Dankesrede

von

Prof. Dr. Patrick S. Moore

anlässlich der Verleihung

des Paul Ehrlich- und Ludwig Darmstaedter- Preises

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Es gilt das gesprochene Wort!

Anrede

I am delighted to take part in your international celebration of science. It is an honor to receive the Ehrlich-Darmstaedter Award and we thank the Ehrlich Foundation and all the Members of the Scientific Council. Over the past 65 years, the Ehrlich Foundation has recognized the fundamental breakthroughs in biomedical research and any scientist would be proud to join this esteemed list of scientific pioneers. The members of this audience also deserve a special word of thanks. As you know, there are disturbing global political trends that are antithetical to modern science and reason. The Ehrlich Prize celebration directly confronts these trends in a positive and affirming way. Carl Sagan, the astrophysicist, wrote a book, called "The Demon-Haunted World" in which he described science as "a candle in the darkness". So we thank you as fellow candleholders.

Yuan described some of our research leading to the discovery of KSHV. I want to continue this story by telling a little about our work on another human cancer virus, Merkel cell polyomavirus or MCV. When we discovered KSHV in 1993, human genomics was in its infancy. But completion of the human genome project provided new ways to discover cancer viruses. It seemed possible to us to directly sequence the RNA from a tumor and to use a computer to subtract out all of human sequences, which might leave the sequence of a virus causing the tumor.

We started working on this approach in 1999, and it took eight years of trial and error before we were ready to apply it to a tumor. We chose a cancer called Merkel cell carcinoma that has many of the features of Kaposi's sarcoma. Although Merkel cell carcinoma is rare, it is more common among immune suppressed patients, including those with AIDS, transplant recipients and the elderly. It is also the most severe form of skin cancer and has a worse prognosis than melanoma but is fortunately less common. After years of preparation, it only took two weeks to find a new virus using this approach and very quickly we could show that this virus is the cause for most Merkel cell carcinomas.

This virus, called Merkel cell polyomavirus or MCV, gives us new insights in how cancers might arise. We think of cancer as a genetic disease, which occurs when genes inside our cells that regulate cell growth and survival become mutated to lose control over healthy cell functions. These mutations can arise from exposure to carcinogens such as cigarette smoke or ultraviolet light, or might even occur as random mistakes that are made when our cells replicate. But clearly there are multiple control pathways that need to be simultaneously inactivated for a cancer cell to arise. Further, evolution has generated cellular circuits that can sense these mutations and the pathways activated by these mutations. Once these cellular sensors are triggered, they dictate for the mutated cell to arrest its cell growth or to commit suicide rather than to turn into a cancer cell that will endanger the host.

Viruses that cause cancer are unique because they inactivate many cancer control pathways all at once—something that a simple carcinogen cannot do. Further, the control networks preventing cancer cell growth are intimately tied into our innate immune system, which some viruses also try to inactivate. By studying MCV, and other tumor viruses, we can identify common cellular pathways targeted by the virus to see if these pathways malfunction in other forms of cancer, including cancers that are not caused by viruses.

MCV has intimately co-evolved with us so that it only rarely causes cancer. In fact, most of us in this room silently carry this virus in our skin and it causes no symptoms or disease. But under the right circumstances, when specific mutations occur to the virus genome, it turns from a harmless passenger virus into the driver for a deadly invasive cancer. Most of you know about the human microbiome—the mass of bacteria that we carry in our guts, lungs and skin—and the critical role the

microbiome plays in our health. There is a less well-understood human virome composed of the viruses we are continually exposed to and transmit, that scientists are just beginning to appreciate. So in the case of Merkel cell carcinoma, cancer arises not from a mutation to our cells but from mutations to a virus that we harbor. It remains to be seen if other cancers might also arise from mutations to viruses we silently carry.

Most of the work we describe here was performed by brilliant graduate students and post-docs in our lab, who also deserve recognition for this year's Ehrlich-Darmstaedter Prize. Forgive me for listing some of them but each scientist was critical to the discoveries that are recognized by this year's award. In particular, I would like to mention Shou-Jiang Gao, Ronit Sarid, Sonja Olsen, Huichen Feng, Masahiro Shuda, Reety, Arora, Anna Guastafierro, Celestino Velasquez, Hyun Jin Kwun and Tuna Toptan who worked to uncover the secrets of KSHV and MCV. We are also indebted to all our colleagues over the past two decades, including Ethel Cesarman, Robin Weiss, Thomas Schulz and Phil Pellett for their generous collaborations. Besides myself, only two of these people were born in America. The others were born in Mexico, Japan, China, India, Germany, Israel, Turkey, Honduras, and elsewhere. There is no clearer statement I can make than this that science is a human enterprise that has no international borders.

And we want to end by thanking Jackson, our son, who is here, and who has shown patience, pluck and support in putting up with two working-scientist parents.