Pandemics and Pathogens

Hannah Bank: Think back to when the pandemic started—during that very first lockdown. When we scrambled to get groceries. To check on loved ones. And to keep up with the news.

Dr. Jean-Philippe Julien rushed to his lab at SickKids. JP, a senior scientist in the hospital's molecular medicine program, and his team had been busy working on molecules to fight viruses—something microscopic yet with the potential for each one to take out influenza, malaria, *and* HIV. Then came the call for labs to lock down everything. And fast.

Dr. Jean-Philippe ("JP") Julien: There was such a focus on shutting things down from an operational perspective—that's a lot of work.

Hannah: They had to organise critical samples from their lab. Take a record of their entire inventory. Then prepare those samples for long-term storage in extremely cold, specialty freezers so nothing degraded or went bad.

JP: Everybody's shutting everything down and making sure that everybody goes home safe and very much aligned with the mandate of following guidelines and restrictions.

Hannah: On a Thursday night that week, JP and his team finish packing up. They arrive home unsure when they might return to the lab.

On Friday, the team talks online: *What if they took their work and broadened their focus to include SARS-CoV-2—the virus behind COVID-19?* One of the team's specialties *is* investigating diseases that stump vaccine makers because the underlying viruses mutate quickly, producing new variant after new variant.

JP: The will was there all the way around. There was the will from the lab and realizing that, yes, we're scientists, we know what we can contribute despite the fear of, you know, going back to work. But the will was also there from the leadership at SickKids and that's when everyone started to move in the direction of making their infrastructure, their knowledge, accessible and open for collaboration.

Hannah: Less than 48 hours after closing everything down, JP and his team reopen their lab. Time to get back to work.

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Hannah: You're listening to SickKids VS, where we take you to the frontlines in the fight for child health. I'm Hannah Bank, and this is SickKids VS Pandemics and Pathogens.

ACT ONE

Hannah: As JP reopens his lab, he quickly assembles a virus-fighting league. Members include his own team, other colleagues at SickKids, plus scientists from outside organizations. There are

virologists, more molecular medicine specialists, and hospital managers who are temporarily redeployed to work with JP.

Together, they share research and resources. They receive specialty equipment to run complex experiments. Then they form new partnerships, like one with a biotech company. Everyone is all in.

JP: It became an endeavour that was highly, highly collaborative. And that's really what I would say drives innovation is this close competition amongst all scientists that at the same time allows for the sharing of information.

Hannah: JP's lab is hardly starting from scratch. They are benefitting from years of investments into scientific research around viruses and vaccines.

In fact, over the past six years, teams collaborating with JP's lab have been screening hundreds of people. Why? To find antibodies capable of neutralizing not just one virus, but many strains. The approach had proven effective when examining influenza, HIV-1, malaria, and other viruses, and JP and his team suspected similar antibodies might also fight certain coronaviruses and SARS-CoV-2. As for the people who have been screened, they are part of clinical trials or living in malaria-endemic regions where they consent to participate in research.

From each of those individuals, there's the potential to discover tens of thousands of antibodies. And those antibodies are important because they're tools for protecting the body. Picture them like microscopic hammers in an endless game of Whac-a-Mole against mutating viruses that just keep popping up.

JP: We said that's great that this one individual makes this antibody and another individual, you know, another antibody. But what if we started to combine them together? The best solution from here and the best solution from somewhere else.

Hannah: Once identified, JP's team takes the best-of-the-best antibodies from all those different people and sticks them together on a super molecule that's kind of like a Velcro ball. Then they test it against variants of a particular virus.

JP: When all these components are assembled on this Velcro ball, then that's when it can be the most powerful. I think we're in a unique position to do this. And that's why, you know, we're at the forefront of these studies at the moment.

Hannah: JP's goal is to eventually turn their top discovery into a drug that's capable of protecting you, me, and everyone from certain existing *and* future infection outbreaks, along with many of their nasty variants. We're talking about molecules for influenza. Malaria. HIV. And COVID-19.

JP: If it's just surveilling in the body, and if you are exposed, then it just stops it right away. So it's the same molecule in theory that could do both.

Hannah: Even better? When the next major pandemic hits, maybe we won't need to wait on treatments with complicated logistics. Imagine just walking into your nearest pharmacy, grabbing something over the counter, and reducing your symptoms, or even gaining immunity.

JP: Yhat would be a transformation. For example, if you knew today that you could go just buy off the shelf the product that you could administer yourself, that you would be protected for six months or a year. This is important for us in Canada, for sure, and in the developed world. But I would say it's probably even more important in the developing world, where the health care infrastructure is not like us.

ACT TWO

Hannah: JP and his team have been trying to jump over two major hurdles while developing their anti-virus super molecules.

