryland:  
Chromosomal deletion in lung cancer.  
E. Stanbridge, University of California, Irvine: Strategies for  
cloning human tumor suppressor genes.  
L. Strong, M.D. Anderson Cancer Center, University of Texas,

Houston: Molecular genetics of the Wilms' tumor locus.  
A. Balmain, Beatson Institute for Cancer Research, Glasgow,  
Scotland: Chromosomal changes during tumor  
progression.

#### **SESSION 6: Oncogene-Tumor Suppressor Gene Interactions**

**Chairperson: M. Ptashne**, Harvard University, Boston, Massachusetts

- E. Harlow, Cold Spring Harbor Laboratory, New York: Protein  
complexes between p105-RB and DNA tumor-virus-  
transforming proteins.  
A.J. Levine, Lewis Thomas Laboratory, Princeton University,  
New Jersey: The p53 proto-oncogene can suppress E1A  
plus *ras*-mediated transformation.  
F. McCormick, Cetus Corporation, Emeryville, California:  
Role of GAP in *ras* transformation.

- M.H. Wigler, Cold Spring Harbor Laboratory, New York:  
Signal processing along the *ras* pathway.  
S. Aaronson, National Cancer Institute, Bethesda, Maryland:  
Growth-factor-activated pathways in the neoplastic  
process.  
J. Massague, University of Massachusetts Medical School,  
Worcester: Control of growth and phenotype by TGF- $\beta$ .

## **Dystrophin**

**April 2 - April 5**

ARRANGED BY

**L.M. Kunkel**, The Children's Hospital, Boston, Massachusetts  
**R. Worton**, Hospital for Sick Children, Toronto, Canada

#### **SESSION 1: The Human Dystrophin Gene: Putting Together a Physical Map**

**Chairperson: L.M. Kunkel**, The Children's Hospital, Boston, Massachusetts

- G.-J.B. van Ommen, University of Leiden, The Netherlands:  
Review of physical map.  
K.E. Davies, John Radcliffe Hospital, Oxford, England:  
Deletions in the central and 3'-end of the dystrophin  
gene: Genotype and phenotype.  
U. Francke, Yale University, New Haven, Connecticut:  
Characterization of dystrophin deletions by cDNA studies  
and long-range mapping.

R.J. Bartlett, Duke University Medical Center, Durham, North  
Carolina; A. Burghes, Ohio State University, Columbus;  
J.S. Chamberlain, Baylor College of Medicine, Houston,  
Texas; M. Koenig, The Children's Hospital, Boston,  
Massachusetts, and A. Speer, Akademie der Wissen-  
schaften der German Democratic Republic: Filling out  
the map.

#### **SESSION 2: Transcriptional Regulation and Expression**

**Chairperson: R. Worton**, Hospital for Sick Children, Toronto, Canada

- J.-C. Kaplan, Institut National de la Sante et de la Recherche  
Medicale, Paris, France: Transcripts of the dystrophin gene.

U. Nudel, The Weizmann Institute of Science, Rehovot, Israel:  
Expression and promoter studies in rodent myogenic cells.





L. Rowland



A. Engel, E. Bonilla

- H. Klamut, Hospital for Sick Children, Toronto, Canada: Human gene promoter and expression in myogenic cells.  
 H. Blau, Stanford University, California: Cell biology of dystrophin.

- R. Brown, Massachusetts General Hospital, Boston: Studies of DMD gene expression in vitro.

### SESSION 3: Dystrophin Structure and Function

**Chairperson: E. Lazarides**, California Institute of Technology, Pasadena

- E. Bonilla, Columbia University College of Physicians & Surgeons, New York, New York: Localization of dystrophin in specialized regions of the muscle fiber.  
 E. Zibrzycka-Gaarn, Hospital for Sick Children, Toronto, Canada: Site-specific antibodies to dystrophin and localization to membrane vesicles.  
 K. Arahata, National Institute of Neuroscience, Tokyo, Japan: Immunohistochemical study of dystrophin in DMD and BMD.  
 M. Cullen, Newcastle General Hospital, England: Ultrastructural localization of dystrophin in human muscle by gold labeling.  
 S. Watkins, Dana-Farber Cancer Institute, Cambridge, Massachusetts: Light and immunoelectron microscopic localization of dystrophin.  
 G.-J.B. van Ommen, University of Leiden, The Netherlands: Dystrophin localization in embryonic, fetal, and adult mouse.  
 K. Campbell, University of Iowa, Iowa City: Purification of dystrophin from rabbit muscle membranes.  
 T.J. Byers, Harvard University, Cambridge, Massachusetts: Relationship of dystrophin to  $\alpha$ - and  $\beta$ -spectrins.  
 M. Koenig, The Children's Hospital, Boston, Massachusetts: Dystrophin structure and possible function.

### SESSION 4: Cytoskeletal Proteins: Structure and Function

**Chairperson: A.G. Engel**, Mayo Clinic, Rochester, Minnesota

- V. Bennett, Duke University Medical Center, Durham, North Carolina: Proteins of the spectrin-based membrane skeleton.  
 E. Lazarides, California Institute of Technology, Pasadena: Control of assembly of the membrane skeleton.  
 D. Critchley, University of Leicester, England: Cytoskeletal proteins linking actin to the membrane in cell matrix junctions.  
 S. Georgatos, Rockefeller University, New York: Nuclear lamina: Organization principles and anchorage functions.  
 S. Craig, Johns Hopkins University Medical School, Baltimore, Maryland: Muscle costameres: Transmembrane linkage between extracellular matrix, sarcolemma, and myofiber bundles.

### SESSION 5: Mutational Spectrum and Clinical Correlates

**Chairperson: K. Davies**, John Radcliffe Hospital, Oxford, England

- K. Fischbeck, University of Pennsylvania Hospital, Philadelphia: Clinical spectrum of defects in the dystrophin gene.  
 A. Burghes, Ohio State University, Columbus: Correlation of genotype and phenotype at the 5' end of the gene.  
 R. Worton, Hospital for Sick Children, Toronto, Canada: Deletions and duplications of exons in DMD and BMD: More on the frame-shift idea.  
 M. Koenig, The Children's Hospital, Boston, Massachusetts: The frame-shift hypothesis: Correlation of mutation type with phenotype.  
 J.S. Chamberlain, Baylor College of Medicine, Houston, Texas: PCR technology for rapid deletion analysis.  
 M. Zatz, Universidade de Sao Paulo, Brazil: DNA and dystrophin studies in Brazilian families.  
 E. Hoffman, The Children's Hospital, Boston, Massachusetts: Dystrophin quality and quantity in DMD and BMD.

## SESSION 6: Animal Models and Disease

**Chairperson: M. Cullen**, Newcastle General Hospital, England, and L.M. Kunkel, The Children's Hospital, Boston, Massachusetts

- G. Karpati, Montreal Neurological Institute and Hospital, Quebec, Canada: Dystrophin expression in mosaic muscle fibers of carrier *mdx* females and transplanted *mdx* males.
- T.A. Partridge, Charing Cross & Westminster Medical School, London, England: Relationship between morphology and content of introduced dystrophin in muscle of the *mdx* mouse.

- J.L. Mandel, Institute of Biological Chemistry, Strasbourg, France: Dystrophin gene and protein in chicken.
- B.J. Cooper, Cornell University, Ithaca, New York: Expression of dystrophin in the *grmd* dog.
- R. Bartlett, Duke University Medical Center, Durham, North Carolina: Studies of the golden retriever muscular dystrophy.

