[SPARK in the time of COVID-19]
The title is borrows from Gabriel Garcia Marquez's novel 'Love in the time of Cholera'.

The talk included three topics:

1. About SPARK - What is SPARK? / Why do we do it? / What are our goals?
2. About SPARK Global - What is SPARK Global and why do it now?
3. About COVID - How SPARK responded to COVID-19.

[**What is SPARK]**
When we are trying to translate academic ideas to products, academicians have lots of challenges, and we have to overcome several gaps.
The first gap is the issue of the value of our invention in the eyes of the VCs or the companies.
The second gap is knowledge. We, in academia, don't learn much about how drugs are developed. Therefore, it is difficult for us to understand what it is that the industry is expecting from us.
And the third gap, a very important gap, is the cultural gap.
SPARK was founded in order to help academician overcome these three gaps. And our goal is simple and straightforward: Take a good idea and make sure that it's benefiting society.
The focus is on increasing the value of the invention, increasing its value in the eyes of the potential partners. The second focus is to make sure that we academician are more knowledgeable in what the industry is looking for, and so on. And the third focus is to ensure that we develop this mutual respect, both groups are scientists. And it's important that we respect each other's work, the solution for these three gaps was extremely simple.
We started this program in 2006 and the solution for these gaps was achieved by simply mixing industry scientist volunteers together with scientists from academia. This mixing occurs every week. We have about 100 industry volunteers that have signed confidentiality agreements with us and are coming to our weekly Wednesdays meeting. In each meeting they work with the scientists on their projects, provide their expertise, share their experience with us and help the projects mature. They also have the opportunity to hear about the most recent advances in basic research from the academic scientists and through that, we all develop mutual respect. Importantly, there is no hierarchy in these meetings; this way, the voice of a very young scientist who may have the best idea that can heard and impact a project of a senior professor or it can help an experienced industry person come to a better solution. It is also really important not to try to build a consensus; when building a consensus, oftentimes a solution of choice is the least creative, the most mundane one. A successful program needs to allow many ideas to be brought forward. Every Wednesday night, we work for two hours on different projects. This format provides an opportunity to learn not only about successes, but importantly also about failures; after all, it is through failures that we get better. And if we share the failures in real time, we make the participants in the program better. We also have an opportunity to hear failures from our colleagues in industry. And that's particularly valuable because failures are almost never published.
In the 15 years of SPARK At Stanford, we have had a 56% success rate. Success is measured by projects that have been licensed either to a startup, or to an existing company, or by projects that are in a clinical trials.
So far, SPARK sparked 46 companies, 18 projects have been licensed to existing companies. and 18 studies are now in clinical trials, either at Stanford or elsewhere.
This level of success rate is extremely high. And if you ask our colleagues from industry, what's the success rate of early projects in their programs that actually progressed by the above criteria, that rate is only around 5 to 10%.
Some of you had the opportunity to use our book that was published a number of years ago. We hope that the book will help you at the early stage of translational research. We try to highlight what is not intuitive and therefore what experts should be consulted in order to make sure that the project is as robust and as ready for the next step, which is translation to impact patients.

[**What is SPARK GLOBAL**]
About seven years ago, quite a few academic institutions showed interest in having SPARK established locally. And now we have about 60 different SPARK throughout the world including, Japan, Taiwan, Germany, Finland, South Africa, and Zimbabwe.
The value of the SPARK Global is based on three principles,

1. A non for profit activity; it's not an incubator that is in for profit activity
2. It is still done within academia.
3. Ensuring that good ideas are matured to impact patients and society.

Participants in SPARK Global are held to the highest ethical values and the work with industry is based on volunteers. If these industry experts were to be paid, the cost of this program would have been prohibitable for most institutions. And if you work within the academic institute, the education goal is also fulfilled – you create generation of scientists that understand and practice basic and translational research – valuable for the institution and providing experience future workforce. Finally, the focus should remain always on the patients and their unmet clinical needs.

But why SPARK Global? We were hoping that a network of scientists in academia that are better familiar with translational research will allow us to respond quickly if there is global health threats. Unfortunately, last year, COVID-19 provided this large challenge. And we are still facing it today, almost a year and a half to the day.

[**SPARK response to COVID-19**]

So what did SPARK do in response to COVID-19?

The first thing that we have done is reach out to our Stanford SPARKees. SPARKees are the scientists who were trained in SPARK. And I got many responses; I received description of 52 different projects focused on COVID-19 among the Stanford SPARKees, and that was for May of 2020. Now the number of COVID19 projects is much higher. 20 of the projects were therapeutic, 9 were in viral evolution and epidemiology, 7 in prophylactic, 8 were focusing on disease pathology; many more recent projects focus on what is termed 'COVID Long Haulers', COVID-19 patients who have long-term symptoms. Then there are 4 in diagnostics, and 4 in distributing healthcare to patients that have COVID-19.

The response of our SPARKees at Stanford in 2020 made me realize that a major challenge remains unaddressed. And the challenge in May 2020, was that the only things that we had to shield ourselves from COVID-19 were masks to stop the spread of the disease.

We also were promised then that vaccines were around the corner. And vaccine were generated in a record time. But it still took many many months for the vaccine to be available. And importantly, vaccines are still not available worldwide. Since 'the world is flat', if we do not stop COVID-19 spread everywhere, we will still face COVID for many years.

