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### **THE IN VIVO EPOCH OF TUMOR TRANSPLANTATION**

A major step toward attaining the primary goal in my life was taken in 1948 when I entered the University of Pennsylvania, as a 27 year old Freshman under the G.I. Bill, AND with a part-time job as a Research Assistant at The Wistar Institute, just across the street

It was apparent at the time, that clinically administered chemotherapy, did not discriminate well between normal and malignant tissues and that cytotoxic specific screening test systems were needed to identify anticancer agents from the multitude of non-specific toxic materials in our environment. At the Wistar, Dr. Helen Dean King, a geneticist, had demonstrated that selective inbreeding of rats for 20 generations, i.e., brother X sister matings with elimination of undesirable phenotypes in each generation, resulted in the evolution of a strong healthy and wild, inbred strain of rats, identified as the King Albino. Dr. Paul M. Apteckman, an organic chemist and Curator of the Wistar Museum, inbred the PA strain of rats and, was able to demonstrate after 18 generations of inbreeding, that not only reciprocal skin grafts taken at random, grew and were permanently maintained, but methylcholanthrene induced fibrosarcomas could be transplanted in continuous serial passage as Individual tumor lines.

Thus, my introduction to experimental oncology began with the chemically induced primary tumors, their induction, transplantation and the somewhat hazardous experience of holding agitated and aggressive tumor bearing animals immobile, while the elderly Scientist, calmly and leisurely measured and treated the tumor. My first publication as a senior author with Dr. Apteckman was published in Cancer Research, Vol.13, 1953. My final publication with this fine man was also in Cancer Research, Vol. 20, 1960, the year I was accepted as a member of The AACR.

My contributions to cancer research spanned the epoch of in vivo human and animal tumor models, their development and use in anti-cancer drug discovery. My laboratory was one of several under contract with the NCI participating in mass drug screening and evaluating the efficacy of newly developed test systems. We also established and maintained a Tumor Bank for the cryopreservation of transplantation established human and animal tumors. Shipment of such tissues to screening labs and qualified investigators was made worldwide.

The drug screening effort literally tested hundreds of thousands of toxic organic and inorganic materials against transplantable murine tumor systems for anti-tumor activity. Drugs with varying degrees of tumor- inhibitory activity were found. But none that would qualify, broadly, as a "CURE".

Discovery of the athymic nude mouse and feasibility of using transplantable human tumors for drug screening revealed that the pattern of tumor responses to test agents obtained with transplantable human tumors was similar to that of the murine tumors.

Therefore, we developed the "SUBRENAL CAPSULE ASSAY" in which the cancer patient provides tissue from his own tumor for further selecting the most effective agent from among several clinically effective and available chemotherapeutic agents. Compared to the effectiveness of IN VITRO testing, when assay results on tissues were exchanged between laboratories, the Subrenal Capsule Assay was found to be more sensitive and had a predictive accuracy of 85%. No transplantation established tumor is involved in final drug selection.

It seems that drug screening with transplantable tumor systems, reveals toxicity as an innate quality of the drug being tested. On the other hand, selection of the most active drug in a panel of active chemotherapeutic agents, by a Patient's tumor, reflects an innate sensitivity of the tumor.

It is somewhat late to bid you an "au revoir", so good luck and "ADIEU"