

“Israel Is Not Like Any Other Country”

An interview with Israeli Nobel Laureate Dr. Aaron Ciechanover

By Michael Kaufman

Aaron Ciechanover, M.D., D.Sc. and Avram Hershko, M.D., Ph.D. made history in 2004 as the first Israelis to win a Nobel Prize in science. Together with Irwin Rose, Ph.D, of the Fox Chase Cancer Center in Philadelphia, the Israeli researchers were awarded the Nobel Prize in Chemistry for their pioneering role in discovery of the ubiquitin proteasome system—the body’s method of removing damaged proteins. Their research, conducted over 30 years, led to a whole new approach to cancer treatment: targeted therapy.

In 2003 the United States Food and Drug Administration (FDA) approved the first drug specifically targeted against the ubiquitin system: Velcade® (bortezomib) for treatment of multiple myeloma (a cancer of the bone marrow).

Since the approval of Velcade®, targeted therapies have been approved by the FDA for treatment of other types of cancer, and new targeted agents are now being studied in clinical trials or are in earlier stages of development. Targeted therapies differ from standard chemotherapy in that they act only on specific molecular targets associated with cancer, whereas most standard chemotherapies act on both normal and cancerous cells.



And unlike standard chemotherapies, which kill cells, targeted therapies are designed to block the spread of cancer cells.

Professor Ciechanover is director of the Lorry I. Lokey Interdisciplinary Center for Life Sciences and Engineering at Technion – Israel Institute of Technology, in Haifa. In addition to the Nobel Prize, he has been the recipient of numerous other prestigious awards, including the Albert Lasker Award for Basic Medical Research (2000); the "Emet" Prize (the Prize for the Arts, Science, and Culture under the auspices of the Prime Minister of Israel) (2002); and the Israel Prize for Biological Research (2003).

A prominent figure in Israel, he is known for speaking out on a wide range of public issues, and has called for a change in national priorities to strengthen the country’s education and higher education systems. “The strength of Israel and its international standing,” says Ciechanover, “depend on extensive investments in the various sciences as well as in the study of Judaism and the history of the Land of Israel.” Ciechanover’s wife Menucha is a physician and director of the geriatric department at Carmel Hospital in Haifa. They have one son, Yitzhak.

Q In the biography you wrote for the Nobel Prize Committee you explained how your childhood interest in biology evolved into your professional career. But you also wrote specifically about growing up in the newly formed State of Israel and extensively about the history that led to the establishment of Israel as a homeland for the Jewish people. Why did you feel it was important to include these historic details about your country of origin?

A *Israel is not like any other country. I was born with the country and I grew up with the country so therefore I put a lot of emphasis on this coincidence. And my parents came from Poland because of anti-Semitism in Poland, not just because they were looking for better economic conditions. They actually*

escaped, predicting—kind of prophesizing—what was going to happen, and by that they rescued themselves. So I thought it would be very interesting for people—as well as for me—to write that down because I never thought about writing a biography. So the fact that I was born in a unique country at a unique time, immediately after the Holocaust, two years after the end of World War II in Europe, when the Jews looked for their own place in which they would be able to protect themselves, and not being victimized by hatred and discrimination. And I was lucky to grow up in an independent country enabling me to protect myself and my colleagues who were serving in the military. I thought it was important for me to put it down.

Q What was the audience reaction?

A *I don't know because it was not a speech. You are asked to write it down and it is posted on the website. I know there are hundreds and thousands of entries—close to a million—at this site in recent years. But I really don't know what the audience thinks. The Nobel Foundation doesn't let people log in and correspond directly with the laureates. But for me it was important: It was the story of my parents, the story of my country, the story of the Holocaust, the end of the Holocaust, the beginning of independence, of free Jewish life.*

Q When you finished your post-doctorate Fellowship at Massachusetts Institute of Technology (MIT) in 1984 you needed funding to be able to continue your research in Israel, and in 1985 you received a Research Career Development Award from the Israel Cancer Research Fund (ICRF).

ICRF has continued supporting your research, and in 2002 and 2003 you and Professor Hershko were awarded Research Professorships, the highest research grant designation given by the ICRF Scientific Review Panel.

How important has ICRF support been to you as well as to other researchers in Israel?

A *Actually it was even better than that. When I left to MIT, before I started my post-doc, I applied for a grant from ICRF. It was then a very young organization and there was a huge discussion there whether to fund somebody who leaves the country rather than somebody who returns to the country, because for them it was supporting scientists working or returning to Israel.*

Q Why support a scientist who goes to work in the United States?

A *I learned in retrospect that after deep discussions, probably difficult ones, they nevertheless decided to give me the fellowship....somehow trusting me that I will come back—that they are going to seed something and though it's not going to be in Israel, this seed is going to grow up and pay off. In retrospect they were right and they were not disappointed, but they did take a risk and they did something that was against their policy at the time. But they probably had the right gut feeling. It was a very rare occurrence. I don't know if they ever repeated it or did it again.*

Q What is the level of government support for research in Israel? How does it compare with the U.S., where concerns over government spending have led Congress to authorize extensive cuts in funding for research?

A *The situation in the United States now is not anything to be proud of. . .but we shouldn't discuss America now. That's your problem. In Israel I would say the support is good. We are also now part of the European community and we have been getting a lot of support from Europe.*

We are contributing but we are getting back. Because Israel has very talented scientists we get more than we contribute. We contribute according to the GDP and we get back according to our brains... so we are gaining from it. Israel has good universities and very good people.

