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It's the rare bird that does science alone. In my case, the research I did and any contributions I made were due in part to my mentors, co-workers, students and technicians. Hence, this is a brief statement of appreciation of those who played major roles in my research career.

I dropped out of high school in my senior year to enlist in the Coast Guard. After a short period of service, I enrolled at the University of Montana in the fall of 1946. When I met my first academic mentor, Professor Ludvig Browman, he seemed glad to enroll a rare pure zoology major. During my sophomore year, Dr. Browman chose me as a lab teaching assistant and he taught me rat anesthesia and surgery. Life was good, and Mayre-Lee and I were married just before my senior year.

When I wished to apply for graduate study in endocrinology, Dr. Browman told me who he thought were the five best experimental endocrinologists. I applied to all five. Professor of zoology Roland K. Meyer of the University of Wisconsin topped Browman's list. He accepted my application and became my second mentor. Early on, he put me in charge of a rat colony that was being chronically treated with estrogen to induce anterior pituitary tumors. The problem was the nature of the physiological events in the various hormone-secreting cell populations during tumorigenesis. I soon learned that Dr. Meyer had an encyclopedic knowledge of biology in general and of experimental design in particular. And a great love of both. R.K. Meyer's group of students was close. Mutual assistance was expected and common. We lunched together daily, organized picnics, male-only beer busts and other enlightening events. Among my closest friends were Tom Roos (deceased, Dartmouth), Bob Breitenbach (deceased, U. Missouri) from whose father we bought our current home, and Lee Hershburger (pharmaceutical research, retired).

My doctoral thesis, accepted in 1955, concluded that estrogen-induced pituitary tumors developed from the prolactin-secreting cell population that continues to secrete prolactin throughout tumor growth. The postulated trigger-like release in proliferation rate of the estrogen-responsive cells after a few months of treatment was not confirmed. The rapidly increasing total pituitary weight was attributable to exponential growth of the initially small percentage of total cells that were estrogen responsive. Initially, when this cell population as small, its increase did not greatly affect total gland size. With accumulation of the responsive cell population, their proliferation progressively increased the rate of increase in total gland weight.

Dr. Meyer urged me to continue research in this area with Dr. Jacob Furth, a pioneer in the study of the biological effects of ionizing radiation. With Meyer's help, I received an American Cancer Society postdoc grant, and was accepted by Dr. Furth, then at the Children's Cancer Research Foundation (now the Dana Farber Cancer Institute) in Boston. Furth became my third mentor. He had isolated a series of endocrine gland tumors that had developed in inbred mice that had been irradiated during atomic weapons tests. The tumors were transplantable in syngeneic recipients, and secreted

specific pituitary hormones. Furth was also interested in the estrogen-induced rat prolactinomas and in radiothyroidectomy-induced mouse thyrotropin-secreting tumors. The concept of dependent and autonomous tumors was developed with this battery of neoplasms. My first manuscript co-authored with Jacob Furth was published in *Cancer Research* in 1956.

Jacob Furth was the most dedicated and most original scientist I ever knew. As Prof. Meyer noted after Furth spoke at a Laurentian Hormone Conference, "He's like spit on a hot stove." *i.e.* gave off ideas in every direction. And his correct percentage of conclusions and interpretations was high. Mayre-Lee and I were soon treated like family by Jacob and Olga Furth, and we continued a close relationship for the rest of his life and as long as her health allowed. During my time in Furth's lab I developed life-long friendships. Among these are Arthur Cohen (who will be present at this meeting), Untae Kim (Snyder, NY), Rita Buffett (deceased), Saburo Ono (Japan, deceased), and Kenjiro Yokoro (Hiroshima, Japan).

Toward the end of my fourth year in the Furth lab, I told Dr., Meyer that I wished to have a faculty position. Shortly thereafter I was invited to attend the University of Wisconsin Medical School where the Department of Radiology offered me a faculty position. Although I had no formal training in radiation biology, I knew the University of Wisconsin and was intrigued with the charge of developing a radiobiology section in parallel with their new radiologic physics section and growing radiation oncology group. I have never been sorry. I joined Prof. Joh Cameron in the development of a graduate program in radiological sciences. John, now deceased, was founder of the department's radiological physics section, and later founder of a world renowned academic department of medical physics. He was a genius in application of physics to medicine.

My initial radiobiological research at Wisconsin was measurement of tumor cell response to irradiation *in vivo* and its dependence on vascularity and oxygenation. Although I have not mentored many graduate students, those that I have had have included outstanding individuals. Among the most important is Randy Jirtle, whose undergraduate degree was in nuclear engineering. Randy, now a Professor of radiation biology at Duke University, is a leader in epigenetics. He is the first to have demonstrated dietary modification of gene function and its heritability without mutation.

