

IN CONVERSATION

From telomere to evolution, in conversation with Nobel Laureate Jack W. Szostak, FRS

Biju Dharmapalan



Jack William Szostak receiving the Nobel Prize from His Majesty King Carl XVI Gustaf of Sweden at the Stockholm Concert Hall, 10 December 2009
(Photo credit: <https://www.nobelprize.org>).

Jack W. Szostak, FRS, is an English-born American biochemist and geneticist who was awarded the 2009 Nobel Prize for Physiology or Medicine, along with American molecular biologists Elizabeth H. Blackburn and Carol W. Greider, for his discoveries concerning the function of telomeres, which play a vital role in determining cell life span. Szostak also investigated the process of chromosomal recombination during cell division and conducted studies into the role of RNA in the evolution of life on early Earth.

Szostak currently serves as a Professor of Chemistry and Chemical Biology at Harvard University, Professor in the Department of Genetics at Harvard Medical School, the Alexander Rich Distinguished Investigator at Massachusetts General Hospital and as a Howard Hughes Medical Institute Investigator.

In this special online interview with Biju Dharmapalan, he talks about wide-ranging topics.

Biju Dharmapalan: *Hi Jack, it's indeed a pleasure to meet you. Greetings and wishes from the team of Science Reporter, India's premier science magazine.*

Jack William Szostak: Nice to meet you online, sorry it's not in person.

Biju Dharmapalan: *Parents and teachers often instil scientific curiosity in our minds during our childhood. Could you recollect some of the memorable events during your childhood that helped you become one of the great scientists?*

Jack William Szostak: I was interested in math and science as early as I can remember, and my parents encouraged

those interests. My father built a small lab for me in our basement where I would do simple chemistry experiments. The experiments I conducted there often made use of remarkably dangerous chemicals that my mother was able to bring home from the company where she worked. With my father's assistance, shortly after the tragic Apollo 1 fire, we prepared and collected a jar of pure oxygen. We then carefully lowered a small quantity of methanol into the oxygen reservoir. The transformation of the barely visible pale blue flame in the air into an intense jet of fire in oxygen was amazing, but also horrifying in the context of the then recent Apollo fire. Less carefully supervised experiments frequently led to explosions, which made



Elizabeth Blackburn, Jack William Szostak and Carol W. Greider after delivering their Nobel lectures on 7 December 2009 (Photo credit: <https://www.nobelprize.org>).

chemistry seem much more dramatic than one would guess from the textbooks. My failure to carefully separate the hydrogen evolved during electrolysis from ambient air led to an impressive explosion which resulted in a glass tube being embedded in a wooden ceiling rafter. I also participated in more biologically oriented projects with my high school friend Joachim Sparkuhl. In the basement of his house, we constructed a small hydroponics garden, inspired, I believe, by the idea that astronauts living on some future space station would need or want to grow their fresh food.

Biju Dharmapalan: *Throughout your life, your areas of interest keep on changing, from chemistry to biochemistry, plant science, ecology, molecular biology and evolution. It seems you were a transdisciplinary person. Has this been your trump card in science?*

Jack William Szostak: The world is full of interesting and important problems. To be successful, you have to stick with a specific problem for long enough to make some progress. However, once I see that a lot of other people are working on the same problem, I tend to move on to some other area.

Biju Dharmapalan: *Many Nobel laureates, including you, often shift the area of research after receiving the Nobel Prize. But in our universities, researchers keep on researching the same topic their supervisor has taught them (or continue their PhD topic). Is this type of research good for science?*

Jack William Szostak: I think this depends on the person and the scientific area. Some people use the same experimental system to investigate different problems over their whole career, while others may make larger shifts into different fields. I do think it's important to be aware of progress being made in other disciplines, as most advances come from combining advances in distinct areas.

Biju Dharmapalan: *You worked in genetic engineering and synthetic biology even during your PhD in 1977. How far did your mentor Dr Ray Wu influence your research career?*

Jack William Szostak: Ray Wu was a wonderful mentor, who allowed and encouraged me to follow my own ideas. At the same time he was always available to talk and to help me when I encountered difficulties.