## SESSION 7: What Does the Future Hold?

**Chairperson: D. Wood**, Muscular Dystrophy Association, New York, New York

- T.A. Partridge, Charing Cross Hospital, London, England: Future of myoblast transplantation: The minimum requirement before consideration of clinical trials.
- L.M. Kunkel, The Children's Hospital, Boston, Massachusetts: Speculation on the function of dystrophin

- and approaches to correction of the defect.
- D. Wood, Muscular Dystrophy Association, New York, New York: Where do we go from here? What is MDA's current response to the 'big' question—how soon will we have a cure?

# Viral Proteinases as Targets for Chemotherapy

April 16 - April 19

ARRANGED BY

**E. Wimmer**, State University of New York, Stony Brook  
**S. Oroszlan**, NCI-Frederick Cancer Research Facility, Maryland  
**H.-G. Krausslich**, State University of New York, Stony Brook

## SESSION 1

**Chairpersons: J.H. Strauss**, California Institute of Technology, Pasadena, and **M.J. Schlesinger**, Washington University, St. Louis, Missouri

- E. Wimmer, State University of New York, Stony Brook: Polyprotein processing in viral replication.
- B.L. Semler, University of California at Irvine: Molecular genetics of picornavirus protein processing.
- P. V. Pallai, Boehringer Ingelheim Pharmaceuticals, Ridgefield, Connecticut: Peptide cleavage by purified 3C.

- E. Wimmer, State University of New York: Poliovirus proteinase 2A.
- A.C. Palmenberg, University of Wisconsin, Madison: Cleavage specificity of the EMC 3C proteinase.
- J. Wellink, Agricultural University, Wageningen, The Netherlands: Processing of the CPMV polyproteins.

## SESSION 2

**Chairpersons: A.C. Palmenberg**, University of Wisconsin, Madison, and **B.L. Semler**, University of California at Irvine

- W. Dougherty, Oregon State University, Corvallis: Molecular genetic analysis of a plant virus proteinase and its conserved cleavage site.
- R.J. Fletterick, University of California, San Francisco: X-ray crystallography of trypsin variants.
- J.F. Bazan, University of California, San Francisco: Viral branches of the trypsin-like proteinase family.
- M.J. Schlesinger, Washington University, St. Louis, Missouri: A second sindbis virus autoprotease: In vitro processing of the viral nonstructural polyprotein.

- J. Strauss, California Institute of Technology, Pasadena: *cis*-Acting structural and nonstructural proteinases encoded by sindbis virus.
- J. Weber, Centre Hospitalier Universitaire, Sherbrooke, Canada: Adenovirus proteinase: Properties of a recombinant enzyme expressed in *E. coli*.
- M. Johnston, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland: AIDS drug discovery and development: Present and future.



### SESSION 3

**Chairpersons:** **K. von der Helm**, University of Munich, Federal Republic of Germany, and **S. Oroszlan**, NCI-Frederick Cancer Research Facility, Maryland

- S. Oroszlan, NCI-Frederick Cancer Research Facility, Maryland: Retroviral polyprotein processing: An overview.
- Y. Yoshinaka, Otsuka Pharmaceutical Co. Ltd., Tokushima, Japan: Retroviral proteinase as an aspartic proteinase.
- R.B. Luftig, Louisiana State University Medical Center, New Orleans: Bacterial expression and activity of the Mo-MLV proteinase.
- M. Hatanaka, Kyoto University, Japan: HTLV-I proteinase.
- M. Roberts, NCI-Frederick Cancer Research Facility, Maryland: Lentiviral proteinases.
- C. Debouck, Smith Kline & French Laboratories, King of Prussia, Pennsylvania: Expression and structure-function characterization of the HIV-1 proteinase and its *gag-pol* substrate.
- M. Graves, Hoffmann-La Roche Inc., Nutley, New Jersey: Characterization of HIV-1 proteinase.
- K. von der Helm, University of Munich, Federal Republic of Germany: Action and inhibition of the HIV proteinase.
- H.-G. Krausslich, State University of New York, Stony Brook: Processing of HIV polyproteins by bacterially expressed HIV-1 proteinase.
- R.I. Swanstrom, University of North Carolina, Chapel Hill: Genetic analysis of the HIV proteinase.
- J.M. Louis, National Cancer Institute, NIH, Bethesda, Maryland: Studies with wild-type and mutant HIV-1 proteinase expressed in *E. coli*.

### SESSION 4

**Chairperson:** **R.J. Fletterick**, University of California, San Francisco

- M.N.G. James, University of Alberta, Edmonton, Canada: Crystallographic studies of AMV proteinase.
- A. Wlodawer, NCI-Frederick Cancer Research Facility, Maryland: Refined structure of a proteinase from RSV.
- M. Navia, Merck, Sharp & Dohme Research Laboratories, Rahway, New Jersey: Three dimensional structure of the aspartyl-proteinase from HIV-1.
- S. Foundling, E.I. du Pont de Nemours & Co., Wilmington, Delaware: Crystallographic analysis of AMV proteinase.
- J. Erickson, Abbott Laboratories, Abbott Park, Illinois: Structural relationships between viral and eukaryotic aspartic proteinases and the implications for retroviral drug design.
- R.S. DesJarlais, University of California, San Francisco: Inhibitor design from known structures.
- S. Oroszlan, NCI-Frederick Cancer Research Facility, Maryland, and R.B. Luftig, Louisiana State University Medical Center, New Orleans: Synthetic nonpeptide inhibitors.

### SESSION 5

**Chairperson:** **E. Wimmer**, State University of New York, Stony Brook

- C.S. Craik, University of California, San Francisco: Expression and characterization of HIV-1 and HIV-2 proteinases.
- S.B.H. Kent, California Institute of Technology, Pasadena: A synthetic approach to the molecular biology of retroviral proteinases: Structure-function studies of the HIV-1 and HIV-2 enzymes and their substrates.
- B.M. Dunn, University of Florida, Gainesville: Kinetic studies on viral proteinases utilizing synthetic peptide substrates.
- J. Leis, Case Western Reserve University, Cleveland, Ohio, and A.M. Skalka, Fox Chase Cancer Center, Philadelphia, Pennsylvania: Biochemical analysis of the ASLV proteinase.
- C. Carter, State University of New York, Stony Brook: Substrate specificity determinants of the HIV-1 proteinase.
- P.L. Darke, Merck, Sharp & Dohme Research Laboratories, West Point, Pennsylvania: HIV-1 proteinase: Substrates, inhibitors, and subunit interactions.
- P. Strop, Institute of Organic Chemistry and Biochemistry, Prague, Czechoslovakia: Specificity and inhibition studies on MAV proteinase.
- M.T. Skoog, Boehringer Ingelheim Corporation, Ridgefield, Connecticut: Substrate specificity of HIV proteinase.
- B.D. Korant, E.I. du Pont de Nemours & Co., Wilmington, Delaware: Potential use of proteinase inhibitors as antiviral agents.

# Molecular Genetics of Early *Drosophila* and Mouse Development

April 20 - April 23

ARRANGED BY

**M. Cappechi**, University of Utah, Salt Lake City

## SESSION 1

W. Bender, Harvard Medical School, Boston, Massachusetts:  
Segmental regulation of the bithorax complex of  
*Drosophila*.

