Dankesrede

von

Prof. Dr. Ada Yonath

anlässlich der Verleihung
des Paul Ehrlich- und Ludwig Darmstaedter-Preises
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Es gilt das gesprochene Wort!

Dear Mr. Kopper, Chairman of the Scientific Council of the Paul Ehrlich-Foundation
Dear Members of the Scientific Council
Dear Members of the Board of Trustees
Dear Secretary of State in the Federal Ministry of Health
Dear Major of Frankfurt
Dear President of the Johann Wolfgang Goethe-University
Dear Guests and Friends

I would like to start with expressing my deep and sincere gratitude and appreciation for this exceptionally prestigious award in life sciences. I feel deeply honored and extremely grateful. Receiving the Paul Ehrlich and Ludwig Darmstaedter Prize has a special meaning for me. By reading about Paul Ehrlich I learned that he was undoubtedly one of the geniuses of his time. He was the first to relate chemical structure with function and among medical scientists of his generation Ehrlich was marked as the most original and stimulating. Importantly, the fruitfulness of his concepts initiated advances in all fields of biomedical research to which they were applied. A superb model to follow!

But this is not the only reason for my gratitude for being this prize winner. I am thrilled because the decision of awarding me this prize was made by peers who are “heroes” in their field, whom I deeply appreciate. Whose creativity, originality and accomplishments have inspired me and played a special role in the progress of my studies. I would like to use this opportunity for thanking the distinguished committee, who selected me as a recipient of this prestigious prize. Indeed, sharing such honor with Prof. Harry Noller adds to my satisfaction.

Winning prizes was very far from the motivation for initiating the studies that eventually brought me here. I was dreaming about revealing the mechanisms underlying a key life process, protein biosynthesis, in which the ribosome is the key player. This enormously complex assembly of RNAs and proteins functions as a nano-machine that translates the genetic code into proteins, the components responsible for almost all life processes, in all living cells. When I initiated my study, this cellular process has been investigated comprehensively by biochemical methods in several Universities, among which the Max Planck Institute for Molecular Genetics in Berlin was considered as a highly respectable leader. However, it was clear that detailed understanding of the mechanisms underlying its function hinges on structural information. In addition, owing to its key role in life, the ribosome is a target for many antibiotics. Hence, revealing the ribosome structure and discovering how the small antibiotics can paralyze its functions, how resistance to antibiotics can be acquired, and how to produce antibiotics that distinguish between the pathogens and the patients with minimum side effects, were my prime scientific goals.

At the end of the 70th, the mere ides of the determination of the ribosome structure met with considerable skepticism since most of the international scientific community could not even conceive its feasibility. Nevertheless, the late Prof. Wittmann, the Director of the Max Planck Institute for Molecular Genetics and myself established a strong collaboration, and undertook this challenge. The specimen required for performing crystallographic studies, are high quality crystal. The main reason for the overwhelming doubt in the fruitarian of ribosomal crystallography stem from repeating failures of leading scientists who were attempting to crystallize ribosomes before I entered this field. At that time the common conception was that they cannot crystallize. The logical explanation for this failure were the ribosomal properties which are unfavorable for crystallization: they are flexible, heterogeneous and unstable.

You may wonder what was the basis for my belief that I will indeed reach this goal. Here I should be thankful for the North Pole bears that hibernate in winters. While hibernating the bears run

limited metabolism and therefore need only a very small number of ribosomes. As ribosomes in living bodies disintegrate within a few days, most of their ribosomes should have vanish during the winter. However, the minute the bear awakens he has to start active life. If no ribosomes remain intact in his cells throughout the winter, how can he come back to life in the spring?

A study which revealed that in the cells of hibernating polar bears the ribosomes are arranged alongside each other, almost like a crystal on the cell membranes, provided the idea that pushed me onwards. We interpreted the close packing as the means nature takes to limit ribosome disintegration. Hence, no only the orderly packed ribosomes remain intact for months, they also maintain functionally active unique conformation, properties that should be favorable for crystallization. Hence, my strategy was to mimic the bears!

For this we identified robust bacterial sources, hoping that their ribosome will disintegrate slower, and searched for ways to maintain them at their active state long enough for crystallization. For this aim, we used procedures developed at the Weizmann Institute by Zamir, Miskin and Elson, and micro crystals diffracting to high resolution were obtained already in 1980! However, even when larger crystals could be obtained, almost a decade later, pursuing the crystallographic end met with enormous hurdles. For instance, once we irradiated the crystals by X-rays, they deteriorated immediately. All biological materials are sensitive to X-rays, including crystals of proteins and other cell components, but in most cases measurements from them are still possible. The ribosomal crystal are, however, exceptionally sensitive, and therefore originally we could not collect their crystallographic data. Can you imagine, ladies and Gentlemen, spending years in order to obtain a crystal, and then watching it vanishing within a faction of a second? We reasoned that the fast decay of the ribosome crystals is due to their loose packing allowing rapid propagation of free radicals that are formed by the X-radiation. Hence, we overcame this terrible situation by introducing the method called cryo crystallography.

