



日本国際交流センター

JAPAN CENTER FOR INTERNATIONAL EXCHANGE

Japan-US Dialogue

Harnessing New Technologies to Battle COVID-19

Co-sponsored by the Japan Center for International Exchange (JCIE/USA)
& the Consulate General of Japan in New York

NEW YORK: OCTOBER 1 (7:00–8:15 PM EDT)

TOKYO: OCTOBER 2 (8:00–9:15 AM JST)

On the evening of October 1, JCIE/USA and the Consulate General of Japan in New York co-hosted an online dialogue featuring Dr. Shinya Yamanaka, the recipient of the 2012 Nobel Prize in Physiology or Medicine. This was designed to share lessons from Japan's relatively successful COVID-19 response and explore possible areas of US-Japan collaboration in battling the epidemic. The meeting started with remarks from Japan's Minister of Economic and Fiscal Policy, Hon. Yasutoshi Nishimura, who is in charge of Japan's COVID-19 response, then moved on to a presentation by Yamanaka and a conversation between him and Pulitzer Prize-winning science writer Laurie Garrett, culminating in a dialogue with roughly 20 top US and Japanese experts on public health, medicine, and international affairs. It was moderated by JCIE/USA Executive Director James Gannon, and Ambassador Kanji Yamanouchi, the consul general of Japan in New York, gave closing remarks.

The Japanese Government's Approach

Minister Nishimura outlined the Japanese government's approach to the pandemic, which stressed the need to prevent the spread of the pandemic while simultaneously maintaining economic activity. In April and May, as the virus began to spread in Japan, the government adopted emergency measures including voluntary closures rather than a mandatory lockdown. They employed two techniques: a retrospective cluster-based approach and a public awareness campaign on avoiding the 3 Cs (closed spaces, crowded places, and close-contact seating). When numbers began to rebound in July and August, Japan turned the tide through a focused, strategic approach. Using genetic analysis, they identified large entertainment areas as hot spots. Those areas were then tested

intensely, and bars and restaurants were asked to close earlier than usual, allowing the country to suppress the spread of the virus without too large of an economic toll.

Nishimura stressed that it is unrealistic to expect COVID-19 to disappear completely, and the goal should instead be a reduction of cases to a level where it can be contained through cluster-based approaches. In order to better understand the effectiveness of various individual measures taken to date, Nishimura created an AI Advisory Board in August to review the big data analyses and artificial intelligence (AI) simulations. (Dr. Yamanaka has been appointed as one of the senior members of this board.) Japan's AI researchers have been studying more than 5,000 cases to better understand the factors that lead to severe infections and

identify potential therapies. They have also used the Fugaku supercomputer in Kobe—the world’s fastest computer—to analyze the spread of the virus through droplets and aerosols, which has led to policy recommendations allowing full attendance at events where



there is little talking or shouting, such as movies and classical concerts, while limiting attendance at events such as sports. Japan’s results to date have been impressive, with only about

84,000 confirmed infections and 1,570 deaths, as compared with more than 7 million infections and more than 200,000 fatalities in the United States. Nishimura expressed his hope that the United States and Japan can learn from one another and work together to battle the unprecedented threat of the virus.

Chasing Factor X

Yamanaka began by noting that he is a scientist working on stem cells rather than a virologist but hopes to contribute to the pandemic response in some way. Until the pandemic struck, he had been commuting monthly between Kyoto University and his lab at the Gladstone Institute of Cardiovascular Disease in San Francisco, and his perspective on the pandemic was thus influenced by the contrasting impact of the virus on those two communities. He noted that more than 200 countries are now suffering from a nearly identical virus, each with different policies and strategies and therefore with different results. But the results have been rather surprising. Comparing the stringency level of measures—e.g., travel restrictions, lockdowns, business and school closings—Japan took a much milder approach than countries such as the United States and the United Kingdom. Testing was also much more prevalent in the United Kingdom and the United States than in Japan, where tests were used strategically and only given to high-risk people. But despite this less stringent approach, the rate of COVID-19 deaths in Japan has remained remarkably low, with just 12 per million people as compared to 622 in the United States and 620 in the United Kingdom.