W. McGinnis, Yale University, New Haven, Connecticut: A  
homeo domain switch changes the regulatory function of  
the deformed protein in *Drosophila* embryos.

M.P. Scott, University of Colorado, Boulder: Genes that  
control pattern formation during development.

M. Krasnow, Stanford University Medical Center, California:  
Transcriptional regulation by homeotic gene products in  
cultured *Drosophila* cells and in vitro.

## SESSION 2

M. Levine, Columbia University, New York, New York: Spatial  
regulation of homeo box gene expression in *Drosophila*.

M. Cappechi, University of Utah, Salt Lake City: Creating  
mice with specific mutations by gene targeting.

A. Joyner, Mt. Sinai Hospital Research Institute, Toronto,

Canada: Molecular genetic approaches to the analysis of  
mammalian development.

P. Gruss, Max Planck Institute of Biophysical Chemistry,  
Gottingen, Federal Republic of Germany: Precision  
mutagenesis by homologous recombination.



## SESSION 3

E. Robertson, Columbia University, New York, New York:  
Developmental potential of embryonic stem cells.

E.F. Wagner, Research Institute of Molecular Pathology,  
Vienna, Austria: In situ analysis of *c-fos* expression in  
transgenic mice.

R. Beddington, ICRF Developmental Biology Unit, Oxford,

England: Using *lacZ* as an in situ cell marker to analyze  
tissue lineages in the midgestation mouse embryo.

F.H. Ruddle, Yale University, New Haven, Connecticut:  
Mammalian Antennapedia class homeo box genes:  
Organization, expression, and evolution.



#### SESSION 4

- B. Hogan, Vanderbilt University Medical School, Nashville, Tennessee: Developmental expression of the murine *vgr-1* gene: A new member of the TGF- $\beta$  multigene family.
- P. Gruss, Max Planck Institute of Biophysical Chemistry, Gottingen, Federal Republic of Germany: The *hox-1.1* promoter directs expression to a specific region of the embryo in transgenic mice.
- G. Martin, University of California, San Francisco: New approaches to identifying genes that control early mammalian embryogenesis.
- D. Duboule, European Molecular Biology Laboratory, Heidelberg, Federal Republic of Germany: The organization of the murine *hox* gene family resembles that of *Drosophila* homeotic genes.
- R. Krumlauf, National Institute for Medical Research, London, England: The murine and *Drosophila* homeo box clusters are derived from a common ancestor based on similarities in structure and expression.

#### SESSION 5

- A.P. McMahon, Roche Institute of Molecular Biology, Nutley, New Jersey: *int-1* and pattern regulation.
- R. Nusse, Netherlands Cancer Institute, Amsterdam: *int-1* and *int-4*, two genes active in mouse mammary tumorigenesis and in normal embryogenesis.

## Sloan Foundation Journalists' Workshop on Applications of the New Molecular Genetics

May 7 - May 9

ARRANGED BY

**J.A. Witkowski**, Banbury Center,  
Cold Spring Harbor Laboratory, New York

#### SESSION 1

- C. Cepko, Harvard University, Boston, Massachusetts: Studies of cell lineages in developing animals using retroviruses as markers.
- N. I. First, University of Wisconsin, Madison: Applications of new methods of embryo manipulation in animal husbandry.
- M. Capecchi, University of Utah, Salt Lake City: Homologous recombination and gene targeting.

#### SESSION 2

- D. Micklos and M. Bloom, DNA Learning Center, Cold Spring Harbor Laboratory, New York: Laboratory experiment and Smithsonian *Search for Life* exhibit.

#### SESSION 3

- M. Martin, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland: Transgenic mice and other animal models for the study of AIDS pathogenesis.
- G.A. Evans, The Salk Institute, La Jolla, California: Cell ablation studies for developmental studies.
- A.N. Rowan, Tufts University Veterinary School, North Grafton, Massachusetts: Ethical issues of the new genetics.



J. Palca, J.A. Witkowski, R. Cooke



D. Barnes, C. Joyce, M. Martin

# Computational Models of Visual Processing Workshop on Computational Neuroscience

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June 26 - June 30

ARRANGED BY

**J.A. Movshon** and **M. Landy**, New York University, New York

## **SESSION 1:** Sampling and the Retina

A.J. Ahumada, Jr., NASA Ames Research Center, Moffett Field, California: Learning receptor position.

L.T. Maloney, New York University, New York: Retinal sampling and early vision.

D.R. Williams, University of Rochester, New York: Photoreceptor sampling and image motion.

D.C. Hood, Columbia University, New York, New York: Models of the human rod receptor and the ERG.

## **SESSION 2:** Central Visual Neurons

P. Lennie, University of Rochester, New York: Construction of chromatically opponent receptive fields.

M.J. Hawken, New York University, New York: Spatial organization of receptive fields in primate V1.

R. Shapley, New York University, New York: Linear and nonlinear contributions to direction selectivity of simple cells in cat area 17.

## **SESSION 3:** Encoding

A.B. Watson, NASA Ames Research Center, Moffett Field, California: Modeling visual neurons.

D.J. Heeger, Massachusetts Institute of Technology,

Cambridge: Nonlinear model of cat striate cortex.

D.J. Field, University of Cambridge, England: Redundancy of natural scenes and its relation to visual coding.

## **SESSION 4:** Channels

D.G. Pelli, Syracuse University, New York: On the nature of the noise that limits visual detection.

J. Nachmias, University of Pennsylvania, Philadelphia:

Ruminations on subthreshold summation.

H.R. Wilson, University of Chicago, Illinois: Spatial mechanisms and visual pattern discrimination.

## **SESSION 5:** Motion and Transparency

E.H. Adelson, Massachusetts Institute of Technology, Cambridge: Analysis of orientation and motion.

N. Grzywacz, Whitaker College, Massachusetts Institute of Technology, Cambridge: Does the visual cortex really

worry about the aperture problem?

D. Kersten, Brown University, Providence, Rhode Island: Transparency: Psychophysics and computation.

## **SESSION 6:** Texture

N. Graham, Columbia University, New York, New York: Low-level visual processes in texture segregation.

C. Chubb, New York University, New York: Expanding the class of distinct textures with identical local average energy spectra.

J.R. Bergen, David Sarnoff Research Center, Princeton, New Jersey: Energy measures, gain controls, and texture perception.

## **SESSION 7:** Three-dimensional Structure

J.P. Frisby, University of Sheffield, England: PMF89, switcher, and needles: A medley of AIVRU's stereo algorithms.

A.J. Parker, University Laboratory of Physiology, Oxford, England: Stereo, surfaces, and shape.

H. Bulthoff, Brown University, Providence, Rhode Island: Integration of depth modules.

S. Ullman, Massachusetts Institute of Technology, Cambridge: 3D object recognition.

## **SESSION 8:** Surface Properties

M. D'Zmura, University of California, Irvine: Constraints on the recovery of surface reflectance.

D. Brainard, Stanford University, California: Predicting the illuminant's effect on color appearance.

# Molecular Genetics and Biology of Alcoholism

October 10 - October 13

ARRANGED BY

**H. Begleiter**, State University of New York Health Science Center, Brooklyn

**C.R. Cloninger**, Washington University School of Medicine, St. Louis, Missouri

## SESSION 1: Genetic Studies I

**Chairperson: J. Sambrook**, University of Texas Medical Center, Dallas

A. Chakravarti, University of Pittsburgh, Pennsylvania:  
Sampling design issues for segregation and linkage  
studies in alcoholism.

