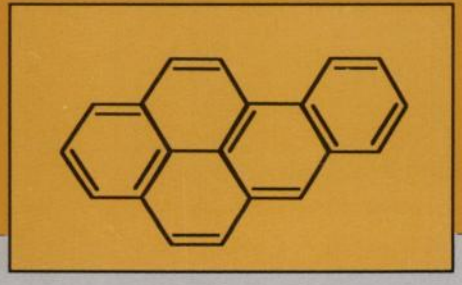
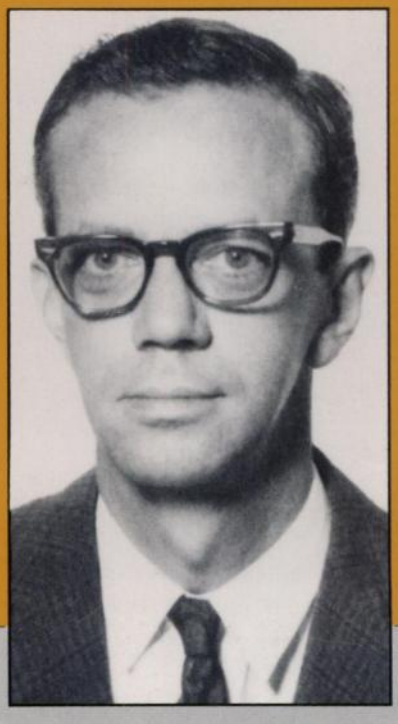
Cancer Research

VOLUME 47 • NO. 21 CNREA 8 • PP 5517–5807

November 1, 1987





Epidemiology and Cancer Registries in the Pacific Basin
—See Epidemiology Section

GRANTS AVAILABLE

for

Research on the Resistance of Human Tumors to Chemotherapeutic Agents

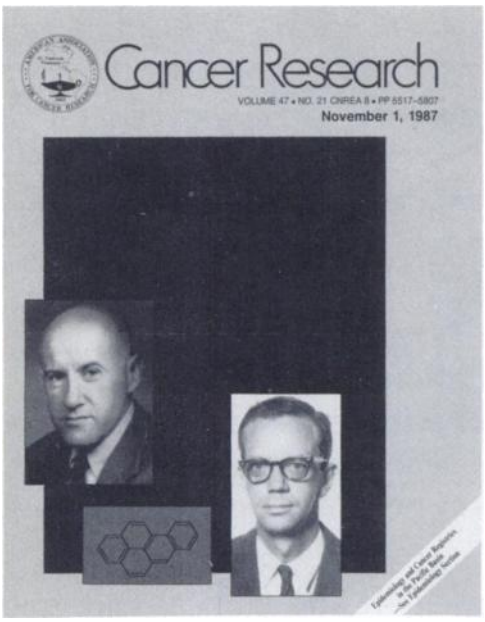
Bristol-Myers Company is pleased to announce a $16,000,000 drug resistance research funding program. The goal of this research program is to identify the mechanisms by which human tumors become resistant to chemotherapy and to develop and test methods of overcoming such resistance. Grants will be awarded in two categories. Laboratory grants will be $100,000 per year for five years. Five year grants of $200,000 per year will be awarded for research which directly tests laboratory findings in human trials.

Applications are invited from qualified investigators worldwide. Applicants may be associated with academic institutions, research institutes, government laboratories or other facilities capable of conducting these types of investigations. Applications will not be accepted from individuals affiliated with or employed in the pharmaceutical industry or engaged in for-profit research.

Applications will be accepted until January 1, 1988 and will then be reviewed by a panel of experts, independent of Bristol-Myers. Awards will be announced on or about April 1, with funding commencing July 1, 1988. Additional information about this program can be obtained by writing:

Mr. Gary Doyle
Program Coordinator
Bristol-Myers Company
5 Research Parkway
P.O. Box 5100
Wallingford, CT 06492-7660
U.S.A.

COVER LEGEND



Cigarette smoking was first established as the major cause of human lung cancer by the epidemiological studies of Wynder and Graham (JAMA, *143:* 329–336, 1950) and of Doll and Hill (Br. Med. J., *2:* 739–748, 1950). The landmark study in experimental tobacco carcinogenesis was the induction of squamous carcinoma of the skin in mice exposed to tobacco tars by skin application (Wynder, Graham, and Croninger. Cancer Res., *13:* 855–864, 1953). These experiments provided the stimulus to organic chemists for a study of the chemical composition of tobacco tar, a complex mixture of chemicals, with the aim of isolating and characterizing its carcinogenic chemicals. Based on characterization by ultraviolet absorption, fluorescence excitation, and emission spectra, Benjamin L. Van Duuren fractionated cigarette tars and isolated by paper chromatography 21 aromatic hydrocarbons, 6 of which were known carcinogens (J. Natl. Cancer Inst., *21:* 1–16, 1958; J. Natl. Cancer Inst., *21:* 623–630, 1958). This list was extended and quantitated by Hoffmann and Wynder [Cancer Res., *13:* 1062–1073, 1960; Cancer (Phila.), *15:* 93–102, 1962]. These early experimental studies on aromatic hydrocarbons as environmental carcinogens from air, water, and other sources are today extended routinely by use of modern instrumentation including gas chromatography, liquid chromatography, and mass spectrometry.

The low concentration of aromatic hydrocarbons in cigarette tars could not account for the observed carcinogenicity in mouse skin, as was shown by Van Duuren (J. Natl. Cancer Inst., *21:* 623–630, 1958) and Leo Orris and coworkers (J. Natl. Cancer Inst., *21:* 557–561, 1958). This led to a search for other carcinogens and cocarcinogens in tobacco tars. Notable among these are aliphatic nitroso compounds and *N'*-nitrosonornicotine (Hoffmann, Dong, and Hecht. J. Natl. Cancer Inst., *58:* 1841–1844, 1977; Brunnerman, Yu, and Hoffmann. Cancer Res., *37:* 3218–3222, 1977).

Van Duuren detected cocarcinogenic agents in tobacco tars at concentrations much higher than benzo(*a*)pyrene and related aromatic hydrocarbons in mouse skin experiments (J. Natl. Cancer Inst., *57:* 703–705, 1973). Remarkable in their potency are catechol, pyrene, fluoranthene, and undecane. These compounds are not carcinogenic and are not tumor promoters in classical two-stage experiments. However, they markedly enhance the carcinogenicity of benzo(*a*)pyrene in mouse skin experiments in which carcinogen and cocarcinogen are applied repeatedly and simultaneously. In humans, the same simultaneous exposure to carcinogens and cocarcinogens occurs in cigarette smoking and is undoubtedly responsible for the enormous toll of lung cancer.

The photographs, taken during the 1950s, show Orris (*left*) and Van Duuren (*right*). The structure of benzo(*a*)pyrene is also shown.