

Mechanisms of DNA Damage and Repair

Implications for Carcinogenesis and Risk Assessment

June 2-7, 1985

DNA is the Beginning and the End

Held at: National Bureau of Standards Gaithersburg, Maryland

Program

Sunday, June 2, 1985

7:00—9:00 p. m.—Reception/Registration
Gaithersburg Marriott

Program Sessions

Monday, June 3, 1985

9:00 a. m.—Welcome

Introduction

- Sanford A. Miller, Ph. D., Director
Center for Food Safety and Applied Nutrition
Food and Drug Administration, Washington,
D. C.
- David P. Rall, M. D., Ph. D. Director
National Institute of Environmental Health
Sciences
Research Triangle Park, NC
- Richard H. Adamson, Ph. D.
National Cancer Institute
National Institute of Health, Bethesda, MD

Mechanisms of DNA Damage

Section Chairman, George Scholes, Ph. D., D.
Sc. U. Newcastle on Tyne,
England

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Session I

Kinetics and Mechanisms of
Free Radical Damage to DNA

Chairman: D. Schulte-Frohlinde, Ph. D. Max-
Planck Institute, Mulheim ad Ruhr,
West Germany

Bacteriophage DNA as a Model for Correlation
of Free Radical Damage to DNA and Biological
Effects—J. Block, Free University, Amsterdam,
Holland

Free Radical Mechanisms of DNA Base
Damage — M. G. Simic, National Bureau of
Standards, Gaithersburg, MD

Fast Reaction Between Thiols and DNA Strand
Break Precursors in Irradiated Cells—B. D.

Michael, Gray Lab, Northwood, England
Comparison of Mechanisms for DNA Strand
Break Formation by OH Radical and Direct

Effect of Radiation—D. Schulte-Frohlinde, Max
Planck Institute West Germany

1:00—LUNCH

Session II

2:00 p. m.

DNA Binding Agents

Chairman: J. W. Lown, Ph. D.

University of Alberta, Canada

Co-Chairman: J. B. LePecq, Ph. D.

Institute Gustave-Roussy, Fra-
nce

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DNA Binding Agents—Introductory
Remarks—J. W. Lown, University of Alberta
Canada

Novel Mono-, Bis-, and Tris-intercalators in
DNA—J. B. LePecq, Institute Gustave-Roussy,
Villejuif, France

Novel Types of DNA-Sugar Damage in
Neocarzinostatin Cytotoxicity and
Mutagenesis—I. H. Goldberg, Harvard U.
Medical School, Boston, MA

Rational Design of DNA Groove Binding
Anticancer Drugs—R. E. Dickerson, UCLA,
Los
Angeles, CA

Tuesday, June 4, 1985

Session III

9:00 a. m.

DNA Damage by Drugs and Chemicals

Chairman: Kurt W. Kohn, Ph. D.
National Cancer Institute,
Bethesda, MD

DNA Modification by Nitrosourea and Sulfur
Mustards and Repair of These Lesions—D. B.
Ludlum, Albany College of Medicine,
Albany, NY

Measurements and Significance of
Macromolecular DNA Lesions: Strand Breaks
and Crosslinks—K. W. Kohn, National Cancer
Institute, Bethesda, MD

Genome Localization of DNA Damage by
Carcinogens—G. N. Wogan, Massachusetts
Institute of Technology, Cambridge, MA

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Sequence Specificity of Drugs That Bind
Covalently in the Minor Groove of DNA—L.
Hurley, U. of Texas, Austin, TX

Pro-oxidant States and Tumot Promotion—
P. A. Cerutti, Swiss Institute for Experimental
Cancer Research, Lausanne, Switzerland

1:00 p. m.—LUNCH

Session IV

2:00 p. m.

DNA Damage in Cells

Chairman: John F. Ward, Ph. D.
University of California
San Diego, CA

Radiation Damage to DNA in Non-Dividing
Tissue. Yields of Damage, Rates of Repair and
Consequences of Long-term Non-repaired
Damage—J. T. Lett, Colorado State University
Fort Collins, CO

Radiation Damage to DNA in Various Animal
Tissues. Comparison of Yields and Repair In
Vivo and In vitro—R. E. Meyn, Jr., M. D.
Anderson Hospital, Houston, TX

Damage Caused by Alkylating Agents, Relative
Yields, Relative Rates of Repair and
Consequences to Biological End-points—K. E.
Erixon, University of Stockholm, Stockholm,
Sweden

Immediate and Repair Induced DNA Double
Strand Breaks in Mammalian Cells—P. E.
Bryant, Abteilung für Biophysikalische
Strahlenforschung, Frankfurt am Main, West
Germany

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Poster Symposium

DNA and Protein Crosslinks

Chairman and Rapporteur: (To Be Announced)

Wednesday, June 5, 1985

9:00 a. m.

