Contents

Asterisks preceding the title refer to studies in humans.

2537 Carcinogenesis—Cellular Evolution as a Unifying Thread: Presidential Address. Emmanuel Farber.


2579 Effects of Whole Blood or Albumin Fraction from Tumor-bearing Rats on Liver Protein Synthesis. Milton Toporek.


2596 Perturbation of Leukemic Cell Population in AKR Mice Due to Chemotherapy. Mitsuhiro Ornine and Seymour Perry.


2624 * Nuclear Binding of Tritiated Actinomycin in Basal Cell Carcinoma and in Normal Human Epidermis. M. Heenen, A. M. Preumont, and P. Galand.

2627 The WIRL-3 Rat Liver Cell Lines and Their Transformed Derivatives. Leila Diamond, Rosemary McFall, Yutaka Tashiro, and David Sabatini.

2637 Effects of Dimethylbenz(a)anthracene and Dihydrotestosterone on Estradiol-17β Binding in Rat Mammary Cytosol Fraction. David D. Keightley and Allan B. Okey.

2643 Morphology and Growth, Tumorigenicity, and Cytogenetics of Human Neuroblastoma Cells in Continuous Culture. June L. Biedler, Lawrence Helson, and Barbara A. Spengler.


2662 Delayed Hematological Recovery after Cyclophosphamide Treatment in the Presence of an Advanced Tumor. William D. DeWys and James M. Mansky.


2677 Blastogenic Response of Lymphoid Cells to Tumor Cells or Tumor Membrane Extracts in Vitro. S. P. Poon and M. N. Cauchi.

2683 * Abnormalities of Platelet Function in Patients with Polycythemia Vera. Sam Berger, Louis M. Aledort, Harriet S. Gilbert, John P. Hanson, and Louis R. Wasserman.

2692 * Analysis of Tissue Esterases from Patients with Hodgkin's Disease and Other Types of Advanced Cancer by Isoelectric Focusing in Acrylamide Gel.

Charles W. Young and Edward S. Bittar.

2701 Effects of Varying the Exposure to Phenytoin on Its Enhancement of 2-Acetylaminofluorene-induced Hepatic Tumorigenesis in the Rat.

Carl Peraino, R. J. Michael Fry, Everett Staffeldt, and Walter E. Kiesielecki.

2706 In Vitro Binding of 63Ga to L1210 Cells.


2714 Some Properties of Adenyl Cyclase from Ehrlich Tumor Cells.

Björn E. Wikström and Gunnar K. Agren.

2721 The Content of the Principal Protein Target of a Hepatic Carcinogen in Liver Tumors.

David M. Mott, Brahma P. Sani, and Sam Sorof.

2726 The Effects of Counting Threshold and Emulsion Exposure Duration on the Percent-labeled Mitosis Curve and Their Implications for Cell Cycle Analysis.

S. E. Shackney, S. S. Ford, and A. B. Wittig.

2732 * The Response of Synchronized Human Lymphoma Cells to Bleomycin and 1,3-Bis(2-chloroethyl)-1-nitrosourea.

B. Drewinko, Barry W. Brown, and J. A. Gottlieb.

2737 Two-Dimensional Gel Electrophoresis of Acid-soluble Nucleolar Proteins of Walker 256 Carcinosarcoma, Regenerating Liver, and Thioacetamide-treated Liver.

N. Raghuveera Ballai and Harris Busch.

2744 Methylhydrazine Tumorigenesis in Syrian Golden Hamsters and the Morphology of Malignant Histioctyotomas.

Bela Toth and Hidesuke Shimizu.

2754 A Growth-stimulating Factor Released by Cultured Mouse Mammary Tumor Cells.

B. K. Nair and K. B. DeOme.

2761 * Isolation and Characterization of Plasma Membranes from Human Leukemic Lymphocytes.

D. Marique and J. Hildebrand.

2768 Spontaneous Tumors in Sprague-Dawley Rats and Swiss Mice.


2774 Elevated Sterol Synthesis in Lymphocytic Leukemia Cells from Two Inbred Strains of Mice.


2779 In Vitro Transformation of Submandibular Gland Epithelial Cells and Fibroblasts of Adult Rats by Methylcholanthrene.

Ashley M. Brown.

2780 Collagenolytic Activities of Squamous Cell Carcinoma of the Skin.

Ken Hashimoto, Yuji Yamanishi, Edgar Maeyens, Mustafa K. Dabbous, and Tamotsu Kanzaki.

