Dr. Coffey’s visionary contributions to urological research in China and Japan

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In deep mourning for Dr. Coffey, we want to bring to readers some of the untold stories from our personal experience of how an extraordinarily talented and kind American scientist of unwavering vision and conviction profoundly influenced urological research and education in China and Japan. This article understandably addresses only a fraction of Dr. Coffey’s legacy in science and education, but the tales told here are vivid and memorable, and hopefully will resonate with thousands of others who also mourn the loss of Dr. Coffey, our Chief, mentor and friend.

Dr. Coffey’s contribution to urological research and education in China (contributed by Leland WK Chung and Haiyen E Zhau)

Dr. Coffey’s curiosity about prostate cancer in Chinese eunuchs was inspired by a conversation he had with Dr. Chieh-Ping Wu, the leading urologic surgeon in China. Dr. Wu was trained by Dr. Charles Huggins from the University of Chicago Ben-May Laboratory, and returned China to serve as the Director of the prestigious Beijing Urologic Institute. Dr. Wu is considered the “father of urology” in China, for several decades the visionary leader and educator of Chinese urologists. He had a special relationship with Dr. Coffey at the Brady Urological Institute of Johns Hopkins to McGill University, we tested this hypothesis by setting up mouse studies to determine the effects of neonatal androgens and estrogens on the development of accessory sex organs and hepatic cytochrome P-450 drug metabolism systems [2-4]. We continued this work at the University of Colorado, further characterizing the effects of sex steroids on prostate epithelial-stroma interaction, and used a tissue recombinant technique to reveal that prostate epithelial growth and differentiation were qualitatively and quantitatively driven by male hormones, androgen receptor, and mesenchymal stromal components in the tissue recombinants [5-7]. These
initial findings paved the way for later concepts that prostate cancer growth and metastasis can be promoted by stromal fibroblasts, and that adjacent cells secreted soluble factors and provided insoluble matrices in the tumor microenvironment [8-15]. This concept gained traction, became popular and is now well-accepted by the scientific community and has been adopted comprehensively for the development of new biomarkers and therapeutics to improve the management of cancer in general and prostate cancer specifically [16-20].

While our lab studies went smoothly and produced promising results, our discussions with the late Dr. G. Miller, a leading genitourinary pathologist, pointed toward an early question we had: Are there fundamental molecular, biochemical and pathologic differences in benign and malignant prostate diseases between the East (China, Japan and Vietnam) and the West (U.S. and European countries)? This question was raised after significant debate with Dr. Miller, in which we were able to convince him that Chinese pathologists indeed had knowledge and expertise in diagnosing prostate cancer. In 1986 we were recruited from the University of Colorado to the University of Texas M. D. Anderson Cancer Center to join Dr. Andrew von Eschenbach to develop a uro-oncology research program. We were most excited when Dr. von Eschenbach shared with us his vision of bridging gaps in our knowledge in the West by studying populations in the East that are exposed to very different dietary, environmental and socioeconomic conditions. At that time China was trying hard to move ahead from a socialist to a more modern capitalistic country. In April 1991, we had the honor of welcoming Dr. Chieh-Ping Wu as a visitor to the M.D. Anderson Cancer Center. Dr. Donald S. Coffey from Johns Hopkins kindly joined us and we shared our visions and exchanged ideas about how to advance the field of urologic science in the U.S. and China (Figure 1). Dr. Wu graciously brought us a rare copy of the Atlas of Cancer Mortality in the People’s Republic of China, published in December 1979. The study was the result of a directive from the late Premier Zhou En-lai. The survey took three years and involved 800 million participants from 29 provinces, with the work conducted by epidemiologists, biostatisticians, and one million medical workers, the so-called “barefoot doctors” who literally walked from place to place to interview and record survey data. The surveyed cancers included stomach, esophagus, liver, cervix, lung, colon and rectum, leukemia, breast, nasopharynx, brain, lymphoma, bladder, penis, and choriocarcinoma. There was no kidney or prostate cancer to be found! Dr. Wu and Dr. Coffey sparked an in-depth discussion of how to formally establish research collaboration between China and U.S. On the U.S. side, the question most often raised was why Chinese men rarely have prostate cancer, when prostate cancer is so prevalent in the U.S. and other western countries? Is this difference contributed by genetic, dietary, environmental, life-style or socioeconomic factors? With our visiting scholars from China, including the pathologists Lian-Sheng Zhao, Hua Yang, and Tongli Xia who worked closely with U.S. genitourinary pathologists Drs. Gary Miller, Patricia Troncoso, and Henry Frierson, we convinced Dr. Miller that indeed Chinese pathologists know how to read pathological slides of prostate cancer!