Biju Dharmapalan: *What inspired you to initiate telomere research in Yeast?*

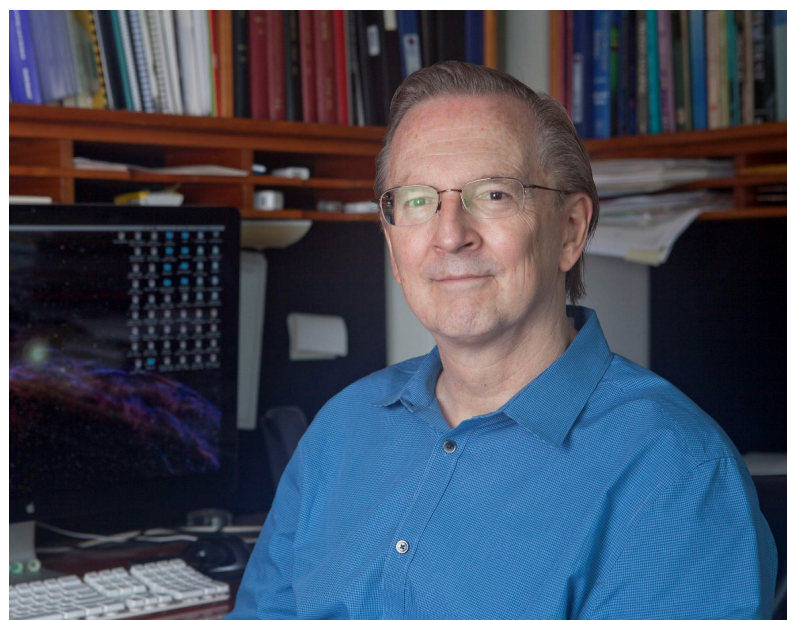
Jack William Szostak: That began as a collaboration with Liz Blackburn, after hearing her give a talk. We realized that looking at telomeres in Yeast could be helpful.

Biju Dharmapalan: *How far has your collaboration with Liz Blackburn helped in your research? Do you think collaboration with different institutions or labs is essential to bring out breakthrough discoveries?*

Jack William Szostak: The collaboration with Liz was essential for our work on telomeres. Some of the other projects that I have worked on have also been collaborations, but many others have benefited from discussions with other scientists while not being close ongoing collaborations.

Biju Dharmapalan: *Carolyn Widney Greider, who was a graduate student at Elizabeth Blackburn, also received the Nobel Prize along with you – this is an infrequent occurrence in the history of science. Why can't the Nobel committee recognize the whole team who worked on the discovery instead of recognizing only the team leader?*

Jack William Szostak: For historical reasons, the Nobel Prize is limited to three recipients. Picking the right three is



often extremely difficult, and there are many cases where the choices are highly controversial. In today's 'big science' we see papers with hundreds or even thousands of authors, so the tendency is to try to recognize the key people who started or drove the larger effort.

Biju Dharmapalan: *Can you mention the key persons associated with your prize-winning discovery?*

Jack William Szostak: Well, I'm biased but I think the Nobel committee recognize the right three people. Of course, many other

people in our laboratories and in other labs around the world contributed to the development of telomere research over the years. In my lab, I would point out that Vicki Lundblad made crucial advances while a post-doc in my group – she did the key experiments showing that defects in telomere biochemistry led to senescence in yeast.

Biju Dharmapalan: *You are a strong proponent of synthetic biology. How can synthetic biology help us solve issues faced by humanity, especially in health care and agriculture?*

Jack William Szostak: Some of the potential applications are obvious, such as producing pharmaceutical drugs and vaccines very cheaply in plants; other applications are less obvious such as developing enhanced methods for diagnostics. In many cases, synthetic biology is really just a collection of tools that help to speed up what is currently done more slowly by classical plant breeding for example.

Biju Dharmapalan: *Can we use synthetic biology to establish living creatures, for example, plants or other organisms, on other potential planets where humans can be colonized?*

Jack William Szostak: That remains to be seen. However, for humans to live on Mars for example will require plants that can survive there to generate food and oxygen. These would be in greenhouses not out in the harsh open environment, but will still require adaptations to lower light, different day-night and seasonal lengths,



Childhood photo of Jack William Szostak with his parents (Photo credit: <https://www.nobelprize.org>)

lower requirements for water and so on. Work is going on now to try to develop systems using algae for the purposes.

