

## Funding above and beyond scientific research

An interview with Thomas R. Cech, President of the Howard Hughes Medical Institute in Chevy Chase, MD

**EMBO reports (ER):** Dr Cech, when you became President of the Howard Hughes Medical Institute did you already have some administrative or managerial experience?

**Thomas Cech (TC):** Very little! I simply ran my research laboratory and I had had some experience in biotechnology. I had founded a biotech company in Boulder so I was somewhat familiar with annual reports, working with a board, doing budgets, human resources and how to deal with employees. This experience was probably more relevant to Howard Hughes than my university experience.

**ER:** Were you the first pure scientist to get this position?

**TC:** Certainly past presidents were also scientists, but they did not continue to do active scientific research after they took the Hughes presidency.

**ER:** In Europe, many scientists complain that those responsible for science administration don't see science the same way as scientists do. Do you think that scientists should get more involved in politics or science administration?

**TC:** I would rather put it the other way round. I think there is value in having practising scientists as leaders of research institutions. In my own case here at Hughes, I feel that I am more in touch

laboratory, keep in perspective questions about having to weigh a very risky and adventurous project against doing some-



thing which is more likely to lead to steady progress, but perhaps not a major breakthrough. The idea is that this will make me a better leader of Howard Hughes than if I were more detached from the realities of doing research. Harold Varmus continued to do research while director of the NIH. Rick Klausner, who is the head of the National Cancer Institute, also has a very robust research group, as

programme while having responsibility as a science administrator.

**ER:** So you think doing research and having an administrative position at the same time is better than just being purely administrative.

**TC:** I think so. You should ask the people who work for me whether they agree that this is successful or not!

**ER:** Do you have less time now for your lab than when you were still in Colorado?

**TC:** Certainly the lab suffers to some extent. I no longer take graduate students, because they in particular benefit from having frequent interactions with a mentor and I am no longer able to provide that. I'll now be working mostly with postdoctoral fellows and I also have several people who are long-term, research technicians or associates who are very important for the continuity of the research.

**ER:** Howard Hughes is building new research facilities near Washington Dulles International Airport. At the same time you are increasing funding for research in Third World countries. In the long term, do you plan to increase investments in investigators in Third World countries and use these new facilities to train and help them to establish their own labs?

**TC:** I think that the new facility may provide some opportunities in terms of bridging what we are doing in our international programme with what we are doing domestically. Whether we will expand either of these programmes in the future really depends to some extent on the stock market and the return on our investments. Unlike other institutions that obtain contributions, or that can apply for

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with the challenges of running a research programme. I keep in perspective how quickly things can move or sometimes how slowly they seem to go in the

does David Baltimore, President of Cal Tech. I learnt from them that it is possible to do what might seem rather crazy, trying to maintain an active research

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federal research grants or have tuition being paid or alumni who give donations, we have none of those things. We operate solely off the income from the investments of the endowment and they are not doing as well as they were in the 1990s, so our immediate goal is to maintain our successful programmes at a healthy level. Expansion is not something we're thinking about.

**ER:** Why was this decision made to support scientists outside the US, in particular in Eastern Europe and the Americas?

**TC:** Let me just start out by describing briefly the organisation at Hughes. By law, we are a medical research organisation, not a foundation. This requires that we support biomedical research with our own employees. So that's the investigators programme, which is entirely within the United States, because it would be impractical to have an employer/employee relationship with researchers around the world. The grants programme is independent of the investigators programme. Once we meet our legal requirement of spending 3.5% on the investigators programme, we are free to spend additional funds above and beyond that. Those funds can be spent on a broader landscape of opportunities, but nonetheless still within our mission of supporting not only scientific research, but also science education. The international programme was started because my predecessor, Purnell Choppin, and the trustees of Hughes at the time thought it was important to keep alive the scientific spirit and infrastructure in countries that have seen hard times and where there has not been much governmental support. Literally, the Hughes funding has allowed the electricity to continue flowing and lights to continue burning in certain parts of the former Soviet Union, Eastern

many of them don't go back to their home countries, so it serves us well but doesn't serve the international scientific enterprise. We think that international science would be at its most healthy and robust if scientists from all over the world could interact as equals with their own local perspective and their own skills and talents. We also encourage their governments to reinvest in science and science education, and already we have seen multiple examples where the leadership of the country has focussed on the fact that their scientists are getting support from Howard Hughes Medical Institute. They take notice and start evaluating the situation and putting in their own resources. Brazil is perhaps the most dramatic example where our researchers now have new facilities being built for them. We think that our funding there provided a spotlight on Brazilian science giving it international recognition, which was in part responsible for the government making such a major investment.