Figure 1. Drs. Donald S. Coffey and Chieh-Ping Wu’s visit of the University of Texas MD Anderson Cancer Center in April, 1991 where Drs. Coffey and Wu presided discussion of the future research and education collaboration between U.S. and China. The participants of this discussion were, from left, Haiyen E. Zhau, Wu Chieh-Ping, John McConell, James Bowen, Margaret Spitz, Andrew von Eschenbach, Gary Miller and Donald S. Coffey.
Shortly after Dr. Wu’s visit, we organized a U.S. delegation consisting of physicians and scientists from three research areas in the urologic sciences (Figure 2): 1) Prostate cancer biology and pathology, Drs. Gary Miller, Andrew von Eschenbach, Haiyen E Zhau, Leland WK Chung, Isabell Sesterhenn and F. K. Mostofi. 2) Benign prostate hyperplasia, Drs. Ying-Lu Guo and Z. Y. Xue; Epidemiology, Drs. Fangliu Gu, R.T. Wang, and K. H. Han. Based on the vision of Dr. Coffey and Dr. Wu, we formed the first such organization, the U.S.-China Urologic Research (UCUR) Group, with the primary goals of exchanging students and faculty to foster close research collaborations between the U.S. and China. We had our first meeting on Sept. 16-19, 1991 in Beijing, China. Dr. Chieh-Ping Wu presided, assisted by his two highly accomplished students, Drs. Fangliu Gu, Ying-Liu Guo, and their colleagues (Figure 3). The delegates from the U.S. were guided by Dr. Coffey behind the scenes. He wrote to all the delegates on August 21, 1991 (Figure 4). This warm encouraging letter from Dr. Coffey showed the depth of his vision and his deep conviction that collaboration with China would bring new knowledge from the East, and his confidence that we as delegates would understand that this was a difficult mission requiring much patience. History shows that Dr. Coffey’s visions and predictions came true. 1) The explosion of research collaborations between the U.S. and China in recent decades resulted in significant exchanges of knowledge at every level in the urological sciences. 2) The active exchanges of faculty and students between the U.S. and China profoundly moved the scientific culture of China toward a more western model and improved our understanding of how research can be translated for the best patient care. 3) As Dr. Coffey foresaw, the success of joint papers published, joint grants funded, and U.S. training for new generations of urologic scientists all over China has been tremendous. One of the ripple effects of these cultural changes is that, in sharp contrast to early
As you, I also have a very deep and abiding belief that the international interaction of urological research should now be realized and that China is a central colleague in this most important endeavor. The opportunities in China to form research collaborations that will answer and test many important questions tremendous potential. Each of you represents an established dynamic aspect of urological research. You are the premier new leaders in American Urology and will initiate the research directions with China that you believe will be most fruitful. It is therefore not appropriate for me at this time, as a mere senior leader who is not actually in the trenches, to detract in any way or complicate any initial interactions that are embryonic and that will form the backbone of this future program. I will certainly work with you and the China program once these contacts are initiated but it must be supportive and not interfere or disturb what you will be building. I salute you for your efforts and I hope you are aware of the long range importance and meaning of this and we all realize how difficult this mission will be. These interactions will call for the utmost patience, wisdom and understanding, and you will be dealing with a great deal of frustration and confusion as you initiate these joint research efforts. Your leadership and determination will certainly be tested to the fullest extent. On behalf of all in urological research, we that you, wish you the best in this difficult mission and send our prayers for a safe and successful visit.

Sincerely,
Your Friend and Colleague,

Donald S. Coffey

Figure 4. The letter from Dr. Coffey expressed his sincere wishes for a successful meeting with our Chinese colleagues in Beijing. He told us it will be a difficult meeting, advised us to have patience and understanding. He placed his full trust and confidence in us, the U.S. delegates.

