Bringing real change to people [1]

Discovery [2]
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Since 2012, Thierry Diagana has served as Head of the Novartis Institute for Tropical Diseases (NITD), a small-molecule drug discovery research institute within the Novartis Institutes for BioMedical Research. In this role, he is focused on discovering new medicines that contribute to the elimination of infectious diseases like malaria. He described his team's progress during a recent conversation about NITD and its future.

What drove you to join NITD?

I joined Novartis in 2007, mainly for malaria. Today, as we see many people infected with drug-resistant parasites, I look back and feel very much validated in my decision to join because there is a growing unmet need for new drugs, which we anticipated at Novartis.

What has NITD achieved with respect to malaria?

We have two drugs in the pipeline that could address the perennial challenge of drug resistance. One of them is KAF156, which could turn out to be a potential game-changing therapy. It not only combats the two main parasites responsible for most malaria deaths but is also active against the blood and liver stages of the parasite's lifecycle. This is what needs to be targeted if we want to both treat and prevent malaria, which kills almost half a million people every year – most of them children.

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How far advanced is this compound?

Currently, Novartis is testing the drug in a clinical trial in Mali together with Medicines for Malaria Venture (MMV) and with the support of the Bill & Melinda Gates Foundation. This is a great step for us, as it means we are making good on promises that we can get the drug to the people who need it most early on. With this step, we are also providing the knowledge and technical equipment for running early clinical trials to doctors and nurses in the most exposed regions. In the past, these regions lacked both the know-how and infrastructure to execute such tests, which are a vital step in the drug development process. This knowledge transfer is of paramount importance if we want to control and eliminate malaria in the future.

How is the other malaria compound progressing?

The second compound, called KAE609 – which we have tested in a small trial in Thailand –

has shown itself to be effective against two parasites, including strains that seemed to be resistant to current malaria treatments. The compound was discovered through joint research with the Novartis Natural Products Research Group, the Genomics Institute of the Novartis Research Foundation, and the Swiss Tropical and Public Health Institute. The research was also supported by the Wellcome Trust, the Singapore Economic Development Board and MMV. It is a great collaboration.

Is this collaborative approach a typical process for NITD?

Thierry Diagana is leading NITD's efforts to contribute to the elimination of tropical diseases such as malaria.

Collaboration and partnership are essential for us. NITD can only thrive if we stay connected and work together with other like-minded organizations. To advance our research programs and make sure that they have an impact, we are very dependent on our partners such as the Gates Foundation, the Wellcome Trust and the Swiss Tropical and Public Health Institute, to name a few. But there are also many grassroots efforts from colleagues within Novartis that are helping to advance our projects. Over the years, many people have come to support our programs. One of them was Eric Francotte, a pioneer in separation technology. He approached us and asked how he could help out and set resources aside to get it all going. He is just one of many people who have come and are continuing to come from all corners of the company to help us achieve our goals.

Has this setup also had an effect on the culture within NITD?

NITD was always a very special kind of environment. It has always attracted people who would have normally gone to a nongovernmental organization (NGO) to provide support and help to the most vulnerable patients. Also, because we are in constant contact with other

NGOs, research labs and Novartis colleagues, we are generally quite open-minded when it comes to embracing and following leads that come from outside. But, of course, we are single-minded when it comes to our mission, which is to contribute to the elimination and eradication of neglected tropical diseases.

Aside from malaria, what are you targeting at the moment?

A key focus is on diarrheal diseases affecting children, such as cryptosporidiosis. This is the second most common cause of diarrhea-related mortality in children under 2. The parasite can cause weeks of watery diarrhea and sets up a vicious cycle of malnutrition and increased susceptibility to infection. Here we have worked with the University of Georgia and Washington State University in the US, using transgenic parasites and novel disease models for drug discovery. Thanks to these tools, we have identified a specific inhibitor: KDU731.

In what other areas are you progressing?

We are also working in the field of kinetoplastid parasites, which include pathogens that cause sleeping sickness, among other diseases. Following the discovery of a compound by the Genomics Institute of Novartis – which is located in La Jolla, California, not far from our own location here in Emeryville, near San Francisco – we are now working on a new compound that targets the proteasomes of three parasites that cause sleeping sickness, Chagas and leishmaniasis. This work is being carried out with support from the Wellcome Trust and in partnership with the University of Washington in the US, and the University of York and the University of Glasgow in the UK. If it is successful, we could make a big difference for hundreds of thousands of patients who today have limited treatment options for these three diseases, which are closely linked to poverty and have been severely neglected. Furthermore, we are in the early stages of developing a fast-acting oral treatment specifically for human African trypanosomiasis, also known as sleeping sickness. The goal is to replace existing drugs, which are administered intravenously and show significant toxicity. An improved oral regimen could help eliminate this disease.

What are your future goals?

NITD’s mission is to contribute to the elimination and eradication of diseases such as malaria. We want to achieve for the rest of the world what has been done for Europe and the United States, where malaria has been eliminated. I am convinced we can achieve this, and we have many associates who are deeply motivated to bring about change. My own relatives have suffered from malaria, and many of our associates are from regions where these diseases are prevalent. They have seen family members suffer and even die. If it was possible to eliminate smallpox in a time when there was no internet, email or other digital tools, then we should aim high and achieve the same for malaria and other diseases.

What makes you so confident?

Today, as we are working in the Bay Area (where I worked for a long time before joining NITD in Singapore), we have a great opportunity to tap into one of the world’s greatest talent pools and aim for disruptive innovation. As Jay Bradner said when we celebrated our move, there are 300 life science companies here, at least four major research universities, and a huge number of startups, which can lead to partnerships and new associates.

Have you already benefited from this?

We benefited from it within just a few weeks of arriving in Emeryville. For example, we have made good progress in expressing proteins that would have been quite challenging to express without the support and expertise of the local protein science team. We are now also better linked with the overall research network of Novartis, which increases our visibility and our ability to interact. And we feel that we are very attractive to many of the Bay Area biomedical research talents. As an institute, we have a unique collaborative approach, and many of our scientists are driven by a personal sense of urgency. Like most scientists, we are driven by the passion for a better world, the passion for doing something with our time that is worthwhile and bringing real change to people. Is there a better way to spend one's life than being a scientist and giving back to society?

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