J.S. Searles, University of Pennsylvania, Philadelphia:  
Methodological limitations of genetic models of  
alcoholism: Critique of extant research and suggestions  
for future directions.

C.R. Cloninger, Washington University School of Medicine,

St. Louis, Missouri: Clinical and genetic heterogeneity in  
alcoholism.

R.E. Tarter, University of Pittsburgh, Pennsylvania: Vulnerabil-  
ity to alcoholism: From individual differences to different  
individuals.

T. Reich, Jewish Hospital of St. Louis, Missouri: Familial  
transmission of alcoholism and related disorders.

## SESSION 2: Genetic Studies II

**Chairperson: P.M. Conneally**, Indiana University Medical Center, Indianapolis

A.C. Heath, Washington University, St. Louis, Missouri:  
Contributions of twin family studies to understanding the  
inheritance of alcoholism.

N.G. Martin, Queensland Institute of Medical Research,  
Herston, Australia: Twin studies of alcohol metabolism  
and sensitivity.

R.J. Cadoret, University of Iowa, Iowa City: Use of the  
adoption paradigm to delineate the role of genes,  
environment, and their interaction in genesis of  
alcoholism.

C.C.H. Cook, Middlesex Hospital Medical School, London,  
England: Candidate genes and favored loci for  
alcoholism.

D. Goldman, National Institute on Alcohol Abuse and  
Alcoholism, Bethesda, Maryland: Candidate loci for  
alcoholism: Cloning and analysis of ethanol metabolic  
genes and tryptophan hydroxylase.

T.-K. Li, Indiana University School of Medicine, Indianapolis:  
Animal models in the study of genetics and biology of  
alcoholism.



### SESSION 3: Putative Markers I

**Chairperson: E. Gordis**, National Institute on Alcohol Abuse and Alcoholism, Rockville, Maryland

- H. Begleiter, State University of New York Health Science Center, Brooklyn: Neurophysiologic markers in sons of alcoholic fathers: Data and criteria.
- M. Schukit, University of California, San Diego: Challenges of children of alcoholics with alcohol or diazepam.
- B. Tabakoff, National Institute on Alcohol Abuse and Alcoholism, Bethesda, Maryland: Neurochemical and peripheral markers in alcoholism.
- D.P. Agarwal, Institute of Human Genetics, Hamburg, Federal Republic of Germany: Human aldehyde dehydrogenases: Genetic implications for alcohol sensitivity, alcohol drinking habits, and alcoholism.
- T.J. Peters, King's College School of Medicine, London, England: Alcohol-acetaldehyde flush reactions in Caucasians: Identification of biochemical defects and genetic aspects.

### SESSION 4: Putative Markers II

**Chairperson: R.S. Sparkes**, University of California, Los Angeles, Health Science Center

- E.P. Noble, Neuropsychiatric Institute, University of California, Los Angeles: Alcoholic fathers and their sons: electrophysiologic, neurophysiologic, personality and family correlates.
- P. Propping, Institute of Human Genetics, University of Bonn, Federal Republic of Germany: Alcohol effect on the EEG: Are there possibilities for applications of molecular genetics?
- V. Hesselbrock, University of Connecticut, Farmington: Social/behavioral factors that may attenuate/potentialize genetic effects.
- E.M. Wijsman, University of Washington, Seattle: Linkage analysis of alcoholism: Problems and solutions.
- J. Ott, Columbia University, New York, New York: Genetic linkage analysis under uncertain disease definition.

### SESSION 5: General Discussion

**Chairperson: A. Chakravarti**, University of Pittsburgh, Pennsylvania

- P.R. Billings, Harvard Medical School, Boston, Massachusetts: Genetics and behavioral disorders: What will be the consequences of identifying a major gene in alcoholism?
- E. Gordis, National Institute on Alcohol Abuse and Alcoholism, Rockville, Maryland: National Institute on Alcohol Abuse and Alcoholism and research on the genetics of alcoholism.

## Applications of Basic Research in Mammalian Development

**October 15 - October 18**

ARRANGED BY

**R.A. Pedersen**, University of California, San Francisco

**A. McLaren**, MRC Mammalian Development Unit, University College London, England

**N.L. First**, University of Wisconsin, Madison

### Keynote Address

N.L. First, University of Wisconsin, Madison: Application of gamete and embryo biotechnology to animal production.

### SESSION 1: Sex Determination

- A. McLaren, MRC Mammalian Development Unit, University College London, England: Sex determination in mice.
- P.S. Burgoyne, MRC Mammalian Development Unit,

University College London, England: Mammalian Y chromosome function in early embryos and male gametogenesis.

### SESSION 2: Gametogenesis

- A.R. Bellve, Columbia University College of Physicians & Surgeons, New York, New York: The thecins, a novel class of proteins associated with the sperm perinuclear matrix.
- C. Racowsky, Arizona State University, Tempe: Regulation of meiotic maturation in hamster oocytes.
- J. Eppig, The Jackson Laboratory, Bar Harbor, Maine: Growth and development of oocytes in vitro.



### SESSION 3: In Vitro Production of Embryos

P.M. Wassarman, Roche Institute of Molecular Biology,  
Nutley, New Jersey: Fertilization in mammals.

J.J. Parrish, University of Wisconsin, Madison: In vitro  
fertilization of laboratory and domestic species.

### SESSION 4: Cryopreservation of Germ Cells and Embryos

W.F. Rall, American Type Culture Collection, Rockville,  
Maryland: New approaches to the cryopreservation of  
mammalian embryos by vitrification.

J. Van Blerkom, University of Colorado, Boulder:  
Consequences of cryopreservation in oocytes and  
embryos.

### SESSION 5: Embryo Multiplication

R.S. Prather, University of Missouri, Columbia: Cloning by  
nuclear transfer in laboratory and domestic animal  
embryos.

V.E. Papaioannou, Tufts University School of Medicine,  
Boston, Massachusetts: Developmental regulation of half  
embryos.

### SESSION 6: Early Embryo Survival

D.G. Whittingham, MRC Experimental Embryology and  
Teratology Unit, St. George's Hospital Medical School,  
London, England: Genetic evaluation of embryos.  
H.J. Leese, Department of Biology, University of York,  
England: Assessment of embryo metabolism.

J. Butler, University of Idaho, Moscow: Metabolism during  
preimplantation development in farm animals.  
R. Wales, School of Veterinary Studies, Murdoch University,  
Western Australia: Energy metabolism during develop-  
ment and differentiation of sheep embryos.

### SESSION 7: Early Embryo Development

R.A. Pedersen, University of California, San Francisco:  
Origin and growth of the extraembryonic cell lineages in  
normal and parthenogenetic mouse embryos.  
S. Heyner, Albert Einstein Medical Center, Philadelphia,  
Pennsylvania: The insulin family of peptides: Expression  
and role in development.

J.D. Biggers, Harvard Medical School, Boston,  
Massachusetts: Regulation of pH in early mammalian  
embryos.  
D. Albertini, Tufts University School of Medicine: Role of  
cytoskeleton in early embryo development.