The a problem of obtaining vaccines worldwide is not only because production is slow, but also because distribution is slow, particularly in low- and middle-income countries. And then there are challenges related to producing the vaccine locally, not only because of IP challenges, but also because of technical difficulties and lack of supply, including even simple things like glass.

To add to these, there is also a challenge for immunocompromised people who cannot benefit from vaccination and those who prefer not to get the vaccine, the so called 'no-vaxxers'.

So we thought that perhaps SPARK Global could help. In April 2020, I wrote an email to all the directors in the 60 SPARK Global sites, and asked them if they have ideas related to this particular problem. I got quite a few responses, but one of these impressed me particularly because it seems to be a very simple, low cost and a logical solution.

It was provided by Michael Wallach, who is a professor in University of Technology, Sydney.

Being an expert in chicken immunity, he suggested a very simple solution, which is to inject the egg-laying hens with a recombinant protein of the capsule of SARS-CoV-2 virus. The hens quickly develop antibodies, and large amounts of these antibodies (called IgY) concentrate in the egg's yolk Those antibodies can be then purified and formulate them in lozenges.

After further consideration, we thought that the better solution is to formulate the IgY into nose drops – the main entry route for the virus, to prevent its entry of to the body. Such a solution, together with vaccines and masks, can provide extra protection from viral transmission.

We first focused on generating the antibodies, but because of both finance and administrative challenges, the project was moved to the US and lead and financed by SPARK at Stanford.

Intranasal IgY are an excellent means to block viral infection as shown by other anti-viral antibodies:

1. They immobilize of the viral particle onto fibers that are present in the nasal mucosa.
2. They hinder the lateral motility of the virus.
3. They agglutinate the virus and prevent its fusion.

The project is now ready to move to efficacy studies:

We have formulated purified IgY using the highest industry standards in dispensers that have enough drops for a one day use. We completed a 28-day rat safety study that found the preparation well tolerated and safe. Importantly, we also completed a phase I clinical study in 48 volunteers, and the study shows excellent tolerability to the treatment. Everything that we've done was at the highest industry standards, using what is called 'good lab practices' and 'good manufacturing practices'. We are waiting now for comments to get started with phase Ⅱ.

The benefit of this intranasal antibodies approach is that they can be used while countries are waiting for vaccine availability. We found that unlike antibodies from immunized subject to one of the commercial vaccine, the IgY antibodies that we have generated are equally effective against the Alpha and the Delta variants of SARS-CoV-2.

Importantly, we found that the hen-derived anti-SARS-CoV-2 IgY antibodies are very stable, can be kept at room temperature for many days and at four degrees, at least for six months.

Such IgY can provide a very low cost solution for any new threats that are transmitted by air. The antibodies can be produced within three to six weeks, and they can be produced locally in low-resource sites. Production does not require fancy equipment or deep refrigeration. We believe that IgY can provide a really good means to respond quickly to epidemic threats before it becomes a pandemic. And there is no IP around IgY, which means that IgY can provide a quick and effective solution everywhere, including in low and middle income countries.

So why does SPARK exist? - It is because SPARK fulfills our social responsibility to ensure that academic inventions benefit society.

And why SPARK Global and why now? - Becuase together we can do better than alone; our network of translational scientists can really make a difference in addressing global health challenges; SPARK Global scientists across our network were important contributors to addressing COVID 19 including in making this IgY project a success.

[Q&A]

Q.

How they can deliver the result of the research to commercialize globally from Japan. So do you have any suggestions? Or do you have any opinion from your experience to spend time in Kyoto?

A.

I spent three months in Kyoto a couple of years ago and noticed firsthand the two challenges that may be more unique to Japan and some challenges that are common everywhere:

The first challenge is lack of time. Researchers need time to do translational research, and if they cannot have time for that, because they are busy seeing patients 24/7, or because they are loaded with other duties they simply have no time to work on translational research.

A second challenge, that perhaps is now changing in Japan, is that it is very common to be employed in company for life. By nature, when you are an entrepreneur, you have to realize that the chances that the company will fail is very high. And this failure is not a real failure because much was learned that will give the next company a better chance for success. Therefore, if culturally, it's recognized that entrepreneur, by definition, are going to have a greater chance of failing than succeeding, I think that it will encourage more people to be courageous and take this path.

A third challenge that I saw in Japan, but is likely true everywhere, including at Stanford, is the lack of conceived value of translational research. There is a sense that this is not a creative work, that it is not the job of academia, that industry should focus on such work, etc. Yet most academic institutions talk about giving back to society. Here is a way to do that in medicine.

Another challenge is that as individual academic researchers, we are rewarded better for publishing in Nature and Science than making a drug that eventually will cure patients; the latter takes so long and is quickly taken out of the control of the researcher. Therefore, academia should re-align the value of giving back to society through translational research for example, through the appointment and promotion process.

And I know that there are a number of innovations in in Japan is just unbelievable; the science in Japan is simply first rate. Unfortunately, Japanese scientists may be leery to become entrepreneurs, because they fear the outcome of a failure.

The solutions to all these challenges are simple. Change the expectation of the leadership of the university about the time dedicated to translational research, and continue to do what you're doing now, which is celebrating the courageous entrepreneurs that have succeeded, celebrate their activities and make sure that you're noticing, rewarding them, encouraging young students to take it on.