Behind the Vaccine

A Conversation with **Satoshi Ohtake** (BS ’00)

The COVID-19 pandemic and subsequent lockdowns drastically changed work conditions for many people around the globe. For some, that meant working from home instead of the office. For others, like doctors, nurses, frontline workers, and those working in public health, it meant steeling themselves for the intense work ahead. For Satoshi Ohtake (BS '00), Pfizer's senior director of pharmaceutical research and development, the pandemic meant finding a way to develop a vaccine against SARS-CoV-2.

Ohtake, who is also president of the Caltech Alumni Association (CAA) Board of Directors, sat down over Zoom with *Caltech* magazine staff writer Lori Dajose (BS '15) to discuss the history-making process of developing a vaccine against SARS-CoV-2, how his Caltech experience prepared him for such a job, and new changes happening within the CAA.

Lori Dajose [LD]: Pfizer has basically become a household name due to COVID-19. What has it been like to work on a vaccine for the virus that has caused this pandemic?

Satoshi Ohtake [SO]: It's been unreal to say the least. To see your work featured on the news is strange. The biggest challenge was definitely the timeline of developing a vaccine from concept to product under tremendous pressure. Another challenge was to unlearn what we do best, which is to develop a product robustly in a stepwise manner. Instead, we tackled many studies in parallel, which really got us thinking both scientifically and strategically.

On top of that, it was a new technology for us. Although we had been investing in the mRNA [messenger RNA, a type of short-lived genetic material that encodes for a protein] technology prior to the pandemic, this was our first product in which we went all in. We had all hands on deck, and I'm really proud of our accomplishment. All credit to our dedicated team of scientists who worked nonstop to successfully deliver the vaccine.

My responsibility at Pfizer is not only focused on the COVID vaccine. We have 50-plus programs that are just as important when you think about the impact they have on people's lives. While we did everything we could, within our capabilities, to accelerate the development of the COVID vaccine, we didn't take a step back in developing the critical programs in our five therapeutic areas of focus: oncology, vaccines, rare disease, internal medicine, and inflammation and immunology. For example, our next-generation pneumococcal vaccine as well as human growth hormone treatment have been filed for registration, and we're placing a lot of emphasis on developing gene therapies using a different technology platform: adeno-associated viruses.

Now that we've been able to develop the COVID vaccine in such a short period, the question has become, can we accelerate all R&D programs in a similar manner? Management discussions are taking place to assess the ability to prioritize and shift our resources accordingly. How do we balance business needs with our colleagues' needs for their development? That is the challenge.

[My team is responsible for only] a very small fragment of COVID vaccine development. Our experts in the vaccine group conduct preliminary research on the compound to be developed. We have a partner line that figures out a way to scale up the production, and then my team takes it from there. More specifically, we figure out how to stabilize the therapeutic compound and then we develop a robust process to manufacture materials to enable clinical trials and eventually commercial production.

[LD]: People are now talking about ways to prepare for the next pandemic. Given your experience with vaccine and therapeutic development, what are your thoughts on the future of the evolutionary battle between humans and viruses?

[SO]: Pandemics have occurred throughout history. Before COVID, there was the Spanish flu about 100 years ago and the black plague about 650 years ago. We learned a great deal from nature that enabled us to advance our medical technologies. Many biotech companies are pursuing the mRNA approach: some are focusing on monoclonal antibodies, while others are looking at small molecules or adeno-associated viruses. Our toolbox has expanded considerably over the years.

But the minute we come up with a good defense for certain types of infections, nature's pretty smart and figures out a way to get around our strategy. We then work on an alternative approach. It's cyclical. Interest in mRNA and gene-therapy technologies has gone hot and cold many times. It's critical that we continue funding fundamental research in academia, which then gets translated to therapeutics or treatments by industrial partners. I think that's how we continue to progress and try to stay one step ahead of nature. Well, maybe it's more accurate to say not get too far behind nature.

