

Prof. George Church

A POLYMATH'S JOURNEY IN REINVENTING SPECIES

Biju Dharmapalan

Prof. George Church is a professor of Genetics at Harvard University and one of the world's leading genomic sequencing method, which resulted in the first genome sequence (the human pathogen, *H. pylori*). He helped initiate the Human Genome Project in 1984 and the Personal Genome Project in 2005. In the early 1990s, Church assisted in the development of an idea for nanopore sequencing that could help make sequencing quicker and more accessible for projects like the Human Genome Project.

Additionally, Church also began developing another sequencing technology called polony sequencing that enabled researchers to sequence millions of DNA strands at once. George invented the broadly applied concepts of molecular multiplexing and tags, homologous recombination methods, and array DNA synthesizers. As of 2021, Church is involved in multiple endeavours using genome engineering to create new biofuels, reverse human ageing, and revive extinct species through a process called de-extinction.

In 2012, Church was involved in promoting and working towards de-extinction, or a process that creates new proxies of extinct species through genetic engineering. That year, he published a book with Ed Regis titled *Regenesis: How Synthetic Biology Will Reinvent Nature and Ourselves*, in which the authors explore how biotechnology can make innovative new procedures possible, such as the creation of new renewable energy, the extension of human life, or the de-extinction of species.

In this special online interview with Biju Dharmapalan, he talks about his journey in science.

Walter Gilbert, George Church's mentor
(Image credit: wikipedia.org)

Biju Dharmapalan: You have been designated as one of the top polymaths of the 21st century, can you tell our readers how one should prepare themselves to reach the position of a polymath?

George Church: Maintain the extreme curiosity of your early childhood. Find a task that requires multiple disciplines to co-exist in one brain — in my case, this task was RNA crystallography.

Biju Dharmapalan: You have played with molecular techniques and tools, especially in genomics when the field was just catching up. What made you focus on this area? Or did you realise that genomics would revolutionise science in future?

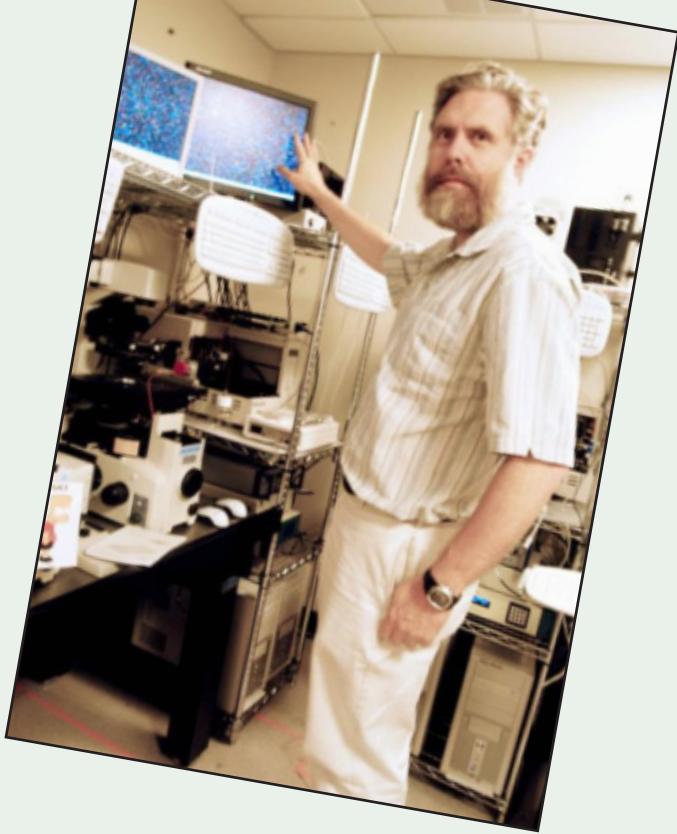
George Church: RNA crystallography led me to RNA sequencing, and hence to genomics. It seemed plausible to me that some automation analogous to what we had in crystallography (e.g. diffractometers) could help accelerate research in other fields of chemistry and biology.

Biju Dharmapalan: You worked along with Nobel laureate Walter Gilbert for your PhD, how was your experience working with a pioneer in the field?

George Church: I enjoyed his multidisciplinary enthusiasm and entrepreneurship — also enjoyed the amazing team that coalesced in his Harvard and Biogen labs in those key years (1977-1984).

Biju Dharmapalan: From Gilbert's chemical sequencing to the polony sequencing Polonator G.007, the sequencing approaches have become more simple and cheaper, how do you foresee the future of sequencing technologies?

George Church: They are definitely NOT simpler. They are cheaper per base-pair analyzed, but much more is spent today on sequencing than ever before.



Biju Dharmapalan: *You have been a proponent of rewriting genetic code and creating synthetic organisms. Won't it create problems in our biosphere?*

George Church: Doing nothing can potentially cause bigger problems. We are blessed with strong regulatory agencies NAS, FDA, USDA, EPA, CDC, WHO, SEC, USPTO, UN.

