CONVERSATIONS WITH MIKE MILKEN

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Mike Milken: Francis, thank you for joining us today.

Francis deSouza: Mike, it's a pleasure to be here. Thanks for having me.

It's been nearly 20 years now since the first human genome was sequenced, but we're still in the infancy of genomics. I think for our listeners, Francis, I'd like to start off by you telling us what Illumina's mission is.

Our mission at Illumina is to improve human health by unlocking the power of the genome. So we make machines that our customers use – and our customers could be hospitals, cancer care centers, consumer companies like 23andMe and ancestry.com. They buy our machines and they put in biological samples – it could be from blood, from tissue, from saliva – and we'll tell you what the DNA in those samples are.

It really has been astonishing to see what's happened over the last 20 years in genomics, and Illumina has certainly been a very central part of that. If you think about 20 years ago when we sequenced the first genome, it took about $3 billion and 15 years to do the first genome. Today you can get a genome sequenced in less than a day and comfortably under a thousand dollars, and we've publicly said that we are in a march to bring the price of doing a genome down to $100.

This interview has been lightly edited for clarity and readability.

Over the last two decades we've seen an enormous amount of discovery done in the research community, and so you're starting to see genomics actually impact human health in a number of areas: in reproductive health, through noninvasive prenatal testing and predisposition testing and carrier screening, but also in oncology where you're using genomics to match patients with the best therapies for them. We're now entering that era of biology where, whether it's genomics combined with immunotherapies or gene therapies, we really are starting to see genomics impact human health very directly for patients.

"We at Illumina were called in to deal with it from the very beginning in December of 2019 by the Chinese CDC. The first genome sequence of the virus that was published on January 12th online was done on Illumina machines, and so we have been working on this outbreak [since] well before it became a pandemic."

Francis, one of the things that you touched on is something we've had a few podcasts about: data. One of the companies was Tempus, which is taking both the biological data and the clinical data and trying to figure out what is the best treatment for an individual. You are central to those efforts. Talk a little bit about the process.

One of the things that we have learned is that there is an enormous amount of data that will be generated through genomics. And that's because if you look at a human genome, each of us has 3 billion base pairs that have to be sequenced and that generates a lot of data per sequence that then has to be connected to clinical data: imaging or other digital data sources. And all of that has to be brought together to try and understand how they all relate. So it's in some sense it's a, it's a ginormous data problem.

Well it doesn't just start and end with the genome. Over the last three decades, particularly, we've been very focused on the microbiome and measuring the type of bacteria, and good bacteria preventing you from disease or having less of a reaction maybe to this virus. We can now look at this information and tell what happens to your body when you eat different foods. We also have treatments now where we've taken good bacteria from one human being and put it in another and found very positive outcomes for many diseases. When we talk about sequencing, how many different things do you believe we could sequence in a human being?

From our base level human genome, we can understand our predisposition to a number of disease states. If we think about diseases today, we believe that 95% of all human diseases have a genetic component, and yet today we only understand 15%. So there's still a lot we have to learn about just starting from a base level genome. How does that alter a person's risk of getting all these different human diseases?

Beyond that though, as you pointed out, there are a number of other factors that differentially determine how that genome converts into diseases. One area that's very exciting that you touched on is the area of the microbiome. We know there are probably at least 10 times as many genomes affecting your body beyond just your own human genome. We know in a number of cases that a disturbance in your gut flora does result in impacting your human health. And as you pointed out, there are a couple of areas where it's then led to treatments. That's one area.

Another area that's incredibly exciting is that although you have a base level human genome, those genomes are expressed differently throughout your body. And so you have really exciting initiatives like the Human Cell Atlas, where we're trying to understand what makes an eye cell different from a cell in the lung, even though they both have the same genome. What proteins are expressed differently between the two?