**ER:** But if you compare research in Second or Third World countries with the United States, Western Europe and Japan, the gap is certainly growing larger. And many governments simply do not have the money to invest as much as they probably wish. Do you feel that non-governmental organisations, such as the Bill Gates foundation, which supports malaria research or George Soros who supported research in the former Soviet Union, will play a more important role in the Third World?

**TC:** Yes, and I think they should play such a role. I think that a small amount of funding can go a long way. You say the gap is getting larger. Maybe in some countries that's true, but in others it's getting smaller. But in any case, without such efforts I think the gap certainly would get very large very quickly. In

to the disease. People don't read about this in books. They have the examples right there on the hospital wards. That of

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course is the place where the research should be done.

**ER:** The pharmaceutical industry does not seem to be interested in serving these countries for the simple reason that the people there can't afford drugs. Shouldn't this be an additional incentive for non-governmental organisations to support this?

**TC:** Non-profit organisations do have a special opportunity to make an impact on the understanding and treatment of these diseases, which are huge problems internationally, and where participation by pharmaceutical companies is limited. There's a crying need there and it's an excellent use of non-profit funds to make an impact in these areas.

**ER:** Is it a long-term plan of Howard Hughes to increase their investment in



disease research in Third World countries?

**TC:** It would be wonderful if we could find the resources to increase our investment in the long term. Right now we are operating on a fixed budget. As I said before, a portion of it is certainly not going to be spent internationally, because our core responsibility is to do biomedical research in the United States with our own employees. In the grants area, we have a number of exciting opportunities in public education in the United States in terms of trying to get the American people

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Europe and certain Latin American countries. Of course, other people said we can help international scientists by inviting them to our laboratories in the United States. The problem is that you contribute to the brain drain. Although it helps the United States to host these scientists,

many areas of parasitology and infectious disease, it makes so much more sense to have the researchers working in the country where the disease is endemic, where the patient population exists and where there is local information about the different types of disease and the body's response

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informed about what medical research is, how it's done, what the opportunities are with the human genome project. There's a great need in this country for more public education.

**ER:** Do you see the same problems as in Europe: the negative public perception of scientific research as in the GMO or the stem cell discussion? Is there an increasingly negative perception of science in the USA?

**TC:** Here, the overall view of the human genome project has been one of great excitement and positive press, but nonetheless there are people who have concerns that are quite reasonable, and sometimes they are frightened of things they don't understand. Some people in this country think that DNA is just in GMO foods, not in regular foods. Certainly one can only expect the public to make reasonable decisions about such social and political issues if they have some fundamental level of understanding. Much of the population went through school before the DNA revolution, others may have learned it but have forgotten it and they're interested in knowing more. I think the public is hungry for more knowledge. Part of the disaster with the GMO crops in Europe was that the public weren't treated with enough respect. People don't like to be treated that way. And personally, I think there are some issues with GMO crops. It's not that I am worried about eating them, it's simply questions of environmental and ecological consequences.

**ER:** So you think there should be more caution, more...

**TC:** There should be more attention paid to scientific research in the ecology area, and I think that such attention to proper environmental concerns would make the public feel much better about it. Think of what happened at Asilomar when American scientists at the dawn of the recombinant DNA era said, "We're entering a new area. Let's step back and let's think about what the consequences might be and what would be an appropriate response".

**ER:** But at the time of Asilomar, you had no corporate interests in DNA technology. Now, you have huge corporate interests in the GMO and biomedical field, which have changed the rules.

**TC:** It's definitely changed the situation. If the corporate interests had taken the same path as the scientists did at Asilomar, they



might have found their interests better served in the long run. I'm afraid that they miscalculated because they thought that

aquariums and other science institutions that try to educate the public as well as school children about scientific method, scientific discoveries, what it's like to be a scientist. Then there are significant ethical issues as well, in terms of who should have the right to see one's DNA sequence and should an employer or an insurance company be able to get access to such information. I think it is quite correct for the public to be concerned about such issues.

**ER:** Do you think that it would be an advantage if scientists rather than the government were involved in public education? Education basically is the responsibility of the government.