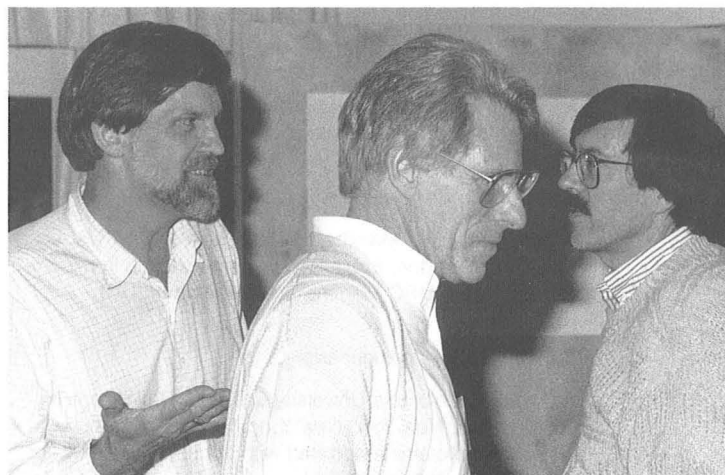
### SESSION 8: Gene Transfer in Laboratory and Domestic Species

K.M. Ebert, Tufts University School of Veterinary Medicine,  
North Grafton, Massachusetts: Present status of  
transgenic livestock.  
C. Spadafora, University of Rome, Italy: Sperm as vectors for  
producing transgenic mice.

J. Kopchick, Ohio University, Athens: Mutagenesis of the  
bovine growth hormone gene: Structure/function studies  
employing transgenic mice.

### SESSION 9: Sex Identification in Agriculture and Human Genetics

K.L. White, Louisiana State University, Baton Rouge: Identifi-  
cation of the sex of preimplantation mammalian embryos.  
A.H. Handyside, Royal Postgraduate Medical School,  
Hammersmith Hospital, London, England: Preimplantation  
diagnosis of human inherited disease.



A. Bellve,  
N. First,  
R. Pedersen

# Molecular Cytogenetics: Bridging the Resolution Gap

October 30 - November 2

ARRANGED BY

**F.S. Collins**, University of Michigan Medical School, Ann Arbor

**D.H. Ledbetter**, Baylor College of Medicine, Houston, Texas

**H.F. Willard**, Stanford University School of Medicine, California



M. Burmeister, K. Davies



T. Hassold, H. Cooke

## SESSION 1: Bridging Technologies

**Chairperson: F.S. Collins**, University of Michigan Medical School, Ann Arbor

M. Burmeister, University of California, San Francisco: Fine structure genetic analysis of human chromosomes by using radiation hybrid mapping.

D.C. Ward, Yale University School of Medicine, New Haven, Connecticut: High-resolution gene mapping by in situ hybridization.

B.J. Trask, Lawrence Livermore National Laboratory, California: Genomic distance estimated from the proximity of fluorescence in situ hybridization sites in interphase nuclei.

B. Horsthemke, University of Essen, Federal Republic of Germany: Microdissection and molecular analysis of human chromosome regions involved in contiguous gene syndromes.

K.E. Davies, John Radcliffe Hospital, Oxford, England: Physical mapping and microdissection in the fragile X region.

A.P. Monaco, Imperial Cancer Research Fund Laboratories, London, England: Human genome linking with cosmids and yeast artificial chromosomes.

## SESSION 2: Chromosome Structure

**Chairperson: H.F. Willard**, Stanford University School of Medicine, California

H. Cooke, MRC Human Genetics Unit, Western General Hospital, Edinburgh, Scotland: Human telomeres.

L. Clarke, University of California, Santa Barbara: Structure-function analysis of centromeric DNA in fission yeast.

H.F. Willard, Stanford University School of Medicine, California: Molecular studies of X-inactivation.

S.D.M. Brown, St. Mary's Hospital Medical School, London, England: Long-range genetic and physical mapping of mouse chromosomes.

P. Goodfellow, Lincoln's Inn Fields, London, England: Structure of the pseudoautosomal boundary.

## SESSION 3: Reverse Genetic Cloning Strategies

**Chairperson: B.S. Emanuel**, Children's Hospital of Philadelphia, Pennsylvania

F.S. Collins, University of Michigan Medical School, Ann Arbor: Lessons from the cystic fibrosis gene search.

B.S. Emanuel, Children's Hospital of Philadelphia, Pennsylvania: Molecular and cytogenetic studies of 22q11.

S.F. Warren, Emory University School of Medicine, Atlanta, Georgia: Isolation of human Xq28 within a somatic cell hybrid by fragile site-directed rearrangement: Application to saturational cloning and genome analysis.

## SESSION 4: Contiguous Gene Syndromes

**Chairperson: D.H. Ledbetter**, Baylor College of Medicine, Houston, Texas

U. Francke, Howard Hughes Medical Institute, Stanford University, California: Contiguous gene syndrome in the Xp21 region.

A. Ballabio, Baylor College of Medicine, Houston, Texas: Contiguous gene syndromes in the distal short arm of the human X chromosome.

R.L. Nussbaum, University of Pennsylvania, Philadelphia:

Identifying human genetic disease by map position:

Application of X-linked ophthalmological disease.

G.A. Bruns, The Children's Hospital, Boston, Massachusetts: Organization of the WAGR region.

D.H. Ledbetter, Baylor College of Medicine, Houston, Texas: Molecular dissection of the Miller-Dieker lissencephaly syndrome.

## SESSION 5: Origin and Mechanism of Chromosome Abnormalities

**Chairperson: T. Hassold**, Emory University Hospital, Atlanta, Georgia

T. Hassold, Emory University Hospital, Atlanta, Georgia: Parental origin effects: imprinting and the parental origin of chromosome abnormality.

R.D. Nicholls, University of Florida College of Medicine, Gainesville: Prader-Willi and Angelman syndromes: Are both parental contributions to chromosome 15q11q13 necessary for normal human development?

W. Reik, Institute of Animal Physiology and Genetics Research, Cambridge, England: Role of DNA methylation

in mammalian genome imprinting.

A. Chakravarti, University of Pittsburgh, Pennsylvania: Analysis of nondisjunction in Down's syndrome and ovarian teratoma.

C. Sapienza, Ludwig Institute for Cancer Research, Montreal, Canada: Genetics of genome imprinting.

J.G. Hall, University of British Columbia, Vancouver, Canada: Genomic imprinting: Relevance for human diseases.

# Control of HIV Gene Expression

November 7 - November 10

ARRANGED BY

**B.R. Cullen**, Howard Hughes Medical Institute, Duke University Medical Center, Durham, North Carolina

**R. Franza**, Cold Spring Harbor Laboratory, New York

**F. Wong-Staal**, National Cancer Institute, Bethesda, Maryland

## SESSION 1: HIV Rev Function

**Chairperson: B.R. Cullen**, Howard Hughes Medical Institute, Duke University Medical Center, Durham, North Carolina

C.A. Rosen, Roche Institute of Molecular Biology, Nutley, New Jersey: Regulation of HIV gene expression by *rev*.

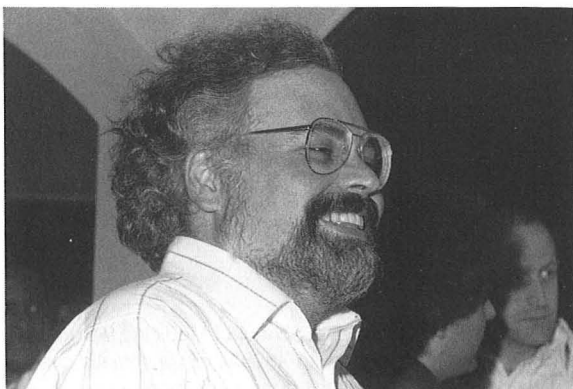
G.N. Pavlakis, NCI-Frederick Cancer Research Facility, Mary-

land: Transcriptional organization and regulation of HIV-1 expression.