Then you add infections created by pathogens. There's a lot of research happening around the coronavirus that we're dealing with. One: understanding it and its mechanism of attack and what type of cells that attacks, what proteins it needs for its mechanisms. But there's a lot of work also going on on the human side. Why do some people seem to get a very serious case of the disease, whereas for some people that's very benign? There's a lot of research happening there to understand the genome of the virus, the host genome, and the interaction between the two.

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Francis, a number of months ago, as I became concerned with what was going on in China and the potential to spread around the world, we called and asked what could Illumina do in diagnostic testing? What could the company do in screening strategies and methodologies? How has the pace and approach of Illumina changed since this coronavirus outbreak?

The coronavirus outbreak has really accelerated everyone's thinking around how we can leverage genomics to combat this pandemic. What we'd like to do is understand which patients are the most vulnerable in the population based on their genome and protect those patients. In addition, there's work going on to use genomics to provide high testing capacity – to say, is there a way we can leverage these genomic machines to deliver high-throughput testing into the market?

Beyond that there is a need for a global surveillance network. What that would allow us to do is help us understand how the virus is spreading around the world and within a community. And that's important for policy decisions. But if you look forward, what the global surveillance network would allow us to do is it'll allow us to identify the next pandemic much more quickly. That could be true whether it was a virus outbreak, like the one we're dealing with today; if it was antimicrobial resistance; or if it was even a bioterror attack. And by identifying this early, you can move very quickly to containment. And that is very, very important in dealing with a pandemic.

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Then there's a lot of work happening right now to leverage genomics as part of a screening strategy to get the economy back to work. We're talking to companies, we're talking to governments, around how to do mass screening of healthy people so that you can feel confident that they're not carrying the pathogen back into the workplace. Genomics can be used to provide that very high-throughput screening of healthy people and do it at a regular pace as we get people back to work.

Francis, there's been a lot of discussion about how the virus is not mutating as fast as others. Why is this important? Can you explain to our listeners why the mutations, and monitoring the mutations of this virus, are so key?

First of all, understanding the mutations gives you a sense for the geographic spread of the virus. Equally importantly though, it allows you to understand whether the diagnostics you're using to tell whether somebody has the virus or not will continue to work. Similarly, by understanding how a virus is mutating, you can watch to see whether the therapies you're using will be effective or will continue to be effective. And so for all those reasons, it's really important that we continue to track the rate of mutations in this virus. Now this virus mutates about the same as other coronaviruses to the best of our understanding so far from the data, which is a lower mutation rate than influenza for example.

So Francis, you also spoke about high-capacity testing. Do we have it in the United States, and if not, when will we have it in the United States?

We're starting to put into place the capacity we need for diagnostics. So if somebody has symptoms and you want to know whether they have the disease or not, there's a lot of work going on right now to put that diagnostic capacity in place, and there's still work to do to make sure that that diagnostic capacity exists throughout the country. But if you think about what it'll take to put 100-million-plus people back to work in this country,

and a much larger number back to work around the world, then you're talking about needing to do millions of tests in a week. That still needs to be put into place, and that's going to have to come in as quickly as possible, but certainly it will come in later this year.

Francis, one of the reasons I turned to you a number of months ago in your company to try to see how you could help in this coronavirus crisis was that you were the leader in the world in this area of sequencing. Give us a feel of your worldwide customers today.

We've really seen the global markets emerge to be a much bigger part of our business in the last five to 10 years. The big applications for genomics are in research, so a number of our customers are funded by government research dollars. In addition to that, we're seeing clinical markets, like cancer and cancer therapy selection.

Reproductive health is a growing application for genomics and noninvasive prenatal testing. There's a demand for genomics in carrier screening as people think about having a child. We're also seeing emergence of a market around genetic disease testing. So we know today, for example, that 5% of all births resulted in a child that has some kind of genetic disease, and even here in the U.S. the state of the art is that that child and that family will go on a five- to seven-year diagnostic odyssey looking for a diagnosis. That's incredibly difficult, as you can imagine, for the child and painful in a lot of cases. It's incredibly stressful for the family and it's financially very difficult. About 10% of those families end up going bankrupt because of this medical odyssey.