2802 Distribution of Radioactivity and Metabolism of Formic Acid 2-[4-(5-Nitro-2-furyl)-2-14C-2-thiazolyl]hydrazide following Oral Administration to Rats and Mice.

Samuel M. Cohen, Arthur Alter, and George T. Bryan.

2810 * N-Demethylation of the Antineoplastic Agent Hexamethylmelamine by Rats and Man.

John F. Worzalla, Bruce M. Johnson, Guillermo Ramirez, and George T. Bryan.

2816 * Distribution of Kinase and Deaminase of 1-β-D-Arabinofuranosylcytosine in Tissues of Man and Mouse.

Dah Hsi Wang Ho.

2821 The Blood Group A-like Site on the Carcinoembryonic Antigen.

J. Michael Gold and Phil Gold.

2825 Adenosine Formation and Metabolism during Adenosine Triphosphate Catabolism in Ehrlich Ascites Tumor Cells.

Christopher A. Lomax and J. Frank Henderson.

2830 Reversal by Melatonin of the Effect of Pinealectomy on Tumor Growth.


2834 Effects of Camptothecin on the Breakage and Repair of DNA during the Cell Cycle.

Susan B. Horwitz and Marshall S. Horwitz.

2837 Binding of 3H-Labeled Benzo[a]pyrene to DNA in Hamster Tracheal Epithelial Cells.

David G. Kaufman, Valerio M. Genta, Curtis C. Harris, Joseph M. Smith, Michael B. Sporn, and Umberto Saffiotti.

2842 Localization of Benzo[a]pyrene-3H and Alterations in Nuclear Chromatin Caused by Benzo[a]pyrene-Ferric Oxide in the Hamster Respiratory Epithelium.

Curtis C. Harris, Joseph M. Smith, Michael B. Sporn, and Umberto Saffiotti.

2849 The Effect of Bleomycin on Survival and Tumor Growth in a C3H Mouse Mammary Carcinoma.

Muneyasu Urano, Nobuo Fukuda, and Sachiko Koike.

2856 The Role of Thymidylate Synthetase Inhibitors in Bromodeoxyuridine-induced Neoplasia in Drosophila.

Rose M. Rizki and T. M. Rizki.

2862 Changes in Glycosaminoglycans of AH-130 Ascites Tumor after Treatment with Cyclophosphamide and Vitamin A.

Toshihiko Suematsu, Nobuto Nakamura, Takekawa Kamada, and Hiroshi Abe.

2867 Inhibition of Purine Nucleotide Metabolism by 6-Methylthiopurine Ribonucleoside and Structurally Related Compounds.

2972 Differences in RNA Formation and Polyribosome Content of AKR Leukemic Cells

2894 The Carcinogenic Activity of 3-Hydroxy-3-Methyl-1-[[(3-Nitro-2-furyl)allylidene]-amino]hydantoin in Rats.

2984 The Basis for the Disparate Sensitivity of LI-210 Leukemia and Walker 256 Carcinoma to a New Triazine Folate Antagonist.

2987 Localization of Human GW-39 Tumors in Hamsters by Radiolabeled Heterospecific Antibody to Carcinoembryonic Antigen.

2983 Microsomal Metabolism of Dimethylnitrosamine and the Cytochrome P-450 Dependency of Its Activation to a Mutagen.

2977 The Effect of Aflatoxin B1 on the Hepatic Structure and RNA Synthesis in Rats Fed a Diet Marginally Deficient in Choline.

2886 Enhancement of Normal Lymphocyte Cytotoxicity by Sera with High Antibody Titers against H-2 or Virus-associated Antigens.

2872 Enhancement of Adenovirus Transformation of Hamster Cells by TV-Methyl-\(\text{N}'\)-Nitro-\(\text{N}'\)-Nitro-1-Amino-1(3-(5-Nitro-2-Furyl)allylidene)hydantoin in Rats.

2903 Specific Estrogen Binding in Vivo in the R3230-AC Mammary Adenocarcinoma of the Rat.

2913 Increased Sialic Acid Density in Surface Glycoprotein of Transformed and Malignant Cells—a General Phenomenon?

2923 Catabolism of Nuclear Proteins in Control and Phytosterol-stimulated Human Lymphocytes, Leukemic Leukocytes, and Burkitt Lymphoma Cells.


2923 Insulin Reversal of Growth Inhibition of Plasma Cell Tumor by Prostaglandin or Adenosine 3',5'-Monophosphate.

2939 Prophylaxis of Spontaneously Developing Mammary Carcinoma in C3H/HeJ Female Mice by Suppression of Prolactin.

2947 Spectrophotometric Analysis of Cytochromes in Morris Hepatomas.

2954 Correlations between Cytotoxicity, Biochemical Effects, Drug Levels, and Therapeutic Effectiveness of Daunomycin and Adriamycin on Sarcoma 180 Ascites in Mice.