[LD]: What were your research interests at Caltech, and how did they lead to where you are now?

[SO]: Professor Mark Davis [Warren and Katharine Schlinger Professor of Chemical Engineering] was the person who helped me start my career in research. He welcomed me into his research group as an undergraduate researcher my sophomore year. I was browsing through the chemical engineering faculty research web

pages (yes, they did exist in the '90s), and I decided to send him a message because I was really curious to learn more about his research. He paired me up with a very talented graduate student, Chris Jones (MS '97, PhD '99), who is now a professor at Georgia Tech, and I learned a lot about catalysis. That was a very different kind of research from what I'm doing now, but I gained a lot of perspective about what it means to be a scientist beyond just doing the scientific coursework.

After Caltech, I went to the University of Wisconsin to study chemical engineering, intending to continue catalysis research. But when I got there, my curiosity led me to change course to research on cryopreservation. We rely on cold temperature storage for many of our therapeutics as well as for tissues and organs for transplant surgery. Nature provides many clues for how best to preserve living organisms. Have you heard about these tiny creatures called tardigrades? Without water, they dry out. Upon rehydration, they come back alive. I'm not sure coming back alive is technically correct since they never ceased to live, but their activity certainly slows down considerably. Trehalose is a [sugar of the] disaccharide [class] found in tardigrades and many desiccation-tolerant organisms. That has spawned a new field of research assessing the role of these sugars and other amino acids in enhancing the stability of biologicals. They have been assessed for their ability to provide protection not only during drying but also during freezing, which is a form of dehydration since water is crystalized.

Satoshi Ohtake at his Caltech Commencement in 2000, with his parents and physicist Stephen Hawking. Ohtake was using a wheelchair because of a broken ankle.

[LD]: Does cryopreservation have anything to do with why the Pfizer vaccine has to be kept at such cold temperatures?

[SO]: In a sense, yes. Most of the biotherapeutic products are sensitive to temperature-induced stress, similar to why food stored in the freezer lasts longer than that left on the counter. As we gain more understanding about the effects of cryopreservation and improve our technology, we can offer the product with enhanced storage stability, sometimes in the form of higher temperature storage, which makes transport and handling easier. An alternative to low temperature storage is drying. We're working on freeze-drying approaches for many of our therapeutics because it enhances the storage stability and ease of transport.

[LD]: You mentioned that your research trajectory shifted a few times. Could you talk about the importance of having that flexibility to switch fields and the freedom to change your mind?

[SO]: Transition is not easy, especially if you've spent so much time and dedication in one field. The unknown can be scary. But in everything that you learn, a lot of the valuable aspects are transferable skills. For example, decision making, the ability to think critically … independent research is just that. When you look at a problem, you derive a hypothesis, propose reasonable assumptions, and set boundary conditions. Does the solution make sense, or do we need to modify any of our assumptions? Or perhaps our hypothesis? Whether you happen to select a topic in, say, catalysis or cryobiology, either way, you approach with the mentality of a researcher. With curiosity.

I've been fortunate to work with many professors and mentors who have made these successful transitions. On the other hand, I've also had many mentors and co-workers who have dedicated their entire careers to one field. In the end, both approaches are valid as long as you're passionate about it. There's really no one correct path.

[LD]: You recently took on the role of president of the Alumni Association Board of Directors. Can you tell us what that role entails?

[SO]: The Caltech Alumni Association is a separate nonprofit organization from the Institute, so we work independently but closely with the Institute and its campus partners. My role is to collaborate with the Alumni Association staff, especially with Ralph Amos, who came on board more than a year ago as our executive director, to enable engagement with our alumni, with the students (our future alumni), and also with the Institute.

[LD]: What is your vision for your tenure in this position?