First, they've been striving to give each molecule *breadth* so that it can defend against all known—and future—mutations of a virus. This approach comes in handy with variants—like the COVID-19 variants that have become key drivers of the pandemic.

JP: We need to demonstrate that the same molecule can block all of the different viruses that have been isolated. One of the biggest challenges that we face in vaccinology is to be able to vaccinate against diversity. And so that is to be able to present something in a vaccine where you're not only able to stop one of the pathogens but all the strains that might be circulating worldwide.

Hannah: The good news? Not all viruses will mutate indefinitely.

JP: The more you understand about the biology of the virus, the more you understand that there are certain things that can't change. The virus doesn't have infinite space of things to explore. It still has to carry out a function. It still has to infect the cell.

Hannah: Having enough breadth is one obstacle. But JP and his team have also been trying to pack as much *potency* into their molecules as possible.

JP: Which means you really don't need much in order to completely block all the viruses.

Hannah: Recently, some antibody treatments have been given to people with mild to moderate COVID-19, especially at the start of their symptoms. But these are typically delivered in a hospital. Through an IV injection. And the process can last up to four *hours*. Why? Because hospitals need to administer a high dose of the medication and can't concentrate everything into a small needle.

JP: That's where we think that our approach of high potency really is transformative. Now you can start envisioning some mode of delivery that can be done over the counter.

Hannah: Last summer, JP and his team assembled one super molecule then tested its strength. They held their breath. Then they studied the results.

What they discovered was astounding: A full vile of medicine would have required the equivalent of up to 10,000 drops—about a small bottle of pop. Now, all they needed was a single drop to get the same, powerful results.

JP: You know, this is way beyond what we were hoping. We saw how drastically more potent the molecule was. How actually very little you needed to completely block the virus. That was a big moment.

Hannah: The finding could be a gamechanger when we think about how much medicine needs to be made—and how expensive it is for developing countries—to prevent a pathogen from getting you sick in the first place.

But what about the molecule's breadth? Late last year, JP's team once again tested it against a bunch of SARS-CoV-2 virus variants. They analysed the data, plotted the figures on graphs, and celebrated: One of their collaborators had discovered an antibody that could really boost both the breadth *and* potency of the team's super molecule.

JP: That really gave us the energy and the sense that we need to keep pushing this forward very hard. We're on track to trying to develop something that can go to the clinical trials to be approved and shown to be efficacious and also safe. But at the same time, we also don't have illusions that we can compete with Moderna or Pfizer or some of these big pharmaceutical companies. Our role as academics is often to uncover basic principles that become the foundation for product development.

ACT THREE

Dr. Michael Ryan: This pandemic has been very severe. It's spread around the world extremely quickly and has affected every corner of this planet. But this is not necessarily the big one.

Hannah: You're listening to a briefing from Dr. Michael Ryan—head of the emergencies program at the World Health Organization.

Michael: This virus is very transmissible and it kills people, and it has deprived so many people of loved ones. But its current case fatality is reasonably low in comparison to other emerging diseases. This is a wake-up call. The planet is fragile. We live in an increasingly complex global society. These threats will continue.

Hannah: And the threats keep pushing JP's lab forward.

JP: Until we have a molecule that is benefiting in our community—and people not being infected and really fighting infectious disease and transmission on the ground—we still have work to do.

Hannah: His team is now trying to make their antibody molecules even more broadly resistant to variants of viruses such as influenza, malaria, HIV, and SARS Co-V2. They're also partnering with other hospital scientists and vaccine makers to advance their findings.

JP: As more and more teams around the world are discovering better and better antibodies, we've now initiated new collaborations where we are leveraging the next best antibodies.

Hannah: JP's team will then test their molecules in living organisms to ensure whatever product they develop can be safely deployed to different communities. They're also taking learnings around how the molecules behave with coronavirus and applying those lessons to their original focus areas of malaria and HIV. Each year, malaria and HIV still kill more than 1 million people around the world—including many kids.

JP: We are hopeful that a lot of the concepts that we solve in the context of SARS-CoV-2 will be applicable to some of these other pathogens that we're targeting.

Hannah: JP is emboldened by what scientists have pulled off to battle the COVID-19 pandemic. But he also knows that he and his peers need to move even faster. Before we get hit by "the big one."

JP: That is medicine at its best. That's science at its best. But at the same time it's also a pandemic at its worst—like we've all suffered in different ways. To have to wait with hopes, highs and downs, and effects on all our daily life. And so as much as we're celebrating the science and the medicine, I think we're also suffering a lot. And so the question is for science and medicine: how can we even do better?

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EXTRO

Hannah: From SickKids Foundation, this is SickKids VS. Thanks for listening.

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