Novartis Institute for Tropical Diseases

Fighting neglected infectious diseases

Infectious diseases, including malaria, diarrheal disease, and neglected tropical infections kill over 8 million people each year, according to the Global Burden of Disease 2015 Study. In an effort to address this burden, the Novartis Institute for Tropical Diseases (NITD) is dedicated to finding new medicines that treat and, ultimately, contribute to the elimination of these pathogens.

"Some of these diseases have been around for thousands of years," says Thierry Diagana, Global Head of NITD. "We now have the opportunity to apply modern drug discovery technologies and find new solutions to this ancient problem. Our vision is to create therapies that can be part of eradication programs for diseases like malaria and human African trypanosomiasis."

As a small-molecule drug discovery research institute within the Novartis Institutes for
BioMedical Research (NIBR), NITD works in collaboration with a number of academic and non-profit partners. NITD research currently focuses on parasitic diseases, such as malaria, cryptosporidiosis, and three major kinetoplastid diseases – human African trypanosomiasis (sleeping sickness), Chagas disease and leishmaniasis.

“I’m proud to work alongside a team of scientists committed daily to solving a very important problem that affects people who we don’t necessarily see every day,” says Diagana.

Accordion:

Malaria

Malaria kills about half as many people as it did two decades ago, yet it remains one of the world’s most deadly infectious diseases. The World Health Organization [1] (WHO) estimates 429,000 people die from malaria each year – mostly young children, pregnant women, and others with compromised immune systems.

Success in controlling infections by malaria parasites has been achieved through substantial investments in bed nets, insecticide campaigns, and artemisinin combination therapies. Now, rising artemisinin resistance threatens this progress.

New drugs with diverse modes of action are needed to combat resistance, as well as to block transmission, prevent infection, and reduce relapse. Such compounds will be used in combination to develop regimens that promote accessibility, compliance, and take into account the needs of particularly vulnerable patients.

In partnership with Wellcome Trust, Medicines for Malaria Venture, the Genomics Institute of the Novartis Research Foundation [2] (GNF), and the Swiss Tropical Public Health Institute, NITD developed two antimalarial compounds that are now in clinical trials (KAF156 and KAE609). Notably, these are the first compounds with novel mechanisms in more than two decades. NITD continues research efforts to strengthen the global antimalarial portfolio.

Cryptosporidiosis

Nearly 1.7 billion cases of childhood diarrheal disease occur each year, according to WHO [3]. These diseases can cause dehydration, malnutrition, stunting, and cognitive defects, and contribute to more than half a million deaths annually.

Cryptosporidium is the second most common cause of diarrhea-related mortality in children under two years old. The parasite can cause weeks of watery diarrhea and sets up a vicious cycle of malnutrition and increased susceptibility to infection. Currently, there is no vaccine and the only available treatment is poorly efficacious in malnourished children.

In collaboration with the University of Georgia and Washington State University, NITD researchers have used transgenic parasites and novel disease models for Cryptosporidium drug discovery. These tools brought about the identification and validation of a potent and specific Cryptosporidium PI(4)K inhibitor, KDU731 [4]. NITD is expanding its drug discovery efforts to identify novel agents to fight cryptosporidiosis.

Kinetoplastid diseases
Kinetoplastid parasites include pathogens that cause human African trypanosomiasis (sleeping sickness), Chagas disease, and leishmaniasis. Together these diseases result in over 50,000 deaths each year worldwide. The kinetoplastids, including *Trypanosoma* and *Leishmania* species, are highly associated with poverty and have been severely neglected in the development of diagnostics, treatments, and vaccines. The challenges facing available drugs include toxicities, limited efficacy, and difficulties in administering them.

One possible opportunity for kinetoplastid drug discovery is that a single compound may have activity against more than one member of the group. Indeed, a collaborative effort led by GNF, supported by the Wellcome Trust, and in partnership with University of York, University of Washington, and University of Glasgow discovered an inhibitor of the kinetoplastid proteasome that has efficacy against *Trypanosoma cruzi*, *Trypanosoma brucei*, and *Leishmania donovani* in preclinical models.

NITD scientists and collaborators are also in the early stages of developing a fast-acting, oral treatment specifically for human African trypanosomiasis. The goal is to replace existing drugs, which are dosed intravenously and show significant toxicities. An improved oral regimen may support elimination of this disease.

Footnotes:

References:


Publication list


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