On return from a year as an NCI Special Fellow at the Karolinska Institute in Stockholm, I began characterization of those mammary cells and thyroid cells from which cancer develops. We developed monodispersion and transplantation procedures to quantitate the cells capable of proliferation and monoclonal organoid formation and cancer development. Michael Gould was my graduate student during the early stages of these studies of mammary cells. He ultimately became a faculty member, colleague and collaborator throughout the remainder of my active research career. Michael, an outstanding scientist, is now a name Professor of oncology in the McArdle Laboratories. Timothy Mulcahey later joined us as a doctoral student and worked on the thyroid cell studies. After completing his Ph.D., Tim also joined our faculty. He is now Vice President for Science at the University of Minnesota.

When I was a grad student I had met Prof. Harold Rusch, and was impressed by his establishment of the McArdle Laboratories and their academic Department of Oncology as well as by their quality. I came to know Dr. Rusch better when he brought together the faculty to establish the new Department of Human Oncology. Our radiobiology section joined the new department. About 40% of the DHO faculty members were laboratory scientists, and the remainder were medical oncologists, radiation oncologists, and a few surgeons. Chaired by Harold Rusch, the DHO was designed to serve as the core department of a Comprehensive Cancer Center. Harold recruited Paul Carbone from the NCI to take over as the departmental chair and Comprehensive Cancer Center Director. The genius of Harold Rusch, a quiet, modest, and unassuming man, was the judgement and organization of people, and in convincing others to support his ideas. And much of the time he was establishing and chairing one or the other of his centers and departments, he also served as editor of *Cancer Research*, known as the best such journal in its area. I was delighted to serve on its Editorial Advisory Board and as an Associate Editor. Dr. Rusch was indeed greatly admired.

I chaired a committee to develop a new graduate degree program in Human Cancer Biology in the Human Oncology Department. Before it was approved, I left to serve for 30 months as Chief of Research and Board Member of the binational Radiation Effects Research Foundation, the successor to the Atomic Bomb Casualty Commission. ABCC/RERF have followed the health of the survivors of the atomic bombings of Hiroshima and Nagasaki, Japan. Their results are the primary biomedical information upon which recommendations and regulations on the use of ionizing radiation are based worldwide. My friendship with Dr. Kenjiro Yokoro developed in Dr. Furth's lab, and was important in my selection for this position and my decision to accept the offer. Ken is just a few months older than I, and one of the smartest and kindest people I know. He is truly international. Soon after returning to Japan from Furth's lab, he was appointed Professor and a bit later, Director of Hiroshima University's Institute for Radiation Biology and Medicine (IRBM). I knew Ken very well, and he served as my educator about how best to bridge the cultural gap between Americans and Japanese.

By my return to Madison, Prof. Gould had achieved the final approval of our graduate program. We prepared a successful proposal for a NCI Training Grant. I chaired the departmental steering committee and administered the grant for 15 years. Professor Yokoro sent me two of his young men as postdocs with whom I still have contact. Hiromitsu Watanabe worked on the thyroid cancer project for three years and has visited us several times. He became a Professor in the IRBM, and was recently retired (because of age!). Ken Kamiya stayed in my lab for five years working on the mammary cell project. He also was made an IRBM Professor and was elected Director of the Institute.

Three additional doctoral students deserve mention. Nam Deuk Kim developed the methodology for sorting the mammary cells and achieved a thirty-fold concentration of them. "Andy" is now Professor and Dean of the School of Pharmacy at Pusan National University, Korea. Frederick Domann worked on the thyroid cell project, and is now a professor of radiation biology at the University of Iowa. Kevin Groch worked on the

effects of goitrogens and iodine-deficient diets on thyroid cells. He became a Hanford National Laboratory scientist.

In addition, two highly skilled and absolutely essential technologists, Joan Mitchen and Jane Yasukawa Barnes, each staffed my lab for 25 or more years, for which I am eternally grateful.

The main conclusions of all the mammary and thyroid studies may be briefly summarized: a) the cancer susceptible mammary and thyroid cells have the characteristics of tissue specific stem cells. b) The first steps (“initiation”) in radiation-induced cancer development in both glands are very frequent events at the susceptible cell level and in some cases may be reversed. c) Radiation-induced cancer initiation in both tissues occurs too frequently to be a mutational event, and is likely to be epigenetic.