Figure 5. Dr. Coffey and Japanese urological doctors and scientists from Chiba University, A. Dr. Coffey’s picture as a souvenir for Dr. Shimazaki. B. Dr. Coffey between Dr. Tomohiko and Ms. Yayoi Ichikawa on June 1, 1991, a couple of weeks before going back to Japan. C. Dr. Coffey and Suyama in front of Dr. Coffey’s Portrait at Suyama’s farewell lunch on Mar 5, 2010. D. Dr. Lupold and Dr. Kurozumi in front of Dr. Coffey’s Portrait just after the lab meeting on February 6, 2018.
synthesis in the rat prostate is controlled by testosterone treatment [21, 22]. In addition to my own experience with Dr. Coffey, I can say unequivocally that Dr. Coffey was a dear friend of mine (Figure 5A), and he had a huge influence and impact on the thought processes of many Japanese urological doctors and scientists from Chiba University. After returning to Chiba, I decided to send Japanese doctors and scientists to Johns Hopkins to work with Dr. Coffey’s protégées, Drs. John and Bill Isaacs, Dr. Steven Ward, Dr. Robert Getzenberg, and Dr. Shawn Lupold. We successfully completed the training of three generations of clinicians and scientists from Chiba at Johns Hopkins. After the trainees returned to Japan, they also successfully achieved their personal goals as academicians or practitioners. Tomohiko Ichi-kawa, MD., Ph.D. (Figure 5B) from 1989 to 1991, was trained under the mentorship Dr. John Isaacs [23-42]. Tomohiko is now the Professor and Chairman of the Department of Urology, Graduate School of Medicine, Chiba University. Yuzo Furuya, MD., Ph.D. [43-51] mentored by Dr. John Isaacs from 1992 to 1995 is now the Director of a private clinic. Hiroyoshi Suzuki, MD., Ph.D., [52-57] mentored by Drs. John and Bill Isaacs from 1996 to 1998, is now Professor and Chief of Urology, Toho University Sakura Medical Center. Akira Komiya, MD., Ph.D. [58-60] was mentored by Dr. Bill Isaacs from 2000 to 2003. Akira is currently the Associate Professor, Department of Urology, Graduate School of Medicine, Chiba University. Takahito Suyama, MD., Ph.D., [61, 62] mentored by Dr. Robert Getzenberg from 2008 to 2010, and he has a picture taken with Dr. Coffey before his departure then (Figure 5C). He is now an Assistant Professor in the Department of Urology at Teikyo University Chiba Medical Center. Most recently, Akira Kurozumi, MD., Ph.D., mentored by Dr. Shawn Lupold from 2017 to present, will also return to Japan with the offer of an academic position (Figure 5D).

Beside exciting academic interactions with Dr. Coffey and the Brady faculty, the students from Japan also enjoyed intimate interactions with Dr. Donald and Eula Coffey and the Brady bunch through parties, getting together and networking to support each other. Dr. Coffey’s passing is a shock to all of us but he and Eula Coffey will live on in our memories.

Memorable moments with Dr. Donald and Mrs. Eula Coffey (provided by Haiyen E Zhau and Leland WK Chung)

In the summer of 2000, Dr. Donald and Mrs. Eula Coffey took a trip with us to Hong Kong, Taiwan, Xian and Beijing, China primarily for scientific conferences. At our first stop in Hong Kong, Dr. Coffey was amazed by the streamlined public transit system, the luxury hotels and restaurants and he proclaimed, “Who said this is a developing country, we Americans are from a developing country!” Dr. Coffey believed in meditation and practiced this art in the basement of his home. While we were in Taiwan, he asked to visit the monks in a Buddhist temple. In Xian, both he and Eula enjoyed Shaanxi Provincial Museum and the famous Terracotta Warriors. Dr. Coffey and Eula were attracted by an oval wooden table set with detailed engravings depicting a scene from Dream of the Red Chamber, a master piece of classical Chinese literature. They acquired the table set and had it shipped to Baltimore. Dr. Coffey enjoyed Chinese food everywhere he went. In Xian, Dr. Dalin He, our highly accomplished student and one of the leaders in the urologic sciences in China, catered a dinner in the Eastern Hotel which was prepared by his close friend, a nationally renowned chef. Dr. Coffey was impressed by every dish, none of which are to be found in Chinese restaurants in the U.S. The last night of his stay in Xian, Dalin asked Dr. Coffey what kind of food he would like. “The same food your friend made the night before”, Dr. Coffey replied. To his and Eula’s amazement, the renowned chef presented them with completely different and equally delicious dishes, and years later they still talked about the Xian meals. Dr. Coffey was deeply inspired by a Zen-Taoist poetry classic by Han Shan, one of the leading poets of the Tang Dynasty. Han Shan retired to Cold Mountain and took its name for his own. He wrote about his solitary Buddha-nature internal life on Cold Mountain, yet cared profoundly about educating the young to prepare them to lead a full life. Dr. Coffey’s practice of deep meditation helped connect him with the nature. Once, driving along Lake Tahoe, he said to us, “Chinese look at the mountains from distance, beyond the cloud, and sink in their minds. We Americans on the other hand want to climb and to ‘conquer’ the mountains”. On many occasions he surprised us with

Don Coffey
his profound understanding of eastern philosophy. Dr. Coffey's wisdom, humor and humanity will forever inspire us!

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References