**TC:** Active scientists absolutely need to be involved in the process. The quality of high school and lower grade science teaching in this country needs much help. Public education also needs a great deal of attention. I think that first of all, working scientists can do a better job of trying to fix the current situation because of their knowledge and because of their interest in the topic. But it's also their responsibility. It's the federal government in this country that pays for

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they could save a billion dollars by doing this quickly. Well, maybe they lost billions instead, because, had it been done differently, then GMO crops would have been embraced rather than outlawed.

**ER:** Again, this is a question of education. How is Howard Hughes practically involved in public education in the USA?

**TC:** We cover the complete spectrum from medical students and graduate fellowships through to undergraduate education; promoting research experiences instead of just classroom experiences. It's not just biology, but also physics and chemistry and other sciences. There are programmes for teachers as well as students. There are programmes to support museums, botanical gardens,

most of the research. So I think it's very reasonable that scientists who are supported by the federal government, by the taxpayers, give something back, not just in terms of their discoveries, but also in terms of interacting with people. In the

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long run, it would serve us well to do so, because if we keep communication open with the public and they can see and meet the people whom they support with their

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tax dollars and feel they helped to pay for some of these great discoveries, I think that will encourage them to continue sup-

porting science through the federal system. We really think it is a good thing for scientists to spend a little bit of their time either in the community or in schools or helping to train a couple of high school teachers over the summer.

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### 'It would be a mistake to invest only in "model organisms" because the diversity of biology is exciting in itself'

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ER: A change of topic. You have received the Nobel prize for the discovery of enzymatic activity in RNA while working on a ciliated protozoan. And you also found the telomerase in...

TC: *Euplotes aediculatus*, which is another ciliate.

ER: So obviously there is value in looking at strange organisms. Do you see, with the current trend in studying model organisms, that there is a lot to be missed?

TC: Let me put it in a positive way. I think there is value in both approaches. Clearly if you decide to put a lot of resources into mouse, *Drosophila*, *Caenorhabditis elegans*, *Arabidopsis* or yeast it makes a lot of sense because you build up the tools, such as genetics, biochemistry, gene chip expression arrays, which all facilitate research. Research can be done very quickly, very rigorously and there's a huge database of information. It is not a mistake to make an investment in a handful of so-called model organisms. On the other hand, it would be a mistake to invest only in those because the diversity

of biology is exciting in itself. I dislike the term 'model organism' because it suggests that one should be interested in yeast only to the extent that it is a model for humans. I think that yeast biology is an important and exciting area as is fruit fly biology— independent of whether they reveal things about humans. And, because all of biology is connected, one can often make a breakthrough with an organism that exaggerates a particular phenomenon, and later explore the generality. The ciliate *Euplotes* has 50 million chromosomes per nucleus instead of about 50, which gives it a million-fold higher amount of telomerase. And this enabled Joachim Lingner, the Swiss postdoctoral fellow in our laboratory, to be the first to purify a telomerase and identify the catalytic subunit. The continuity of biology allows one to find a protein in the organism that's the most amenable experimentally and then use databases to jump around to other biological systems. That's just as good a paradigm for successful research as focussing on the few so-called model organisms. We need to continue to support both approaches.

ER: How would you advise a student who wishes to apply for work on single-celled algae or on a ciliated protozoan, rather than working on *Arabidopsis*?

TC: The NIH and the Howard Hughes Medical Institute are open-minded about the organisms that people want to study.

But if you want to study one of these strange organisms, you had better have a good justification. It's not good to say I want to study gene organisation in some obscure insect that no one's ever heard about if the same work could be done in *Drosophila*. But if the other organism has some unusual developmental pathway and you think this could illuminate the formation of the body plan in a way that will add value to what's known in *Drosophila*, then there's a reason. If you simply say I would like to do the same work in a strange plant, which I could do ten times more easily in *Arabidopsis*, then they'll probably say they'd rather fund the persons working on *Arabidopsis* because they will be able to make much faster progress.

ER: Do you think your Nobel prize has helped to support such a view in granting agencies?

TC: I don't know that it has, but I would like to think that.

ER: How much has the Nobel prize changed your life?

TC: It's been a good thing for me because it's given me more opportunities; for example, I'm very excited about my new job. It's been one of the highlights of my life and has given me opportunities that I have very much appreciated.

ER: Dr Cech, thank you for the interview.

The interview was conducted by Holger Breithaupt.

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