

TRANSLATION
Acceptance Speech
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Co-Winner of King Faisal International Prize
For medicine 2003/1423H.

Tuesday 8.3.2003 (15.1.1423H)

It is with great pride that I stand before you today to accept the 2003 King Faisal International Prize for Medicine from the King Faisal Foundation. Through the commitment and dedication of the foundation, the King Faisal International Prize has established itself as one of the world's outstanding multi-disciplinary awards.

On behalf of myself and all my colleagues with whom I have worked with throughout my career, may I thank the King Faisal Foundation for the great honor you have bestowed on me. Through the foundation's on-going recognition of advances that affect the lives of many within the world – your support of Science, Medicine, Arabic literature and Islamic studies - you are bravely following a path for the good of all and long may you continue to do so.

Truth, wisdom and compassion were cornerstones of King Faisal's philosophy. These three features have been shown to be fundamental components of the King Faisal Foundation since its inception. I am delighted to be working in a field which also encompasses these virtues – the constant quest for understanding how nature works, the application of knowledge and intuition to the discovery of biological processes and their application to the field of modern medicine so that diseases such as breast cancer can be better treated for the good of all mankind.

King Faisal noted that in each of us lies the seed that will bring mankind's hope to life. This observation is also the key force that drives a scientist such as myself along the road of scientific discovery and its application in medicine. The seeds of hope have grown and through the application of individuals with support and recognition of organizations such as the King Faisal Foundation, we are now in a position to harvest the results and thus reap the rewards. What began as a journey into the biological unknown has brought us to the position where we are today – the ability to create new treatments for diseases that affect hundreds of thousands of patients world wide.

The scientific work for which I have been awarded the King Faisal International Prize for Medicine 2003 began more than 25 years ago when I arrived in San Francisco to join the laboratory of Dr. Howard Goodman at the University of California Medical Center. Shortly before a new scientific method had been developed at Stanford University which was controversially discussed regarding its potential benefits and dangers: "Genetic Engineering". Among others this new technology promised major breakthroughs in the treatment and cure of major disease, such as diabetes and cancer. At this very early time I, a naïve but optimistic young scientist, decided that I wanted to help to make this promise come true. 1977, in the laboratory of Howard Goodman, I succeeded together with my colleagues John Shine, John Chirgwin and Raymond Pictet, to isolate DNA which encoded the hormone insulin. Several years later, in 1985, this breakthrough in bio-medical research led to

the first genetically engineered pharmaceutical “Humulin”, human insulin for the treatment of diabetes. This development was the result of a cooperation between academic scientists, a small biotechnology start-up company, Genentech, and a large established pharmaceutical company, Eli Lilly, and represents until today the paradigm for biopharmaceutical therapy development. After joining Genentech in 1978 as one of the first scientists, I continued on the track I had taken with insulin and eventually in 1983 I focused on the challenge to isolate gene sequences encoding a molecule that is able to generate a biological signal, the cell surface receptor for a factor, designated EGF, that controls the growth of cells and thereby the regeneration of tissues in the human body. The EGF receptor cloning project represents a prime example of how research can lead to completely unexpected findings that open up new dimensions of understanding the wonders of life. This breakthrough, which was only possible through the cooperation with Drs. Michael Waterfield and Julian Downward at the ICRF in London, Josef Schlessinger and Yosef Yarden at the Weizmann Institute and Peter Seeburg at Genentech, was a major step towards the understanding of the complex molecular communication network that is essential for the development and maintenance of a living organism such as the human body. The elucidation of the EGF receptor structure also connected previously discovered oncogenes with human cancer. This work, although at the time not obvious in its applied potential was generously supported by the visionary founder of Genentech, Robert Swanson, who tragically died of cancer at a young age. An unexpected by-product of the EGF receptor project was the accidental discovery of another, related gene which we named HER2. Following the clue provided by the EGF receptor homology with the chicken oncogene v-erbB I set out to investigate whether human cancer tumors were also driven by oncogenes. For this I needed the cooperation with a clinical oncologist who had access to human tumor tissues. Through lucky circumstances I met Dr. Dennis Slamon from UCLA and convinced him to join in this effort. The rest is history: In the mid eighties we discovered that in 30 percent of breast tumors the HER2 was overactive and produced up to fifty times more HER2 receptor protein than normal cells. Most importantly we were able to demonstrate that this abnormal characteristic of breast tumor cells determined the severity of the disease and its rate of progression. This demonstration of a connection between a genetic defect in tumor cells and a clinical characteristic of cancer patients led eventually to the development of the first gene-based target-specific therapy for a defined subgroup of breast cancer patients -HERCEPTIN-, by Genentech. In 1998 the FDA of the United States approved Herceptin for the treatment of advanced breast cancer and in the meantime close to a hundred thousand women have been treated.

Here I would like to express my deeply felt appreciation and thanks to some of the many individuals who believed in me and supported me at times when the basis of scientific and medical application potential of my research was not evident. One key event in my professional and personal life was my move from Germany to San Francisco in 1975, which was only possible through the generous support by the German Research Association, DFG. My time at Genentech included the privilege to work with a number of outstanding scientists and biotechnology pioneers such as David Goeddel, Herbert Heynecker, Peter Seeburg, Arthur Levinson and many others. They made this time from 1978 to 1988 incredibly exciting and unforgettable. The translation of our basic discoveries in the laboratory to a cancer therapy “Herceptin” was

only possible through the dedication and commitment of many outstanding people, especially Dennis Slamon, Robert Hudziak, Michael Shepard, Paul Carter and Arthur Levinson, the current CEO of Genentech.

I'm grateful to the Max-Planck-Society for providing me with outstanding conditions to continue my work upon returning to Germany after fourteen years in the USA. Last but not least I want to say that I would not be standing here to receive this great honour from the King Faisal Foundation without the continued support from my family and life-long friends of which two are here with me to share this wonderful experience.

Being awarded the King Faisal International Prize for Medicine 2003 tremendously strengthens my determination to move forward on the path that began more than 25 years ago towards the translation of scientific knowledge into the betterment of life of hundreds of thousands people worldwide.