Laudatio

von

Professor Dr. Ruth Arnon

anlässlich der Verleihung

des Paul Ehrlich- und Ludwig Darmstaedter-

Preises

2013

an

Professor Dr. Mary-Claire King

Paulskirche, Frankfurt am Main

14. März 2013

Es gilt das gesprochene Wort.

Mr. Thomas IIka, the Undersecretary of State, representing the Ministry of Health, Mr. Michael Boddenberg, Minister of the Federal State of Hesse, Prof. Dr. Felix Semmelroth, Municipal Councilor, City of Frankfurt, Mr. Charisse Phillips, Deputy General Consul of the USA, Prof. Wilhelm Bender, the Chairman of the Scientific Council of the Paul Ehrlich and Ludwig Darmstaedter Foundation, my colleagues in the Scientific Council, Ladies and Gentlemen,

It is a great honor for me to present today the Laudazio for this year's winner of the Paul Ehrlich –Darmstaedter Prize, Prof. Mary-Claire King, a Professor of Genetics at the University of Washington in Seattle, who has a remarkable scientific career.

She has been a leader in the field of human molecular genetics to revolutionize work in molecular evolution, the genetics of breast and ovarian cancer, and the genetics of deafness. Her research has been translational in providing diagnostic solutions and has changed clinical practice for inherited cancer. Most compelling, Prof. King used her techniques, often newly developed in her laboratory, for the resolution of human rights violations.

She started as a mathematician, getting her B.A. degree in mathematics at Carleton College. But, upon starting her graduate studies at Berkley University she was persuaded by her supervisor, Prof. Alan Wilson who (by the way) was a close friend of mine, to change her field to Genetics. The results of her doctoral thesis revolutionized evolutionary biology: Through comparative studies of proteins, she proved that human and chimpanzee genomes are 99% identical. Since differences between species are due to a small number of mutations, affecting gene regulation and timing of gene expression, this places the divergence of the two species from a common ancestor at about 5 million years ago, rather than the 10 million years ago, as previously thought. It is very clear that her strong mathematical background was quite important and helped her to reach the important conclusion of her genetic analysis.

Prof. King's postdoctoral and professorial research has had also more immediate ramifications. In 1974, she began to study the DNA of families in an attempt to find out whether breast cancer might be hereditary. Her colleagues were skeptical, believing instead that an indefinable combination of various genes and environment were the cause. Over years of painstaking research, She searched for a genetic "marker" --- that is, an identified gene that tends to accompany the gene being searched for --- that would flag the presence of the hereditary breast cancer gene in a chromosome. In 1990, after assessing 183 possible markers, Prof. King and her research team found the right one; in fact, they found that the marker was linked to a gene responsible for a number of different inherited breast and ovarian cancers. This allowed her and others to pinpoint two important cancer-causing genes, known as BRCA1 and BRCA2. The isolation of these genes has led to direct diagnosis of about 10% of all breast cancer as hereditary. Furthermore, it showed that most inherited cases of breast cancer are associated with abnormal versions of these two genes.

Everyone has BRCA1 and BRCA2 genes. Their function is to repair cell damage and keep breast cells growing normally. But, when these genes contain abnormalities or mutations that cause instability and are passed from generation to generation, the genes don't function normally and breast cancer risk increases.

Having abnormal BRCA1 or BRCA2 does not mean that one will be diagnosed with breast cancer, but it increases the chances of hereditary breast and ovarian cancer, and

close follow-up testing is recommended for the purpose of diagnosis and early treatment. This is a lifesaver for numerous women with breast cancer family history around the world. Just as important, Mary-Claire King's discovery has given geneticist insights into the nature of cancer-caused genetic mutations in general. This allowed the use of BRCA genes to develop a number of cancer testing, screening and therapeutic procedures.

The discovery of the "breast cancer gene" revolutionized the study of numerous other common diseases: prior to and during Mary-Claire King's 16 years working on this project, most scientists had disregarded her ideas on the interplay of genetics with complex human disease. Genetics had been used in diseases with a single genetic tie, such as Huntington's disease, cystic fibrosis, and sickle-cell anemia, but researchers were skeptical about genetics' utility in the more common kinds of diseases that included multiple genetic factors and environmental factors as well. Mary Claire King opened the road for following this direction.

Since 1990 Mary-Claire has also begun working in collaboration with scientists around the world to identify genetic causes of hearing loss and deafness. They successfully cloned the first nonsyndromic deafness-related gene in 1997. Towards this goal, she is working with scientists such as Karen Avraham in Israel and Moien Kanaan in the West Bank. The reason is that hereditary deafness is common amongst Arab communities, in this region, amounting to 1-2 cases per 1000, providing good study populations to understand the genetics. Most recently she became involved in the study of schizophrenia, applying her skills in human genetics and her passion for identifying genes and genetic mutations. Her revolutionary approach to the identification of genes has had an impact on other devastating diseases as well, such as colon cancer and coronary heart disease.

Mary-Claire has also participated in the Human Genome Diversity Project, which seeks to delineate the distinctions between individuals in order to further understanding of human evolution and historical migrations.

For her many contributions in genetics, she has won numerous awards, prizes and honors, including the Heineken Prize in Medicine, the Weizmann Women & Science Award, and many others. She was also elected woman of the Year of the Glamour Magazine.

Beyond all her scientific achievements, one of the really special tributes of Mary-Claire King is that she has applied her genetics skill to human rights work, starting in 1984 when she and her lab began working with Abuelas de Plaza de Mayo (Grandmothers of Plaza de Mayo) in Argentina to identify missing persons, ultimately identifying and returning to their homes more than 50 children. Most of them were born to women targeted and "disappeared" by the Argentine military dictatorship 3 during the eight-year "dirty war" of the 1970s and 1980s. These children, after being removed from their imprisoned mothers, were often illegally "adopted" by military families without their mothers' consent. Las Abuelas ("the Grandmothers") had gathered data trying to identify the children, and every Thursday marched to the central plaza in Buenos Aires ("Plaza de Mayo") to demand the return of their grandchildren. The Argentinian government would not return the children without "proof" of kinship, this was provided by Mary-Claire King's technique using dental mitochondrial DNA. This led to the ultimate reunification of dozens of families with

their stolen children. Since 1984, this technique has become a major method for genetic identification of the decreased as well as the living. Mary-Claire King employed the technique to identify the remains of individuals massacred in the village of El Mozote, El Salvador. Her lab has also provided DNA identification for the U.S. Army, the United Nations, and the U.N.'s war crime tribunals. Thus, in a unique way, Professor King has applied her scientific discoveries to correct social and humanitarian injustices.

For all her scientific achievements, and her many other contributions, Mary-Claire is an ideal candidate for the Paul-Ehrlich Darmstaedter Award and I am so pleased and proud that she is the prize winner today.