[SO]: One aspect is implementation of digital technology and its many offerings. Due to COVID, many of our alumni are now more digitally savvy. We had a four-fold increase in the number of alumni who joined our first virtual Seminar Day last year, in comparison to the year prior. While I'm not advocating to carry on with only virtual events, I hope we can adopt a hybrid approach. We know the capability that digital tools can offer us, allowing us to connect with our alumni across the globe, but I still find it difficult to replace in-person interactions. Maybe I'm just old school.

Many of our alumni reside outside of Pasadena, so we want to make sure that there are ways in which they can stay connected and engaged with us. We are looking to increase the diversity of the board to better represent the diversity of our alumni community. Over 50 percent of our living alumni graduated post-'90s, and we have observed an increase in the diversity of our graduating class year after year. Correspondingly, our board should shift its composition and mentality.

We look forward to having international alumni serve on the board, and we will benefit from having a wider global perspective. The end result is better programming that caters to the interests of our diverse alumni.

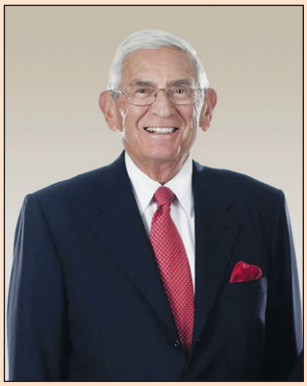
[LD]: How do you envision the alumni–student relationship?

[SO]: The level of rigor at Caltech is, bar none, the highest I've ever seen. It trains you well because the standard is so high. And I think it's good that they keep it high. The challenge is adaptation. Student life at Caltech does not necessarily translate well to life in the real world. Not everything can be solved with rationale or logic. And it's going to be difficult to find another place in the world in which you will find yourself surrounded by people just as smart as you, if not smarter. This is an area in which seasoned alumni can help students better prepare to be successful in the next stages of their careers, to share their perspectives about what it's like after graduation. I've enjoyed getting to know many undergraduates and graduate students [who are] considering careers in the pharmaceutical industry. I've also connected with those considering a career transition. For those alumni who have yet to utilize the new CAA website and Alumni Portal, which is like LinkedIn for Techers, please take a moment and connect.

We're evolving as an organization as well. If there are alumni who have any interest, whether it's serving on the board or collaborating with the board on our diverse programs, please reach out. We're more than happy to connect, whether it's on a personal basis or just to look for ways in which we can have an impact on the Caltech community.

In Memoriam

Read more about his life at **magazine.caltech.edu/post/in-memoriam**



Eli Broad 1933–2021

Eli Broad, founder of SunAmerica Inc. and KB Home, former member of the Caltech Board of Trustees, and a Life Member of the Caltech community, passed away on April 30, 2021. He was 87 years old.

An entrepreneur, civic leader, and philanthropist, Broad was an influential advocate for and generous benefactor of life sciences research, public education, and the arts. Throughout his life, he worked to create and foster new businesses, education organizations, scientific research institutions, and museums.

"Eli Broad's distinctive vision and influence shaped the landscape of Los Angeles, cultivating the arts, education, and science, and enriching our society," says Caltech president Thomas F. Rosenbaum. "At Caltech, Eli and Edye catalyzed research in the life sciences, helping our faculty and students illuminate nature and improve the human condition."

Broad's commitment was most evident at Caltech through his leadership on the Board of Trustees and his long-standing investments in the Institute. In partnership with his wife, Edythe, Broad donated more than $40 million to the biological sciences at Caltech through the Eli and Edythe Broad Foundation. Their generosity helped to establish the Broad Center for Biological Sciences, an interdisciplinary campus hub that houses research groups exploring diseases, disorders, and medical treatments and therapies, and provides flexible funding for professors to pursue bold new areas of science.

"His generosity and concern for the city of Los Angeles, for the arts, and for the biomedical sciences was on a scale that was qualitatively different than anyone else," says Caltech president emeritus and distinguished professor of biology David Baltimore. "And while he had no scientific background himself, his belief in and commitment to the people around him enabled him to move forward the kinds of biological science—stem cell science, genomic science—that have made a huge difference the last couple of decades."