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AACR Employment Register Forms Inside

CANCER RESEARCH HAS A NEW ADDRESS

Please note that the Cancer Research Editorial Office, along with the American Association for Cancer Research Headquarters Office, has moved its location. Effective September 12, 1988, our new address and phone number are:

Cancer Research Editorial Office
530 Walnut Street
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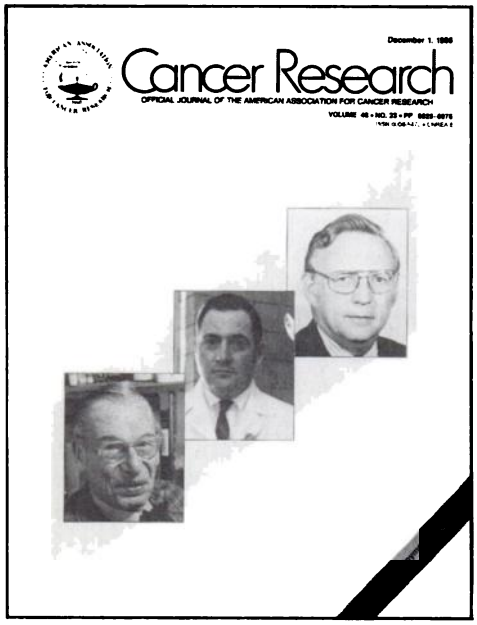
Send all future correspondence, including new submissions, revised manuscripts, page proofs of articles, and letters, to us at the above address.

COVER LEGEND



One of the ironies of nature is the manner in which protective mechanisms, developed over eons of evolution against the multitudes of toxic agents to which organisms are exposed, can be subverted to cause cancer. We now know that a number of nonspecific enzymes are responsible for the oxidation of endogenous substrates, such as steroids, hormones, fatty acids, and biogenic amines, and a wide range of xenobiotic substances that includes many drugs, nitrosamines, and polycyclic aromatic hydrocarbons the oxidation products of which are carcinogenic. The discovery and identification of the functional role of these enzymes are therefore of historical importance.

In the presence of an oxidizable substrate, together with the flavoprotein enzyme cytochrome reductase and NADPH, substrates are oxygenated, usually to hydroxides or epoxides; these may be active carcinogens, capable of binding to DNA and thereby initiating neoplasia. Many other enzymes have been implicated in the hydroxylation of both endogenous and xenobiotic substrates. One of these is the mixed function oxidase cytochrome P-450, so named by Omura and Sato (J. Biol. Chem., *237:* 1375–1376, 1962), because it combines with carbon monoxide to form an inactive adduct with an absorption band at 450 nm. The inactive coadduct is most efficiently dissociated by light of the same wavelength, with restoration of activity. Cytochrome P-450 is located in microsomes, the cellular organelles formed by mechanical disruption of the endoplasmic reticulum and separable from other particulate components by differential centrifugation.

The functional significance of cytochrome P-450 in microsomal oxidation was first discovered by a team headed by David Y. Cooper, Otto Rosenthal, and Ronald W. Estabrook at the Harrison Department of Surgery and the Johnson Foundation of the University of Pennsylvania [R. W. Estabrook, D. Y. Cooper, and O. Rosenthal, Biochem. Z., *388:* 74–75, 1963; D. Y. Cooper, S. Levin, S. Narasimhulu, O. Rosenthal, and R. Estabrook, Science (Wash. DC), *147:* 400–402, 1964]. They found that the carbon monoxide inhibition of the oxidative demethylation of codeine, the hydroxylation of acetanilide by rat liver microsomes, and the hydroxylation of 17-hydroxyprogesterone by bovine adrenocortical microsomes were relieved by light of 450 nm. Spectral and kinetic properties of these hydroxylations were entirely compatible with the enzymatic participation of cytochrome P-450.

Pictured are, *bottom* to *top*, Rosenthal, Cooper, and Estabrook. We are indebted to Dr. Cooper for the photographs.

Sidney Weinhouse