But this was not our last problem. Unpredictable as well as foreseen difficulties kept appearing. Combating these difficulties required establishing novel technologies and the development of innovative and sophisticated procedures, well beyond the limits of biological crystallography of that time. Thus, everyday had its problems but at the same time, almost everyday has its own rewords. For me and my group, every step forward was a little victory. We felt as if we are putting together an enormous puzzle. However, every time we thought that I have reached the highest mountain, we kept realizing that a higher peek is still in front of us. With all of these colossal obstacles on our way, recognition at the level of prizes seemed far and totally unrealistic. In fact, now I am wondering, how would my scientific life proceed if my sole incentive was winning prizes? Surely not the way it went. I would certainly pick a simpler and more “doable” project….

With your permission, I would like to cite one of the greatest scientists, Isaac Newton. He believed that almost everyone can reach heights in their work if they focus on a single endeavor to the exclusion of all else. Newton claimed no more for himself than the ability to concentrate. Apparently, he could afford it. In our days how can people focus when they face so many destructions? When for mere survival, all scientists must report frequently and display their successes?

Some of you may know that my scientific history is somewhat different from what is considered to be the “usual path”. For a long time I was allowed to focus on ribosome crystallography, and was tolerated as long as have demonstrated some progress towards reaching my ultimate goal. Thanks for are due:

- to the Max Planck Society that blessed and supported the initiation of these studies, kept on with the original collaboration even after the sad death of Prof. H. G. Wittmann, and established an independent research unit for Ribosomal Structure at the DESY Campus, to avoid the need to transport crystals and thus facilitating efficient progress of this project;
- to the Weizmann Institute for supplied a permanent home for me despite my intensive collaboration with the Max Planck Society which necessitated frequent travel to Berlin, Hamburg and synchrotron stations around the world;
- to Ms. Helen Kimmel for establishing the Kimmelman Center for Macromolecular assembly, which elevated structural biology at the Weizmann Institute to heights not known previously;
- to Unite States National Institute of Health (NIH) who financed my "dream" from its embryonic stage, despite the severe doubt expressed by most (but, obviously, not all) of the scientific community worldwide; and continues to do so even after several prominent USA groups stepped into this field;
- to the members of my groups in Hamburg and in Israel, for their devotion and enthusiasm in good and, more often, bad times;
- to the administrative staff in Hamburg who directed me through the German bureaucracy;
- to my dear friend Renate, who is here today, who opened her heart and her house to me although at times I was falling asleep while she was taking care of me;
- and to my family, who supported me throughout with no questions or complains, although not always my mind was solely given with them …, which includes:
- my parents, who were brought up far away from science; especially my mother, who experienced enormous difficulties in raising and educating my after my father's death, when I was still a child;
- my young sister, Nurit, her husband Mati, who is here today, my daughter, Hagith, who had to tolerate me in my presence and my absence, and to my granddaughter, Noa, who at the age of 5 invited me to her kindergarten class, in order to explain how the ribosome works.

Before ending I would like to ask your permission to mention the names of the few scientists who encouraged me at the very beginning of this seemingly impossible endeavor. Among them are the late Sir John Kendrew, the former EMBL director General who permits us to use the EMBL station although for a long time we did not show dramatic progress; Prof. Ken Holmes, from the Max Planck Institute for Medical Research; Prof. Volker Erdmann from The Free University Berlin, who supplied us with high quality ribosomes and valuable advice; Prof. Aaron Klug, from the Medical Research Council at Cambridge, UK; Prof. Alex Rich at MIT; and Prof. Christof Kunz, who is with us today, who not only provided the means to reside at HASYLAB, but also took care of all student in our group whose primary education was Physics.

With time, more scientists became ware of the significance of our studies and a growing number of them provided assistance and advice. The time is too short to mention all of them, so I will refer to only those who enabled my studies in Germany, namely the directors replacing Prof. Wittmann in Berlin as well as the MPG Presidents; the DESY and HASYLAB directors; The BMBF administration and many scientists at different universities and research centers, who conducted fruitful discussion from which a benefited tremendously.

I guess that you have heard similar speeches from other awardees, and the clichés and slogans that I was using sound prosaic, trivial, ordinary and dull. But, what can I do, they truly describe my feelings.