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## Es gilt das gesprochene Wort

## Tak W. Mak Paul Ehrlich and Ludwig Darmstaedter Address

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"I sleep better at night knowing scientists can clone sheep", Jeff Ayers once said.

Today, with this kind of cynicism and short-sightedness, some thunder that research should only be done if it is clearly targeted at curing disease or saving the planet or boosting the economy.

Unfortunately, we seldom know where and when the next great discovery will occur, and how it may benefit humankind.

Under funding pressure, my own research has progressively become more and more practical over the years, and I do enjoy, at some level, the very real prospect that our findings may one day be applied to treating diseases.

Nevertheless, my message today is that it is still so important to "let a thousand flowers bloom", because it is basic scientific research that is the essential engine churning out the fundamental discoveries which are later applied in the clinic or on the shop floor.

In 1978, Werner Arber was studying the exchange of genetic material between bacteria and unexpectedly discovered enzymes that cut DNA at specific sites. This seemingly simple observation spawned the break-through of recombinant DNA technology, which in turn led to the mapping and cloning of genes, the establishment of the biotechnology industry, the decoding of the blueprint of the human genome, and the development of advanced approaches for the diagnosis and treatment of many diseases.

Please also consider the fascination of Sydney Brenner, John Sulston, Robert Horvitz and others with the lowly worm. In 1986, Horvitz took advantage of the relative simplicity of this organism to identify the genes controlling programmed cell death, or apoptosis. We've since learned that defects in apoptosis can lead to cancer and degenerative diseases, and today, treatments designed to promote the apoptosis of tumor cells are important cancer therapies.

Thus, we cannot afford to underestimate the role of serendipity in scientific discovery, and society cannot afford to starve basic research by curtailing funds.

Those who would reduce funding for basic research in epidemiology, virology and microbiology have the very real spectres of the HIV and West Nile viruses and the SARS epidemic to give them pause.

Recent global events have clearly warned us not to be complacent about infectious diseases, and not to shut down an avenue of research just because we cannot see its practical application at that very moment. We should all take a lesson from the

fundamental work of Paul Ehrlich and Ludwig Darmstaedter, which so elegantly established the foundations of chemical structures, pathogen identification, and demonstrated how to target these pathogens to conquer infectious diseases.

I believe we have entered into a golden age of medical research. It took 100 years of discoveries in physics to place a man on the moon. It has taken only 30 years of discoveries in molecular biology to bring us tantalizingly close to curing both infectious diseases and cancers. The rise of this field has enabled us to peer directly into the workings of a cell, to probe its DNA and determine how its proteins work. With such mechanistic insights, we can rationally design drugs that work precisely on cellular defects, sparing normal cells and processes. Indeed, in the past 5 years, we have seen the development of targeted therapeutics that are making real and dramatic differences in the lives of cancer patients.

For example, Gleevec is a drug that was designed to specifically inhibit the activity of the rogue kinase that drives chronic myelogenous leukemia. Without the basic research that identified the chromosomal translocation giving rise to this rogue kinase, and the basic research that determined how its intracellular signaling could transform cells, these patients would all now be dead. Similarly, treatment with the drug ATRA rescues patients with acute promyelocytic leukemia, since basic research showed that the effects of the tumorigenic transcription factor causing this disease could be countered by flooding with trans retinoic acids.

These advances would not have been possible without adequate funding for basic research, and stable, generous support for studies in molecular biology, molecular genetics and biotechnology must be provided if our progress in this direction is to continue. We have the tools to find cures for so many scourges of humankind; we need ongoing moral and financial support to use these tools to their best advantage.

Finally, I would like to remind my fellow basic scientists that the work we do does not exist in a vacuum. We are responsible to the greater world around us, and if we are to realize the great advances that I believe are imminent, we must continue to be forthright and rational ambassadors for our type of science. We must also always keep in mind the ultimate goal of all research, the betterment of the human condition.

I'll close with a quote from the very wise, if not scientific, Mahatma Gandhi: "The things that will destroy us are: politics without principle; pleasure without conscience; wealth without work; knowledge without character; business without morality; science without humanity; and worship without sacrifice".

The Paul Ehrlich and Ludwig Darmstaeter Foundations have been established in just such a context, with the goal of rewarding scientists in a broad range of fields who do work that might initially appear esoteric but which may ultimately benefit us all.

I am humbly grateful to be included among these scientists, and I thank the Foundations, as well as my family, my late wife, Shirley, my children, Julie and Jennifer and my wife Lillian for their love and support; the students and post-doctoral fellow (many from Germany and some even in the audience) who were in our laboratory for their dedication and wisdom, as well as friends and colleagues for their friendship and advice, from the bottom of my heart.