

Dankesrede
von
Prof. Dr. Yuan Chang

anlässlich der Verleihung
des Paul Ehrlich- und Ludwig Darmstaedter- Preises
2017

in der Paulskirche Frankfurt am Main
14. März 2017

Es gilt das gesprochene Wort!

Anrede

We are honored to be the recipients of the Paul Ehrlich and Ludwig Darmstaedter Prize and would like to thank the Paul Ehrlich Foundation for its support and commitment to medical research. Foundations have a unique and critical role in advancing the highest aspirations of our society. We thank the Members of the Scientific Council Selection Committee, it is an added honor to have been selected by members of such a distinguished panel of scientists chaired by Professor Harald zur Hausen.

I am deeply grateful for the communities I have been part of both personally and professionally at each stage of my life and career which have allowed me to arrive at this point. I was an immigrant to the United States. My parents, both educators, left a comfortable life in Taiwan, for an uncertain future to give their children broader opportunities to succeed. During college, medical school, and fellowship training – friends and mentors appeared from the most unexpected of places as enablers who molded my approach to life and the choices I made. One of those friends was Pat who has not only proven to be a great scientific collaborator, but also a superb life partner and father to our son.

Both Pat and I started our careers in academics with varied backgrounds and had the good fortune to train in several different disciplines that have enriched our approach to science. I fell in love with Pathology in medical school, a visually oriented field. In fact, Pathology is a field indebted to Paul Ehrlich who started his career developing and mastering the staining principles differentiating sub-cellular structures now ubiquitously used in microscopy.

Studies on viruses have been the foundation for much of molecular biology and cancer research. Kaposi's sarcoma was an enigma in the early 1980's. Even before the AIDS epidemic, the spectrum of its clinical behavior was confounding. KS was the most common tumor in some parts of Africa yet it cropped up as only a medical oddity in European and American populations. It was (and still is) rapidly fatal in African children, but presented mainly as a slow-growing tumor in elderly men in Europe and America. With the onset of the AIDS epidemic, Kaposi's sarcoma had an unprecedented presentation in which a cancer became epidemic striking previously healthy gay, young men. Tackling this bewildering range of clinical presentations, Valerie Beral and Harold Jaffe developed epidemiologic predictions that began to shed light on this enigmatic disease. They predicted that an infectious agent causes KS, and further, that infection by this KS agent is common in Africa but uncommon in the general populations of developed countries. Also, the KS agent has transmission risk factors highly correlated with sexual activities in men-who-have-sex-with-men, but is poorly transmitted by blood exposure.

To discover this agent, we chose a molecular technique that would identify the virus' genes, rather than the whole virus, in a tumor. This was fortuitous because we eventually came to understand why virus culturing failed. The discovery of KSHV clarified one of the important general principles of tumor virology: cancers associated with viruses arise as biological accidents and the virus, although going into the cell as an infectious agent, cannot replicate to high copy numbers and cannot come out of the tumor cell as amplified infectious particles. The fundamental process of viral replication itself kills any host tumor cells. While the virus is present as a latent genome in tumor cells, and it produces oncoproteins that drive cell proliferation, it does not generally produce infectious virus particles. Hence looking for a tumor virus that is in this latent, stealth mode in tumors is similar to hunting for a cellular oncogene.

The discovery of KSHV underscored a second feature of tumor viruses, which is the critical role of the immune system in cancer prevention. The importance of the immune system in suppressing viral tumors has been shown repeatedly since, and is now widely accepted - even taken for granted. This concept has now been generalized to genetic cancers as well. We now know that many cellular immune pathways also directly prevent tumors by controlling proliferation and death pathways in nascent cancer

cells. Many of these dual immune and tumor suppressor pathways have been uncovered by research on the virus that causes Kaposi's sarcoma.

While this award is given to us, it actually recognizes the accomplishments of the large group of scientists from many countries working in this field over the past few decades. The astonishing progress made in understanding this virus and the cancers it causes is not the work of any one group. In our own laboratory, we are indebted to the hard work and skill of technicians, students and post-docs responsible for our research.

I feel extremely lucky to be here, and consider it a privilege to do science. It has been a wonderful experience for me to be involved in a global community of scholars and to be involved in investigations that have not only been deeply, personally satisfying but also just plain fun. When I began my research, I never imagined that I would be here in Germany in this place celebrating science. Thank you again.