The support from both Europe and the Israeli government is good. You cannot compare it to America of today because America is nothing like it was 20 years ago.

Q Some scientists view religion as antithetical to their understanding of science.

In your Nobel Prize commentary you explained how your upbringing provided a liberal modern orthodox Jewish education as well as an excellent general education. You noted that you and some other physicians and colleagues meet regularly for lessons taught by a rabbinical scholar regarding the relationship between Jewish law and the moral and ethical problems of modern medicine and science.

How do these studies help in your pursuit of scientific knowledge?

A *I am Jewish and a proud Jew and I think Jewish traditional scholarliness is something to be proud of. Clearly the success of the Jewish people is due to a large extent to scholarliness that has been developed almost to perfection over centuries. Jews were persecuted. They were not allowed to own land or to learn certain things. They were always discriminated against, so the only thing they could do once they were kicked off their place was to bring only one item, which is called head. So they took their head with them.*

But in order to take their head they had to develop it to become a good head. So over the generations, from the days of the Temple and the

Mishna and Talmud, scholarliness was really a hallmark. And it's highly appreciated. Jews always thought about what they do. They had to reason. They always ask questions....what to do in this situation or the other situation.

They never accepted anything for granted. It was always questioning, inquiring and investigating. And for me it's the call of life.

So here I am, a Jew, finding that my core roots are already deeply implanted in the ground by my centuries-old predecessors, therefore the big appreciation for this culture.

Q Is there any one aspect of your work that you find most gratifying?

A *There is no one moment of 'Eureka.' It is hard work, going for decades, and you never know at the moment, even if you find something that looks exciting. You may think it's exciting but you certainly don't know whether it's important because it's new and there is no time perspective. Only time can tell. And mostly time not that it is not so much via your work but via work of others that take it further, and who further distill it, and bring it to the next stage and the next stage and then, finally to a drug or something that can benefit humankind.*

Q So do you feel the connection between your work and the targeted therapy that is now increasingly being used to extend lives and improve quality of life of cancer patients?

A *Yes, it is a major source of satisfaction. But the connection was not seen at the beginning. It took 30 years. There was no way to prophesize or predict it. It came after many years. But when you do it you are doing it because you're driven by curiosity. And I'm still driven by curiosity.*

All I want to know is the secrets of God, the secrets of nature. So I am curiosity driven and then good things come out of it in the eyes of the public. But as a good scientist I am interested in dueling with God or with nature or whoever God is, it doesn't matter, and understanding the secrets of creation.

If something good comes out of our work, let it be. Many good things have come out of our work and many will come. But that is not necessarily the drive because you don't know when you do it that something will come out. When you do it you are driven by curiosity and I am still driven by curiosity

and I'm happy that it ended up with beneficial drugs for people. It is a major source of satisfaction.

But I did not start out with the intent to do it. But it happens. That is the beauty of science . . . that you cannot predict. You just have to push hard and then it happens. There is a Hebrew saying, Mitoch shelo lishma ba lishma ("From [doing a mitzvah] without proper intent, one will come to do it with proper intent.")

You don't have a purpose, you are just driven by curiosity and then something good comes out of it, you achieve something. It also reflects humbleness I believe.

Q You serve on the board of Tufts University's Science Training Encouraging Peace – Graduate Training Program (STEP – GTP), which provides graduate and post-graduate-level health and science education to pairs of graduate students comprised of one Israeli and one Palestinian.

How meaningful are programs of this kind in helping to one day achieve peaceful co-existence?

A *I believe that even if politically you don't agree with your neighbors, the minority, at the end of the day what the mother wants for her family is for her children to grow up and have good health services, a good education, and to see them flourishing. So the idea is to take people and not to push them down but to lift them up.*

Science is a language of peace. The drugs that were developed following our discovery don't have a message on the package that says "Aimed for Jews only." They are drugs for people. And I believe that people are people anywhere in the world.

Q Isn't it true that the more we learn about genetics the more we see how similar people are to each other?

A *I don't even care about genetics so much. I care about the human spirit and soul. Therefore I believe that pushing up the Arab minority . . . is something very important for the Israeli nation.*

Q Has the recent strife set back collaboration between Israeli and Palestinian medical professionals?

A *I am not a practicing physician so I cannot attest to it but I believe it is very difficult now, especially after the summer atrocities. Hopefully it will change for the better one way or another. But we are still faced with the problems caused by Islamic fundamentalism.*

Look at ISIS, the Islamic State, the cruelty, the lack of education, the beheadings.

Q What is the quality of the healthcare system in Israel and how does it compare with that of the United States?

A *It's a good system. Israel has a very advanced healthcare system, much better than the United States. You are spending so much money, 18 or 19 percent of GDP, and the average citizen gets very little. (Israel spends less than eight percent.) You have very good physicians and medical centers but to get there costs you a lot of money.*

Israel has a public system. Everybody is entitled to the same service and you pay out of your salary.

Even if you don't earn anything and don't pay anything you get the same service in the public system as a rich person.

You can obviously buy additional private services if you want: private room, color television hanging from the ceiling, anything you want. And we have very good physicians, nurses and equipment.

That is not to say that there are no problems. We are running short of physicians and therefore many people have to wait a long time to get this good treatment. There are physicians who just go into private practice; they don't want to serve in the public sector But the law is very good, the system is very good and the people are superb: We have very good physicians in Israel.



**For more information about ICRF visit our website at
<http://www.icrfonline.org>**