J. Rusche, Repligen Corporation, Cambridge, Massachusetts: Biochemical characterization of HIV-1 *rev* interaction with the RRE.

M. Emerman, Fred Hutchinson Cancer Center, Seattle, Washington: Regulation of HIV envelope gene expression/mechanism of *rev* gene action.

M. Hatanaka, Kyoto University, Japan: Nucleolar targeting signals in HIV.



G. Pavlakis

## SESSION 2: HIV-1 *tat* Function

**Chairperson: F. Wong-Staal**, National Cancer Institute, Bethesda, Maryland

B.M. Peterlin, Howard Hughes Medical Institute, University of California, San Francisco: Activation and *trans*-activation of HIV.

A.P. Rice, Cold Spring Harbor Laboratory, New York: *tat* regulation of HIV-1 LTR-directed gene expression.

- A. Frankel, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Biochemistry, activity, and inhibition of the *tat* protein from HIV.
- K.T. Jeang, National Institutes of Health, Rockville, Maryland: Activation of the HTLV-1 and HIV-1 LTR by viral and cellular factors.
- A.J. Kingsman and S.M. Kingsman, University of Oxford, England: Activation of the HIV LTR by *tat* in *Xenopus* oocytes.

### SESSION 3: Other HIV Gene Products

**Chairperson: M.A. Martin**, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

- W. Haseltine, Dana-Farber Cancer Institute, Cambridge, Massachusetts: HIV-1 *vpr* gene function.
- M. Rosenberg, Smith Kline & French Laboratories, King of Prussia, Pennsylvania: Role of HIV-1 proteinases.
- L. Ratner, Washington University, St. Louis, Missouri: HIV regulation by *nef*.

- N. Sonenberg, McGill University, Montreal, Canada: Function of the *tar* sequence in posttranscriptional control of HIV-1 gene expression.
- M. Green, St. Louis University School of Medicine, Missouri: Functional *tat* protein domains and inhibition of viral gene.

### SESSION 4: Cellular Factors in HIV-1 Gene Regulation

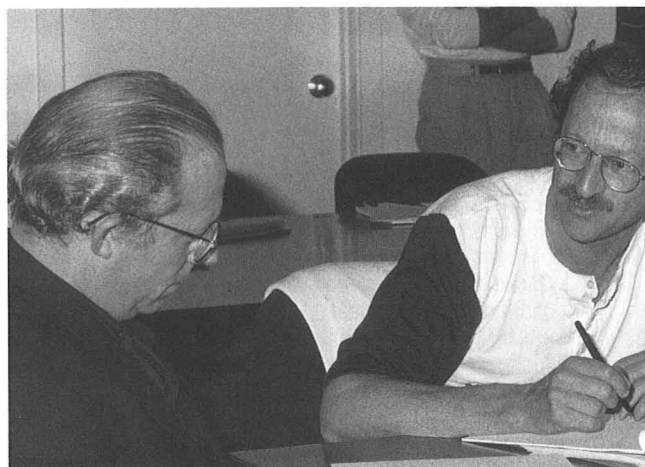
**Chairperson: R. Franza**, Cold Spring Harbor Laboratory, New York

- A.S. Fauci, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland: Effects of lymphokines on HIV-1 gene expression.
- G.J. Nabel, Howard Hughes Medical Institute, University of Michigan Medical Center, Ann Arbor: *kB* binding proteins: Heterogeneity and mechanisms of activation.
- R. Gaynor, University of California, Los Angeles, School of Medicine: Transcriptional regulation of HIV.
- A. Rabson, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland: Role of LTR regulatory sequences in HIV replication.
- M. Feinberg, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Mutational analysis of LTR function in HIV replication.
- E. Verdin, Free University of Brussels, Belgium: Identification of an inducible intragenic enhancer in HIV-1.
- I. Chen, University of California, Los Angeles, School of Medicine: HTLV gene regulation.

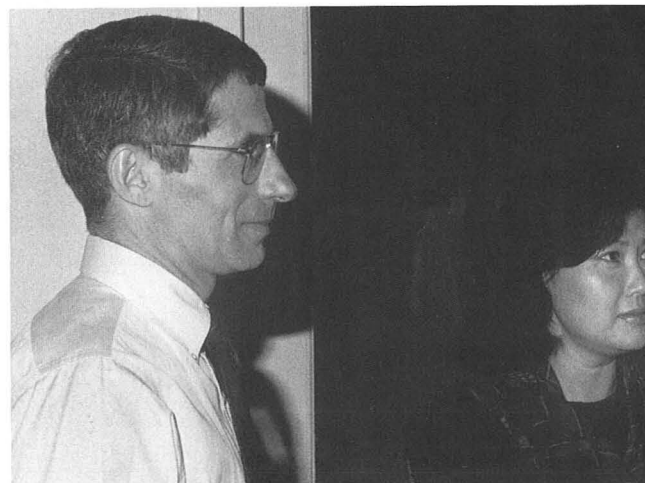
### SESSION 5: HTLV and Animal Lentiviruses

**Chairperson: M. Yoshida**, Cancer Institute, Tokyo, Japan

- W.C. Greene, Howard Hughes Medical Institute, Duke University Medical Center, Durham, North Carolina: Mechanism of HTLV-I *rex* action.
- J. Hauber, Sandoz Research Institute, Vienna, Austria: Functional analysis of the HTLV-1 *rex* gene regulation.
- J.E. Clements, John Hopkins University School of Medicine, Baltimore, Maryland: Regulation of gene expression of visna virus by *tat* and cellular factors involves AP-1 recognition sequences.
- D. Derse, National Cancer Institute, Frederick, Maryland: EIAV *tat* is structurally and functionally related to HIV and SIV *tat* proteins but lacks a methionine initiation codon.



W. Haseltine, H. Varmus



A. Fauci, F. Wong-Staal

# Mutation Induction and Heritability in Mammalian Germ Cells

November 12 - November 15

ARRANGED BY

**J.W. Allen**, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina

**M.J. Moses**, Duke University Medical Center, Durham, North Carolina

**L.B. Russell**, Oak Ridge National Laboratory, Tennessee

## SESSION 1: Germ-line Properties Affecting Mutation Induction and Recovery

**Chairperson: M.A. Handel**, University of Tennessee, Knoxville

L.D. Russell, Southern Illinois University, Carbondale:

Structural evidence for entry of substances into the seminiferous tubule.

I.B. Fritz, University of Toronto, Canada: Cell-to-cell interactions in the seminiferous tubule.

D.G. De Rooij, University of Utrecht, The Netherlands:

Relation between the proliferative activity of spermatogonial stem cells and their sensitivity to irradiation and adriamycin and to translocation induction.

M.A. Handel, University of Tennessee, Knoxville: Heritable

mutations in the analysis of spermatogenesis.

N.B. Hecht, Tufts University, Medford, Massachusetts:

Regulation of postmeiotic genes.

G. Sega, Oak Ridge National Laboratory, Tennessee:

Molecular targets, DNA breakage, DNA repair: Their roles in mutation induction in mammalian germ cells.