Various factors must be at play here to explain the discrepancy, which Yamanaka referred to as “Factor X.” There are two key questions: First, “What is Factor X?” Is it related to Japan’s habit of wearing face masks, some pre-existing immunity, or genetic differences? And second, “Will Factor X continue?” If Factor X does not continue through the coming flu season, Japan could be in trouble. Scientists, including Yamanaka, are now searching for the answers to those questions.

About 14 years ago, Yamanaka and his team developed a new stem cell technology, induced pluripotent stem cells, or iPS cells. Previously, stem cell research had relied on ES cells, or embryonic stem cells, which raised ethical issues and politicized the field. The iPS cells are identical to ES cells but are derived from a patient’s own skin or blood cells and can be converted into virtually all types of cells found in the body, such as neurons, heart cells, muscle cells, and so on. With the support of the Japanese government, he has been able to share the technology and give impetus to regenerative medicine and drug development. Now, he is trying to use this technology to help identify Factor X. By converting peripheral blood cells from individuals in the United States and Japan into iPS cells, they can create lung organoids (mini lungs) and test the impact of SARS-CoV-2 on that organoid. The iPS cell technology provides the ability to conduct these tests in



a Petri dish in the lab instead of in humans.

Yamanaka concluded his initial presentation by noting that the travel restrictions have reinforced our tendency to focus on only our own country’s battle with the pandemic, but the fact that countries around the world are applying different policies and strategies to an identical virus and having different results demonstrates the need to think globally and learn from one another.

In interviewing him, Laurie Garrett asked about the factors that are being considered in the search for Factor X and noted that all of the countries that experienced the 2003 SARS outbreak seem to have been faring relatively well in this pandemic, with

the exception of China. She asked Yamanaka what he thinks is the most significant aspect of the 2003 experience that has informed the response capacity of those countries to COVID-19. He noted that the countries that experienced SARS and MERS were well prepared in terms of PCR testing, contact tracing, and, most importantly, having the proper mindset. Those were important advantages. Garrett also



noted that SARS was a nosocomial disease, meaning that it was often acquired within a hospital setting, and so those countries greatly improved infection control in their medical facilities. Yamanaka agreed, stressing that the United States and Japan should be sure not only to overcome this pandemic but to learn from it so that we are better prepared for pandemics in the future.

Turning back to Factor X, Garrett pointed out that while COVID-19 was initially thought of as a respiratory disease, it has become increasingly clear that it is more of a cardiovascular disease, and that recent research has shown that the virus infects and denucleates the heart cells. Given that fewer Japanese people tend to have high blood pressure, high cholesterol levels, obesity, or other cardiovascular issues, and that the fish-heavy Japanese diet offers some protections, she wondered if Factor X could lie somewhere in those areas. She also wondered whether stem cells

can be used to help deal with some of the long-term cell destruction caused by the virus.

Yamanaka explained that, in his work at the Gladstone Institute, they are making heart cells using iPS cells as well and have found that the virus does infect heart cells—more so, probably, than lung cells. Many of those who have recovered from COVID-19 in the United States and Europe are experiencing heart dysfunction. But Japanese doctors are reportedly not seeing as strong an impact on the hearts of patients in Japan, so that is one area that is being studied using heart cells created with iPS cells from Japanese and American people. There might be some difference between populations in terms of the number of ACE2 receptors—a protein on the surface of cells that is the entry points for the virus—found on heart cells, for example. These are good candidate theories for Factor X.

Japan-US Dialogue

The discussion was then opened up to the full panel of roughly 20 experts for a dialogue that focused on possible explanations for the relative success in Japan and elsewhere in Asia, as well as opportunities for deepening US-Japan cooperation on the pandemic.



Understanding Factor X

At the start of the dialogue session, Dr. Victor Dzau, a cardiovascular researcher who is the president of the National Academy of Medicine (NAM), emphasized that, in searching for Factor X, it may be more important to focus on the social determinants of health rather than biological differences between Asians

and North Americans. There are many Americans of Asian descent, like himself, yet the outcomes in the United States have been markedly worse for these populations than in Asia. The NAM has been preparing a report on vaccine allocation, and as part of this they have looked into whether biology and ethnicity are the most significant factors or whether it is social indices (crowded living conditions, comorbidities, poverty, etc.). They have concluded it is really social vulnerability that is most important. Yamanaka was in complete agreement, noting that he believed social determinants are critical. For example, people in Asia—not just Japan—generally have had lower cases and lower per capita death rates, but Asians living in America have seen high rates, which shows that the primary factor is not genetic.