Biju Dharmapalan: *I think you are interested in creating a synthetic human genome? How will it benefit humanity at large?*

George Church: One of our main applications is making human stem cells resistant to all viruses by changing the genetic code. This could help prevent viral infection in manufacture as well as in cell therapies and transplants — even newly emergent viruses for which we don't yet have any experience.

Biju Dharmapalan: *Is it possible to create immortality in humans?*

George Church: Unlikely to happen soon (by definition). But we might be able to get ageing reversal therapies available soon (for example Rejuvenatebio).

Biju Dharmapalan: *You hope to revive the long-extinct woolly mammoth, what's the need to revive extinct species?*

George Church: We are not aiming for reviving a species, but rescuing endangered species (Asian and African elephants). The 'need' is to reduce a runaway feedback loop in warming the Arctic causing methane release (which is 30-fold worse than carbon dioxide).

Arctic elephants could help restore high reflectance (albedo) of grass (relative to current trees), high-cold-conductance *via* trampling, and higher carbon capture *via* higher efficiency photosynthesis.

Biju Dharmapalan: *Species extinction is the rule of nature. Then why should we need to focus on that?*

George Church: 'Natural' doesn't always mean desirable for human goals — e.g. pandemics, invasive species, killer asteroids, etc. Rescuing (nearly) extinct species that are also 'keystone' species can also help save or restore whole ecosystems — some of which may be crucial for human well-being (for example, sequestering the Arctic carbon).

Biju Dharmapalan: *The emergence and usage of AI technology has made humans dependent on technology, won't this adversely affect the cognitive skills of our species?*

George Church: It could enhance cognition as we interact with AI which can be programmed to be more patient and more communicative than most human mentors. We also could benefit from computers handling the routine, boring, time-consuming tasks so that we can focus our intellect on creative and out-of-the-box tasks that are not the forte of AI. We will likely also develop new technologies to biologically augment our brains.

Biju Dharmapalan: *Space colonisation seems to become a reality in the near future, what would be the role of omics technologies in the space era?*

George Church: We need to deal with human-to-human and day-to-day variation in our physiology, especially points of new challenges — dysbioses due to low microbial diversity, low gravity effects, psycho-social issues from confined and/or highly alien environments.



Image credit: Channel 4



Biju Dharmapalan: *Most of our scientific discoveries and innovations have been objected by the ruling/peer community of the time. Human genome editing has been objected by scientists across the globe and even He Jiankui has been persecuted for the work. Do you think gene-edited babies will become a new normal in the near future?*

George Church: The issue is not 'human genome editing' or even 'edited babies', but germline editing. There is not yet a clear medical need. Most diseases that can be prevented or fixed via germline editing can also be handled for lower cost and impact via genetic counselling pre-conception or pre-natal. We can treat babies or even fetuses if it doesn't affect the next generation.

Biju Dharmapalan: *Science graduates from India often complain about the lack of employment opportunities in science even after doing a PhD, can you suggest a few tips to our youngsters for getting good employment in science?*

George Church: Good social and language skills, willingness to travel while young, picking the right field (slightly ahead of the crowd, but not too far ahead).

Biju Dharmapalan: *What was the biggest hurdle in science for you when you started your research career?*

George Church: My mediocre communication skills coupled with many counter-intuitive and premature ideas.

Biju Dharmapalan: *Humanity is badly affected by pandemic; can you give a few insights for overcoming future pandemics?*

George Church: Since the cost of bio-surveillance has dropped 20 million-fold we have the opportunity to do a lot more bio-weather-mapping for emerging



zoonotic diseases, resistance to drugs or vaccines, for any alterations in distribution, etc. The gene therapy vaccines (AstraZeneca, Moderna, Pfizer) are helping the safety, cost, efficacy and speed of clinical trials.

Biju Dharmapalan: *People across the globe are concerned about the recent IPCC report that raises serious concerns about our environment. Can biotechnological interventions reverse climate change?*

George Church: I think so, but it requires focusing on carbon sequestration. One good location is some subset of the 20 million square kilometres of Arctic and similar sized regions in deserts.

Biju Dharmapalan: *Molecular tools have made scientists don the role of creator, will someone start a religion with scientists as 'GOD' in future?*

George Church: Doubtful. Maybe a minor prophet. Humans have for many millennia in the past seen key creators/engineers — breeding for agriculture and animal labour, spreading out over earth, deep seas, and space.

Biju Dharmapalan: *Your mentor was a Nobel laureate, you have touched upon almost every aspect of biology and made significant contributions anyone would envy, did you ever dream of getting a Nobel prize?*

George Church: This has not been a concern. Unclear how that would help the world or my research. I am very grateful for the support that I have had for many years from many friends, collaborators and funding sources — and for seeing the positive impacts on our society. These are more than sufficient.

Thank you for this enjoyable discussion.

Biju Dharmapalan: *Thank you Prof. Church for sparing your time for our readers.*

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