A. Wyrobek, Lawrence Livermore National Laboratory, California: Detection of specific locus mutation in human sperm.

## SESSION 2: Aberrant Chromosome Structure/Behavior

**Chairperson: M.J. Moses**, Duke University Medical Center, Durham, North Carolina

I.-D. Adler, GSF-Institut fuer Saeugetiergenetik, Neuherberg, Federal Republic of Germany: Clastogenic effects of acrylamide in different germ cell stages.

M.J. Moses, Duke University Medical Center, Durham, North Carolina: The synaptonemal complex as an indicator of chromosome damage.

J.W. Allen, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina: Mutagen effects on the synaptonemal complex.

M.E. Dresser, Oklahoma Medical Research Foundation, Oklahoma City: Structure-function relationships in meiotic chromosome behavior: An experimental approach.

B.F. Brandriff, Lawrence Livermore National Laboratory, California: Human sperm cytogenetics and the one-cell zygote.

M.T. Davisson, The Jackson Laboratory, Bar Harbor, Maine: Chromosome aberrations associated mutations: Effect on mapping new mutants.





### **SESSION 3: Variables Affecting the Rate and Nature of Mutations**

**Chairperson: L.B. Russell**, Oak Ridge National Laboratory, Tennessee

B.M. Cattanach, MRC Radiobiology Unit, Didcot, England:  
Factors affecting the recovery of mutations from mouse spermatogonial stem cells following X-irradiation.

J. Favor, GSF-Institut fuer Saeugetiergenetik, Neuherberg, Federal Republic of Germany: Mutagenic action of ENU in germ cells of the mouse as interpreted from specific locus mutation results.

S.E. Lewis, Research Triangle Institute, Research Triangle Park, North Carolina: Electrophoretically detected mosaic mutants in the mouse.

J. Peters, MRC Radiobiology Unit, Didcot, England:

Comparison of electrophoretic and specific locus mutation responses and analysis of glucose phosphate isomerase mutants in the mouse.

J.D. McDonald, McArdle Laboratory for Cancer Research, University of Wisconsin, Madison: Investigation of inborn errors of phenylalanine metabolism by efficient mutagenesis of the mouse germ line.

L.B. Russell, Oak Ridge National Laboratory, Tennessee: Relation of germ-cell stages to nature of induced mutations.

### **SESSION 4: Nonmutational Genetic Effects on Early Development**

**Chairperson: M.F. Lyon**, MRC Radiobiology Unit, Didcot, England

D. Solter, The Wistar Institute of Anatomy and Biology, Philadelphia, Pennsylvania: Genomic imprinting and mammalian development.

L.M. Wiley, University of California, Davis: A chimera embryo assay reveals a decrease in embryonic cellular proliferation induced by sperm from X-irradiated mice.

W.M. Generoso, Oak Ridge National Laboratory, Tennessee: Developmental anomalies: Mutational consequences of zygote exposure.

O. Smithies, University of North Carolina, Chapel Hill: Manipulation of the mouse genome by homologous recombination.

### **SESSION 5: Utilization of DNA Techniques in the Detection of Germ-line Mutations**

**Chairperson: H. Mohrenweiser**, Lawrence Livermore National Laboratory, California

H. Mohrenweiser, Lawrence Livermore National Laboratory, California: Detection of insertion, deletion, and rearrangement mutations in the genome.

B.W. Kovacs, University of Southern California School of Medicine, Los Angeles: Quantitation and characterization

of human germinal mutations at hypervariable loci.

N. Arnheim, University of Southern California, Los Angeles: Analysis of DNA sequences in individual gametes.

R. Woychik, Oak Ridge National Laboratory, Tennessee: Insertional mutagenesis in transgenic mice.

### **SESSION 6: Genetic Risk Estimation**

**Chairperson: W. Russell**, Oak Ridge National Laboratory, Tennessee

W. Russell, Oak Ridge National Laboratory, Tennessee: Problems and possibilities in genetic risk estimation.

V.L. Dellarco, U.S. Environmental Protection Agency, Washington, D.C.: Quantitative genetic risk assessment: Induction of heritable translocations by ethylene oxide as an example.

M.C. Cimino, U.S. Environmental Protection Agency, Washington, D.C.: Use of germ cell mutagenicity data at the U.S. Environmental Protection Agency.

J.B. Bishop, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina: Mammalian heritable effects research in the National Toxicology Program.

P.B. Selby, Oak Ridge National Laboratory, Tennessee: Importance of the direct method of genetic risk estimation and ways to improve it.

B.A. Bridges, MRC Cell Mutation Unit, University of Sussex, Brighton, England: Meeting summary.

## **Molecular Clocks of Evolution**

**November 28 - December 1**

ARRANGED BY

**D.J. Melnick**, Columbia University, New York, New York

**M. Goodman**, Wayne State University School of Medicine, Detroit, Michigan

**R.J. Britten**, California Institute of Technology, Corona del Mar

## **SESSION 1: Paleontological Calibration of Critical Taxonomic Branch Points with Particular Reference to Molecular Data**

**Chairperson: P.G. Gingereich**, University of Michigan, Ann Arbor

L.L. Jacobs, Southern Methodist University, Dallas, Texas:  
Geological dating and molecular clocks.

E.C. Olson, University of California, Los Angeles: Calibrations  
of ancient vertebrate origins.

J. Lake, University of California, Los Angeles: Origin of the  
multicellular animals.

E.S. Vrba, Yale University, New Haven, Connecticut: Using  
molecular and morphological evolutionary rates to study  
evolutionary processes in a group of mammals.

E. Mayr, Museum of Comparative Zoology, Harvard  
University, Cambridge, Massachusetts: General  
discussion.

## **SESSION 2: Specific Applications of Molecular Clocks**

**Chairperson: R.E. Pollack**, Columbia University, New York, New York

T. Gojobori, National Institute of Genetics, Mishima, Japan:  
Molecular evolutionary clocks of viral genes.

W.-H. Li, University of Texas, Houston: Molecular clocks and  
mammalian phylogeny.

R. Cann, University of Hawaii, Honolulu: Human mtDNA,

calibrating evolutionary rates, new technology for  
detecting natural selection.

V. Sarich, University of California, Berkeley: General  
discussion.

## **SESSION 3: Rate Variation within and between Genomes**

**Chairperson: W.M. Brown**, University of Michigan, Ann Arbor

J.R. Powell, Yale University, New Haven, Connecticut:  
Intragenomic heterogeneity in rates of DNA evolution in  
*Drosophila*; a note on DNA clocks in higher primates.

R.J. Britten, California Institute of Technology, Corona del  
Mar: Differences in rate of evolution between regions of  
the *Drosophila melanogaster* genome.

T.I. Bonner, National Institute of Mental Health, Bethesda,

Maryland: Evidence for unequal rates of DNA evolution  
in primates.

T. Ohta, National Institute of Genetics, Mishima, Japan:  
Nearly neutral mutations and the molecular clock.

T.H. Jukes, University of California, Berkeley: General  
discussion.

## **SESSION 4: The Effects of Selection on Rates of Molecular Evolution**

**Chairperson: M. Goodman**, Wayne State University School of Medicine, Detroit, Michigan

W.M. Fitch, University of Southern California, Los Angeles:  
When do clocks go wrong? How often? How badly?

M. Goodman, Wayne State University School of Medicine,  
Detroit, Michigan: Darwinian evolution and the accelera-  
tion/deceleration pattern in rates of mutation and fixation.

M. Riley, University of Massachusetts, Amherst: Effects of  
natural selection on nucleotide polymorphism.

M. Nei, University of Texas Health Science Center, Houston:  
Effects of positive and negative Darwinian selection on  
molecular clocks: Data from the MHC and immunoglobu-  
lin families.