DNA Repair and Consequences

Section Chairman: Lawrence Grossman, Ph. D.
Johns Hopkins University
Baltimore, MD

Session V

Repair of Bulky Adducts in DNA

Chairman: Lawrence Grossman, Ph. D.
Johns Hopkins University
Baltimore, MD

Regulation of Excision Repair in Prokaryotes—
David Mount, University of Arizona, Tucson,
AZ

Characterization of Non-induced Excision Re-
pair
Systems in Bacteria—Robert Grafstrom,
Frederick Cancer Research Center, Frederick,
MD

Characterization of Inducible Excision Repair
Systems in Bacteria—Lawrence Grossman,
Johns Hopkins University, Baltimore, MD

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Thursday, June 6, 1985

Session VII

9:00 a. m.

Program

Repair of Mismatched Bases in DNA—Paul
Modrich, Duke University, Durham, NC
Characterization of Eukaryotic Repair Genes—
Errol Friedberg, Stanford University School of
Medicine, Stanford, CA

1:00 p. m.—LUNCH

Session VI

2:00 p. m.

Repair of Alkylation and Oxidation Damage in DNA

Chairman: Tomas Lindahl, M. D.
Imperial Cancer Research Fund
London, England

Adaptation of Bacterial and Mammalian Cells
to

Alkylation Damage—Leona Samson, Harvard
School of Public Health, Boston, MA

Enzymatic Mechanisms of Repair of Damaged
DNA—Tomas Lindahl, Imperial Cancer
Research Fund, London, England

Replication Mechanisms Through Apurinic
Sites—Lawrence Loeb, University of
Washington, Seattle, WA

Repair Mechanisms Responding to Metabolic
Alterations—Bernard Weiss, Johns Hopkins
University, Baltimore, MD

6:00 p. m.—Banquet
Smokey Glen Farm

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Session VIII

Measurement of Exposure to Genotoxic Compounds

Correlations Between DNA Damage Mutagenesis and Carcinogenesis

Chairman: Franklin Hutchinson, Ph. D.
Yale University
New Haven, CT

DNA Repair and Mutagenesis—M. Radman,
Inst. Jacques Monod, U. Paris, France

Sequence Specificity of Mutagenesis by Various
Agents—F. Hutchinson, Yale University, New
Haven, CT

Activation of ras Oncogenes by Chemical
Carcinogens—M. Barbacid, National Cancer
Institute, Frederick Cancer Research Center,
Frederick, MD

Activation of the myc Oncogenes—M. Cole,
Princeton University, Princeton, NJ

1:00 p. m.—LUNCH

Risk Assessment

2:00 p. m.

Section Chairman: Arthur D. Upton, M. D.
Institute of Environmental
Medicine, New York Univer.
sity Medical Center
New York, NY

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Background Levels of DNA Damage in the
Population—R. L. Saul and B. N. Ames,
University of California, Berkeley, CA

DNA Damage as an Indication of Carcinogen
Risk Assessment—R. M. Santella and F. Perera,
ICR, Columbia University, NY

Chairman: Steven R. Tannenbaum, Ph. D.
Massachusetts Institute of Techno-
logy
Cambridge, MA

Measurement of DNA Adducts from Aromatic
Amines—Fred Kadlubar, National Center for
Toxicological Research, Jefferson, AR

Mutational Spectra in Human Blood Cells as a
Means to Recognize Specific Exposure—
William G. Thilly, MIT, Cambridge, MA

Blood Proteins as Alkylation Dosimeters—
Steven R. Tannenbaum, MIT, Cambridge, MA

Urinary N-nitroso Amino Acids as Indices of
Endogenous Formation of N-nitroso
Compounds—Helmut Bartsch, IARC, Lyon,
France

Monoclonal Antibodies for Detection of
Carcinogens and Their Adducts—John
Groopman, Boston University School of Public
Health, Boston, MA

Friday, June 7, 1985

Session IX

9:00 a. m.

Scientific Basis for Genotoxic Risk Assessment

Chairman: Peter N. Magee, M. D.
Temple University
Philadelphia, PA

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Session XI

Risk Assessment in Legal Decision Making for Food

Chairman: W. Gary Flamm, Ph. D.
Center for Food Safety and Applied

Interpretation of Genotoxicity Data in Assessing the Risks of Genetic Diseases—C. L. Denniston, University of Wisconsin, Madison, WI

The Role of Pharmacokinetics in Risk Assessment—R. H. Reitz and P. G. Watanabe, Dow Chemical Company, Midland, MI

1:00 p. m.—LUNCH

Session X

2:00 p. m.

Risk Assessment and Regulatory Decisions

**Chairman: Bernard D. Goldstein, M. D.
Environmental Protection Agency
Washington, D. C.**

Use of Models in Low-dose Extrapolations—J. Van Ryzin, Columbia University, NY

Problems in Inter-species Extrapolation—R. Wilson, Harvard University, Cambridge, MA

The Time-to-Tumor Approach in Risk Assessment and Risk Management—R. E. Albert, New York University Medical Center, NY

Nutrition

**Food and Drug Administration
Washington, D. C.**

Poster Session

Persons interested in presenting a poster paper should send in an nnfolded abstract before April 15, 1985. Abstracts should be typed with a 12 pitch typewriter, single spaced on $8\frac{1}{2} \times 11$ inch paper. The length (including text, references, acknowledgements, title, author's names and affiliations) should be one page. Figures are permitted if included in the text. Each poster presenter will have a 3 foot wide by 7 foot high free standing surface for display.