Biju Dharmapalan: *As a student, did you ever dreamed about getting a Nobel Prize?*

Jack William Szostak: It never occurred to me as a student that I would one day receive any prizes, let alone the Nobel Prize.

Biju Dharmapalan: *We always teach our students Darwinian Theory of evolution and object to Lamarckian theory? In this technology-dependent world, many cognitive skills of the present generation get badly affected. Does this show Lamarck was correct?*

Jack William: No. Biological evolution is Darwinian, but cultural evolution is quite different.

Biju Dharmapalan: *We are often taught in our textbooks about Stanley Miller and Harold Urey's experiment as proof of the origin of organic life. Can we use the same experiment to create new biomolecules?*

Jack William Szostak: The famous Miller-Urey experiment was a breakthrough in that it showed that some of the building blocks of biology could be made in simple ways. However, that experiment actually generated a very large number of other compounds, in trace amounts. Nowadays we have much better and more sophisticated ways of generating new molecules when we are searching for a molecule that will do something useful.

(Photo credit: <https://www.salk.edu/>)



Vicki Lundblad

Biju Dharmapalan: *Most present-day scientific concepts and observations are similar to statements mentioned in some ancient texts published in our early civilizations during BCE? Can we infer that these are the output of some great scientists who lived during that time, or is it some fiction written by literary figures?*

Jack William Szostak: I think you have to be careful when looking back – it's easy to cherry-pick statements that seem to anticipate modern advances or understanding. You have to look at the context of the time to understand if some historical statement really reflected a prescient understanding of how the world works.

Biju Dharmapalan: *Every religious text speaks about the end of life on this planet? Based on the current scientific evidence, how do you see the future of life on this planet? Is the extinction of Homo sapiens imminent, or we shall overcome it through science?*

Jack William Szostak: The problem is that we have the scientific understanding and the engineering ability to overcome environmental crises such as climate change and global warming. The problem is political and social – we won't survive if people cannot look beyond short-term and local advantages.

Biju Dharmapalan: *In many countries, policymakers give over-emphasis to applied research, often neglecting fundamental research. In your opinion, should researchers follow their passion or follow the needs of funding agencies?*

Jack William Szostak: I think both are important, and the same person can often contribute to both basic and applied science. If funding agencies go too far in favour of immediate gains from applied science then they are sacrificing future advances for short-term gain. So it is important that the correct balance be struck.

Biju Dharmapalan: *There is always a wide gap of 20 to 30 years between the period of research and recognition by*

the Nobel committee. Shouldn't this gap be reduced by 1 to 5 years so that the researcher gets immediate credit for his work rather than at the fag end of life?

Jack William Szostak: In most cases, it's just not possible to tell what advances will be the most significant in such a short time frame.

Biju Dharmapalan: *Your student Jennifer Anne Doudna is also a Nobel Laureate, do you ever tell your students strive to become Nobel Laureates?*

Jack William Szostak: You can't tell someone to try to become a Nobel laureate – people who aim for recognition rather than aiming to follow their own interests are seldom successful. Jennifer was an amazing scientist even as a student in my lab, and she followed her own instincts throughout her subsequent career by working on problems that she thought were interesting and exciting.

Biju Dharmapalan: *Science graduates often complain about the lack of employment opportunities in science even after doing a PhD or Post-doc. Can you give a few tips to our youngsters for making them employable in the current world?*

Jack William Szostak: Sure, there are many career paths open to scientists. I would say that one of the most important talents to develop is good writing. The ability to communicate effectively will lead to success in any area you choose.

Biju Dharmapalan: *Can we expect another breakthrough discovery in evolution from you, possibly another Nobel Prize?*

Jack William Szostak: I think the work we are doing on the Origin of Life is very exciting, so I am hoping that we will make some significant advances. I'm focused on improving our understanding of how we got here in the first place. It's not helpful to think about future prizes.

Biju Dharmapalan: *Can we always remain young by caring for our telomeres?*

Jack William Szostak: Ageing is not the result of any one thing going wrong. Many factors contribute to ageing, so telomeres are just one part of the larger overall picture.

Biju Dharmapalan: *Thank you, Jack, for your valuable comments and time.*

Jack William Szostak: Thank you for your wide-ranging questions.

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