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Responsible Investigator: Kathryn F. Fink

University Department: Biophysics

Financial Support 1954-55: UC $ 7,496.00.

Title of Project: A Chromatographic Search for Specific Substances Excreted by Cancer-bearing Animal and Patients.

Accumulated evidence from numerous laboratories suggests that the nucleic acids (the fundamental components of the self-duplicating units--genes, viruses, bacteriophage, and the bacteria transforming factors) may be of basic importance in neoplasia. Our interest was focused on this phase of biochemistry as an outcome of research supported by this grant. A new urinary amino acid was detected, isolated and identified, and its metabolic origin traced to thymine, a component of desoxyribonucleic acid. By a variety of biological studies (clinical, animal, tissue slices, bacteria, and purified enzymes) and development of new analytical methods, the following previously unknown metabolic scheme was demonstrated:

$$\text{Thymine} \overset{2H}{\rightleftarrows} \underset{(DHT)}{\text{Dihydrothymine}} \overset{H_2O}{\rightleftarrows} \beta\text{-ureidoisobutyric acid} \xrightarrow{H_2O} \underset{(BAIB)}{\beta\text{-aminoisobutyric acid}}$$

Analogous reactions were similarly shown for uracil (found in ribonucleic acid) with formation of β-alanine.

Studies to date indicate that liver is the only normal tissue which can convert thymine to BAIB, but the

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intermediates do not accumulate to permit detection by highly sensitive chromatographic methods. In contrast, when tumor tissue is incubated with thymine, a compound with the chromatographic behavior of DHT has been noted. The observations suggest that there is an abnormal reduction of thymine in tumor tissue, and this may be reflected in the high BAIB excretion often noted in patients with cancer, when the disease is in an active state.

Biological investigations are now underway, using radiothymine synthesized in this laboratory, and radioformate (a precursor of one of the carbon atoms of thymine) with the aim of extending our knowledge of these nucleic acid derivatives in normal and neoplastic processes.

Publications:

Fink, K., and McGaughey, C. Reductive Pathway for Pyrimidine Metabolism in the Rat. Fed. Proc., 13:207, April 1954.

Fink, R. M.; Cline, R. E.; and Koch, H. M. G. Chromatographic Detection of Pyrimidine Reduction Products: Microbiological Application. Fed. Proc., 13:207, April 1954.

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