

August 17, 1966

MEMORANDUM

TO: The committee comprising Dr. Reimann, Chm., Dr. Little and Dr. Sommers

FROM: Robert C. Hockett

SUBJECT: New grant application from T. Timothy Crocker, M.D. of the Cancer Research Institute, University of California Medical Center - No. 572.

We enclose herewith an application from Dr. T. Timothy Crocker of the University of California.

This application was prepared following considerable correspondence and a long conference at the Denver meeting of the A.A.C.R. in April, 1966. A copy of my letter dated March 24, 1966 is enclosed.

The Council has supported a number of tissue culture studies and these have returned many observations of scientific value. None so far, however, has succeeded in coming directly to grips with the key problem of comparing effects of known carcinogens upon tissue or organ cultures and upon corresponding tissues of organs in vivo. Crocker seems to have made a promising beginning in studies of this kind. These have proceeded to such a point that a start at comparing effects exerted by tobacco smoke condensates would seem justifiable and promising, especially since human tissue can be studied by this method.

Crocker apparently agrees with me that the ultimate test for "malignant change" in cells, tissues or organs treated with agents in vitro must be made by retransplant into whole animals for direct observation of their ability to grow, invade and metastasize. The work he is already doing along these lines impressed me very considerably and we both want to see it extended. However when we estimated the costs of doing all that he proposes here and the regrafting also at the same time, the figures were rather staggering. It seemed more reasonable to extend the organ culture work to other species first and to concentrate initially on the question whether histopathological changes induced by the same agent in vivo and in vitro do quite generally show the parallelism that he has seen in the experiments so far. It is also reasonable to make comparative observations on the effects of cigarette smoke condensates before proceeding too far with larger scale plans.

The regrafting phase of this study has therefore not been abandoned but deferred for consideration when the inter-species comparisons have been carried farther and some observations made on smoke condensates. Since the final step of regrafting cannot be performed with humans, it seems all the more important to extend the preliminary observations across species lines and especially to include primates (particularly in view of Leila Diamond's report).

A study of this kind may aid considerably in the interpretation of the histopathological changes described by Auerbach (and of others) in the lungs of smokers. The key problem seems to be whether, or in what sense, these changes are to be regarded as "precancerous".

MEMORANDUM - T. Timothy Crocker, M.D.

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The application tells its own story quite effectively with the support of the reprints and manuscripts submitted. These are as follows:

1. Duration of Bronchial Squamous Metaplasia Produced in Dogs by Cigarette Smoke Condensate. Tipton and Crocker, J. Nat'l. Cancer Inst. 33, 487 (1964).
2. Carcinogenic Hydrocarbons. Crocker, Nielsen and Lasnitzki. Arch. Environ. Health, 10, 240 (1965).
3. The Effect of Carcinogenic Hydrocarbons on Suckling Rat Trachea in Living Animals and in Organ Cultures. Crocker and Nielsen (Manuscript)
4. Specificity of Effects of Carcinogenic and Non-carcinogenic Hydrocarbons on Respiratory Epithelium. Crocker and Nielsen (Abstract in manuscript).
5. Organ Culture Followed by Grafting of Rat Tracheas Exposed to Hydrocarbons. Crocker and Nielsen. Proc. Am. Assoc. Cancer Research, 7:16, April, 1966.

R. C. H.