E. Zuckerkandl, Linus Pauling Institute of Science and  
Medicine, Palo Alto, California: General discussion.



E. Olson, F. Ayala, H. Carson



R. Pollack, E. Mayr

**SESSION 5: Molecular Consequences of Behavior, Demography, and Biogeography**

**Chairperson: R.L. Honeycutt**, Texas A & M University, College Station

H.L. Carson, University of Hawaii, Honolulu: Hybridization of species may confound the molecular clock.

R. DeSalle, Yale University, New Haven, Connecticut: Hawaiian *Drosophila*: Biogeography and molecular clocks.

D.J. Melnick, Columbia University, New York, New York: Rapid rates of molecular change as a consequence of behavior and biogeography.

F.J. Ayala, University of California, Irvine: General discussion.

## Immunological Aspects of AIDS

**December 4 - December 7**

ARRANGED BY

**M. Oldstone**, Scripps Clinic and Research Foundation, La Jolla, California

**S. Putney**, Repligen Corporation, Cambridge, Massachusetts



**SESSION 1: HIV Genomic Variability**

**Chairperson: B.H. Hahn**, University of Alabama at Birmingham: Determinants of pathogenicity in naturally occurring strains of HIV-2.

S. Wain-Hobson, Institut Pasteur, Paris, France: Genetic variation of HIV-1 in vitro.

C.-Y. Ou, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Georgia: HIV evolution and transmission in infected persons.

G. Myers, HIV Sequence Database, Los Alamos, New Mexico: HIV protein pattern analysis.

S. Putney, Repligen Corporation, Cambridge, Massachusetts: Variation of the neutralizing determinants of HIV-1.

**SESSION 2: HIV-Cell Interactions**

**Chairperson: R.A. Weiss**, Chester Beatty Laboratories, London, England: HIV neutralization and interaction with receptors.

E.G. Engelman, Stanford University School of Medicine, California: Mechanisms responsible for CD4<sup>+</sup> T-lymphocyte dysfunction and depletion in HIV-injected patients.

M.A. Martin, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland: Structural and functional relations of the HIV envelope gene.

Y. Riviere, Institut Pasteur, Paris, France: Study of the primary cellular immune response to HIV-1, using recombinant vaccinia viruses.

M. Oldstone, Scripps Clinic and Research Foundation, La Jolla, California: Anatomy of CTL vaccine.

A.S. Fauci, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland: Cytokine modulation of HIV expression.

D.E. Mosier, Medical Biology Institute, La Jolla, California:  
Consequences of HIV infection of hu-PBL-SCID mice.

J.M. Coffin, Tufts University School of Medicine, Boston,  
Massachusetts: Genetic variation in retroviruses.

### SESSION 3: HIV-Immune System Interactions: Antibody

**Chairperson: J.J. Skehel**, National Institute for Medical Research, London, England

P.L. Nara, NCI-Frederick Cancer Research Facility, Maryland: HIV-1 neutralization: A humoral paradox.

J. Salk, The Salk Institute for Biological Studies, San Diego, California: Strategies for the control of HIV infection and/or disease using an envelope-depleted inactivated HIV immunogen.

R. De Mars, University of Wisconsin, Madison: A human mutant cell - gene transfer system for studying immune responses to HIV proteins.

D.D. Ho, University of California, Los Angeles, School of Medicine: Quantitation of HIV-1 in the blood of infected persons.

R.S. Fujinami, University of California, San Diego, La Jolla: Common determinant between HIV gp41 and human astrocytes.

### SESSION 4: HIV-Immune System Interactions: CTL

**Chairperson: M. Oldstone**, Scripps Clinic and Research Foundation, La Jolla, California

B.D. Walker, Massachusetts General Hospital, Boston: Specificity of HIV-1-reactive CTLs.

F. Gotch, Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, England: Are HIV-specific CTLs terminally differentiated in HIV-seropositive patients?

S. Koenig, National Institutes of Health, Bethesda, Maryland: Cell-mediated immunity in HIV-seropositive individuals.

J.A. Berzofsky, National Cancer Institute, NIH, Bethesda,

Maryland: Viral sequence variation and MHC polymorphism in immune control of virus and viral escape.

J.L. Whitton, Research Institute of Scripps Clinic, La Jolla, California: Virus sequence requirements for induction of cytotoxic and lymphocytes and for CTL-mediated antiviral immunity.

J. Chiller, Eli Lilly and Company, Indianapolis, Indiana: General discussion.

### SESSION 5: Viral Pathogenesis: Lessons from Animal Models

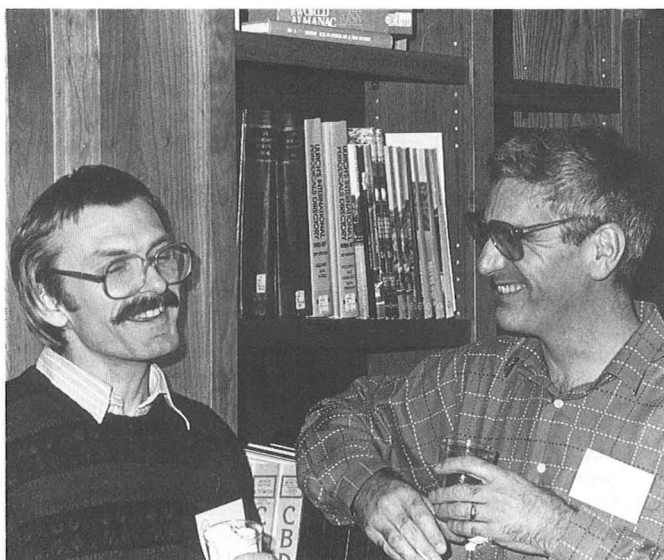
**Chairperson: O. Narayan**, Johns Hopkins University School of Medicine, Baltimore, Maryland: HIV-1 neutralization: A humoral paradox.

N.L. Letvin, Harvard Medical School, Southborough, Massachusetts: The CD8<sup>+</sup> lymphocyte response in SIV-infected rhesus monkeys.

J.N. Coffin, Tufts University School of Medicine, Boston, Massachusetts: Genetic variation in retroviruses.



J. Salk, S. Putney



S. Wain-Hobson, R. Weiss

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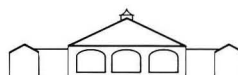
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## Banbury Center 1989 Publications from Meetings



A Banbury Center Meeting

### Banbury Reports

*Banbury Report 32* DNA Technology and Forensic Science  
*Banbury Report 33* Genetics and Biology of Alcoholism  
*Banbury Report 34* Biology of Mammalian Germ Cell Mutagenesis

### Current Communications in Molecular Biology

Cytoskeletal Proteins in Tumor Diagnosis  
The Pancreatic  $\beta$  Cell  
Therapeutic Peptides and Proteins  
Plant RFLPs  
Polymerase Chain Reaction  
Molecular Genetics of Early *Drosophila* and Mouse Development  
Recessive Oncogenes and Tumor Suppression  
Viral Proteinases as Targets for Chemotherapy

### Other Titles

Applications of Basic Research in Mammalian Development

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Environmental Protection Agency	Mutation Induction and Heritability in Mammalian Germ Cells	1989	45,000*
<b>OFFICE OF NAVAL RESEARCH</b>	Computational Eye Movement Workshop	7/88-6/91	62,125
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