Amb. Mark Dybul, former director of the Global Fund to Fight AIDS, Tuberculosis and Malaria, argued that 90 percent of the difference can be explained by good policies and bad, and he stressed that much of the appallingly poor response in the United States can be accounted for by policy choices. Still, he still feels it is worthwhile exploring if there may also be genetic factors that play a role, noting that AI-based research on issues like bradykinin and interferon receptors can be particularly important.

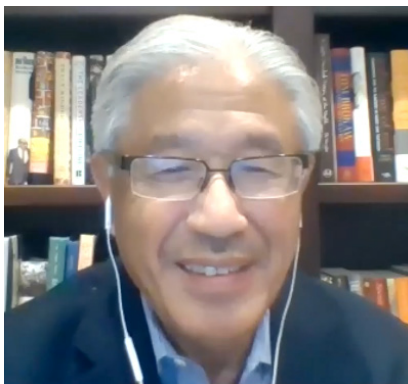
Yamanaka agreed, noting that even after accounting for the many non-biological issues that appear to be primary drivers of the disparities in outcomes, it is still important to explore whether there are biological factors. For instance, San Francisco has had a very effective response, and it has one of the lowest death rates among major US cities. But mortality rates in Tokyo, Osaka, and Kyoto are still much better than

San Francisco, implying that there may still be biological factors at play. In addition to pulmonary and cardiovascular effects, Yamanaka noted, COVID-19 is an immunological disease so it is also important to look at immune responses, including whether they are different for different populations.

Participants discussed the need to expand comparative research beyond just Japan and Western countries to take into account the successes in suppressing the spread and mortality rates in other countries around Asia, such as South Korea, Thailand, and Vietnam. Dr. Dennis Carroll, who chairs the Global Virome Project, spoke about the profound differences between the United States and Europe, on the one hand, and East Asian countries on the other. Yamanaka stressed that he does not believe that there is one single Factor X, but that there are multiple factors. Some responses, such as widespread mask wearing, are common throughout Asia, while other approaches, such as extensive testing programs, have been implemented in places such as South Korea—which quickly implemented drive-through testing and strict contact tracing using GPS—while other countries like Japan have not pursued these, without much difference in overall outcomes. The impact of these approaches, Yamanaka argued, needs to be investigated further so that we can learn from one another.

Opportunities to Deepen International Collaboration

Several participants, starting with Dr. Sheila Smith of the Council on Foreign Relations, expressed the hope that US-Japan partnerships and dialogues that include scientists alongside policymakers and experts



from other sectors of society can advance meaningful collaboration on the COVID-19 response and share information that leads to better policies and more effective care. Dr. Peter Kilmarx, deputy director of the Fogarty International Center at the National Institutes for Health, explained that there is already a strong foundation for US-Japan collaboration, noting that in the past year, the NIH has been supporting 487 active US-Japan collaborations with 387 investigators at 184 organizations, there are 134 Japanese postdoctoral researchers at the NIH, and there are numerous formal collaborative arrangements with Japanese organizations in place. Thanks to those established relationships, some degree of US-Japan collaboration on the pandemic is already underway. The National Center for Global Health and Medicine in Japan is part of the adaptive COVID-19 treatment trials, for example. NIH has also been providing extensive support for AI, with hundreds of millions of dollars in funding, and so Kilmarx felt it is worthwhile exploring the expansion of this to US-Japan collaborative efforts. Yamanaka also noted that Japan's AI Advisory Board comprises only Japanese experts and that it should pursue greater collaboration with American and other researchers around the world.

Dr. Robert Yanagisawa of the Icahn School of Medicine at Mount Sinai drew on his experiences caring for COVID-19 patients in New York City to propose that more attention be given to applying AI in practical ways to assist front-line clinicians. For example, by identifying social and genetic factors as

well as clinical and lab findings, compiling these, and analyzing these using AI, we could more accurately assess which patients are at risk of stroke or kidney failure. The data is coming too fast at the moment for those in the field to fully read, digest, and apply, but researchers involved in international collaborations utilizing AI can point to ways to improve care. Yamanaka added that sharing US data on the multiorgan impact of COVID-19 can be particularly helpful for Japanese researchers, who have seen much fewer cases of this in their work.