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What we know today, though, even with today's technology is that if that baby was sequenced within days of birth, in some cases up to 50% of the time you can actually get a diagnosis right there. And in some cases you can do an intervention to actually help prevent the development of the condition. Less than 1% of kids with genetic diseases have ever been sequenced. But I think if you look forward, we're going to see a much bigger adoption there.

Let me turn back to the coronavirus. The world has been dependent on your ability to create these machines to do research. How have you dealt with this virus and your own workforce?

Our first priority has been to focus on the health and safety of our employees and also to live up to the commitments that we've made to partners and customers, because a lot of them are doing essential work to fight this pandemic. About 25 to 30% of our workforce continues to come into our facilities. And that's because they're actually building the products that we're selling to our customers or their work is essential and requires them to access the lab.

We've put a number of measures into place, including personal protective equipment, installing thermal scanners at doors and enforcing social distancing. We upped the level of deep cleaning at our facilities, and we continue to actively monitor the community in which each of those facilities is based in. For our employees working from home, we've done a number of things around upgrading the IT infrastructure, increasing bandwidth, making sure they have access to equipment to work from home. And overall, although it's been challenging, and it's been a big change for people, I've been incredibly inspired by how the whole company has rallied and is still continuing to deliver this essential work.

As we think about bioscience being the defense companies of the 21st century we've been talking about data storage and the idea that you might be able to store everything that's ever been recorded in the world on some strands of DNA and fit it in a shoe box. Talk a little bit about the process.

If we look at the different ways that we store media today, whether it's on tape or in memory chips. One of the challenges that we're grappling with is that the media itself degenerates over time. And if you talk to people who are on large data centers, they'll tell you that if they spend a bunch of their time just replacing spindles in the drives or re-imaging tapes because the tapes are deteriorating.

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One of the things we've realized is that one of the most stable media that nature has perfected over a hundreds of millions of years is DNA. DNA has an incredible capacity to be stored for an extraordinary long time.

Another challenge that we have in storing data today is that the mechanisms we use to read the data become obsolete. Anybody here who has looked for a way to read a floppy drive or a tape drive knows exactly what I'm talking about. Or even a CD rom, right? It's very difficult to get access to reading tools that we were using a decade ago or two or three decades ago. Whereas we know we will always be able to read DNA.

Those are the two big advantages, and the fact that you can do it so extraordinarily cheaply has created a bunch of work around how to use DNA as a storage mechanism. I believe it will ultimately happen. There's still work to be done to get there, but DNA has been optimized by nature to be the best storage medium out there, and it's only a matter of time before we use it ourselves for the data that we generate.

Frances, when did you realize this coronavirus had the risk of becoming a pandemic? It was mid-March by the time the World Health Organization declared it a pandemic. When did you and your team begin to focus on this?

We at Illumina were called in to deal with it from the very beginning in December of 2019 by the Chinese CDC, and so we were working with the Chinese CDC starting then. The first genome sequence of the virus that was published on January 12th online was done on Illumina machines, and so we have been working on this outbreak well before it became an epidemic, well before it became a pandemic. We are currently working with CDCs around the world. We are working with researchers around the world and with hospitals around the world on a number of aspects of it.

We're continuing to monitor it from a surveillance perspective like we did at the very beginning. We are helping our customers sequence the genome and publish those genomes publicly in a tool called GISAID so that anybody around the world can access the genomes and understand how the virus is spreading and how it's evolving. And we're currently involved in surveillance and screening and testing and in the research activities associated with understanding how the virus acts.

Well, Francis, I want to thank you for joining us today. I also want to thank you and your team for being so responsive when I called a number of months ago out of the fear that this virus was going to become a pandemic, and we look forward to seeing what you can do in the future, all the best.

Thank you for having me on today. Thank you for all the work you do, and thank you for your continued support of the work we do at Illumina.