2959 Polyamine Content of AKR Leukemic Cells in Relation to the Cell Cycle.

2965 Differences in RNA Formation and Polyribo-some Metabolism in Serum-starved Normal and Transformed Cells.

2977 The Effect of Aflatoxin B1 on the Hepatic Structure and RNA Synthesis in Rats Fed a Diet Marginally Deficient in Choline.

2886 Enhancement of Normal Lymphocyte Cytotoxicity by Sera with High Antibody Titers against H-2 or Virus-associated Antigens.

2872 Enhancement of Adenovirus Transformation of Hamster Cells by TV-Methyl-\(\text{N}'\)-Nitro-\(\text{N}'\)-Nitro-1-Amino-1(3-(5-Nitro-2-Furyl)allylidene)hydantoin in Rats.

2903 Specific Estrogen Binding in Vivo in the R3230-AC Mammary Adenocarcinoma of the Rat.

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2923 Catabolism of Nuclear Proteins in Control and Phytosterol-stimulated Human Lymphocytes, Leukemic Leukocytes, and Burkitt Lymphoma Cells.


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Aflatoxin is a historical landmark in chemical carcinogenesis. It is a potent environmental carcinogen from "natural" sources rather than from industrial contaminants or synthetic chemistry.

In 1961, there occurred two epizootic outbreaks. In England, thousands of turkey poults, ducklings, and chicks died of hepatic necrosis. In the northwestern United States, rainbow trout, the favorite game fish of the region, died with hepatomas. Initially, there was no evident relationship between these outbreaks (cf. Advan. Cancer Res., 8: 191, 1964).

The fowl epidemic of hepatotoxicity was traced quickly to food sources, then to peanut meal, and finally to the contamination of the food by a common fungus, *Aspergillus flavus*. M. C. Lancaster, F. P. Jenkins, and J. McL. Philp, of the Unilever Laboratories in England, fed rats with food containing the toxic material and, in 6 months, 9 of 11 survivors developed hepatomas (Nature, 192: 1095, 1961).

Two teams of chemists, one in England (Nature, 195: 1062, 1962) and the other in the United States (J. Am. Chem. Soc., 85: 1706, 1963), isolated and identified the active chemicals, the aflatoxins (*A. flavus* toxins). These compounds, on a molecular-weight basis, are among the most active hepatocarcinogens in the rat; they produce sarcomas at the site of s.c. injection and have other carcinogenic effects.

Hepatomas in trout also were rapidly related to food sources. Fractionation of fish diets for the carcinogen was initiated by John E. Halver at the Western Fish Nutrition Laboratory of the United States Department of Interior at Cook, Washington. Isolation of aflatoxin from *A. flavus* contamination of poultry food kept under warm, humid conditions pointed to this possibility of a similar etiology of trout hepatomas.

To test this relationship, concurrent experiments were arranged. Hepatomagenic fish diets were sent to Gerald N. Wogan at the Massachusetts Institute of Technology, Cambridge, Massachusetts, for analysis for aflatoxin, and aflatoxin was likewise sent to Dr. Halver for feeding to trout. Crystalline aflatoxin B, prepared by Wogan produced hepatomas in rainbow trout, and there was an almost perfect relationship between the appearance of hepatomas in trout and the aflatoxin content in the food (J. E. Halver and I. A. Mitchell, eds. In: Trout Hepatoma. Research Conference Paper 70, United States Department of the Interior, Bureau of Sports, Fisheries and Wildlife, Washington, D. C., 1967). Hepatomas were later produced in the rat and duckling.

Epidemiological investigations in Africa by M. E. Alpert et al. (Cancer, 28: 253, 1971) and in Thailand by R. C. Shank et al. (Food Cosmet. Toxicol., 10: 171, 1972) show correlations between the prevalence of hepatoma in man and the aflatoxin levels in the food. Aflatoxicosis thus appears to be an important environmental carcinogenic hazard in man.

The historical events and developments are presented in *Mycotoxins in Foodstuffs* (MIT Press, Cambridge, Mass., 1964). Pictured are M. C. Lancaster, b. 1930 (upper left), John E. Halver, b. 1922 (right), and Gerald N. Wogan, b. 1930 (lower left), who are among the many key investigators of aflatoxin, especially its carcinogenic aspects. The structural formula of aflatoxin B, and a photomicrograph of a trout hepatoma are also included.