There was also consensus that priority should be placed on utilizing the predictive capabilities of AI for emerging diseases. Dr. Florian Krammer, a virologist, pointed out that zoonotic infections had not been seen for a long time, but in recent years we have witnessed SARS, MERS, and now COVID-19, so AI can be helpful in predicting where and when such viruses might emerge by looking at population density, circulation of viruses in different animals, etc. That would require stronger international collaboration, an expanded exchange of data, and a global network to support this.

In closing, Ambassador Kanji Yamanouchi noted that COVID-19 is far from over and reiterated the importance of greater international collaboration in responding to the pandemic. He expressed his belief that there is much more that Japan and the United States can do together in a cooperative manner, building on this dialogue, not just for the citizens of their own countries, but also for the international community.



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AGENDA

Opening & Welcome

Mr. James Gannon, Executive Director, JCIE/USA

Special Remarks by the Minister in Charge of the COVID-19 Response

Hon. Yasutoshi Nishimura, Minister of State for Economic and Fiscal Policy; Minister in Charge of Economic Revitalization; Member, House of Representatives of Japan

Conversation with 2012 Nobel Laureate Shinya Yamanaka

[Featured Speaker]

Dr. Shinya Yamanaka, Director, Center for iPS Cell Research and Application (CiRA), Kyoto University; 2012 Nobel Laureate in Medicine; Member, AI Advisory Board on COVID-19 to the Cabinet Secretariat of Japan

[Moderator/Interviewer]

Ms. Laurie Garrett, Pulitzer Prize-winning author of *The Coming Plague*; Science Contributor, MSNBC; Columnist, *Foreign Policy*

Japan-US Dialogue with Dr. Shinya Yamanaka

[Moderated by Mr. James Gannon, Executive Director, JCIE/USA]

Dr. Dennis Carroll, Chair, Leadership Board, Global Virome Project; former Director, Pandemic Influenza and Other Threats Unit, USAID

Dr. Lincoln Chen, President, China Medical Board

Ms. Kate Dodson, Vice President for Global Health Strategy, United Nations Foundation

Amb. Mark Dybul, Co-Director, Center for Global Health Practice and Impact, Georgetown University; Member, WHO Independent Panel for Pandemic Preparedness and Response; former Executive Director, Global Fund to Fight AIDS, Tuberculosis and Malaria

Dr. Victor Dzau, President, National Academy of Medicine

Ms. Erika Elvander, Director, Asia Pacific, Office of Global Affairs, US Department of Health and Human Services

Dr. Harvey Fineberg, President, Gordon and Betty Moore Foundation; Chair, Standing Committee on Emerging Infectious Diseases and 21st Century Health Threats, National Academies of Sciences, Engineering, and Medicine; former President, Institute of Medicine

Dr. Hajime Inoue, Deputy Director General, Office for Novel Coronavirus Disease Control, Cabinet Secretariat of Japan

Dr. Claudia Juech, CEO, Cloudera Foundation

Dr. Peter Kilmarx, Deputy Director, Fogarty International Center; Associate Director for International Programs, National Institutes of Health (NIH)

Dr. Florian Krammer, Professor of Microbiology, Icahn School of Medicine at Mount Sinai

Mr. Akio Okawara, President & CEO, JCIE/Japan

Dr. Ariel Pablos-Méndez, Professor of Medicine, Columbia University Irving Medical Center; former Assistant Administrator for Global Health, USAID

Dr. Makoto Shimoaraiso, Cabinet Secretariat of Japan

Dr. Sheila Smith, Senior Fellow for Japan Studies, Council on Foreign Relations

Hon. Keizo Takemi, Member, House of Councillors of Japan; former Senior Vice Minister for Health, Labour, and Welfare

Mr. Shoji Watanabe, Assistant Director General, Office for Novel Coronavirus Disease Control, Cabinet Secretariat of Japan

Dr. Andrew C. Weber, Senior Fellow, The Center on Strategic Weapons; former Assistant Secretary of Defense for Nuclear, Chemical and Biological Defense Programs.

Dr. Shinya Yamanaka, Director, Center for iPS Cell Research and Application (CiRA), Kyoto University

Dr. Robert T. Yanagisawa, Professor of Medicine, Endocrinology, Diabetes, and Bone Disease, Icahn School of Medicine at Mount Sinai

Closing Remarks

Hon. Kanji Yamanouchi, Ambassador, Consulate General of Japan in New York