Dedicated to discovering new medicines

The Novartis Institute for Tropical Diseases (NITD), part of the Novartis Institutes for BioMedical Research (NIBR), is dedicated to finding new medicines to treat neglected, infectious diseases. As a small-molecule drug discovery research center, it combines the drug-discovery expertise and cutting-edge technologies of Novartis to fight infectious tropical diseases, including Dengue fever, Human African Trypanosomiasis and Malaria.

Located in the Biopolis in Singapore, NITD is home to 100 researchers and business associates who work closely with other NIBR sites in China, Europe and US, and with academic and industrial collaborators.

Our Drug Discovery Process

Understanding the biology of the disease – One of the challenges of discovering medicines for diseases of the developing world is the lack of basic research into the underlying causes of these diseases. An example is dengue fever which is caused by any one of the four serotypes of dengue viruses transmitted by mosquitoes.

The challenge in discovering drugs to treat dengue is the limited knowledge about virus infection cycle and the relationship between virus volume and disease progression.

Making better drugs for tropical environments – Drugs developed for developing world diseases need to meet additional challenges aside from efficacy and safety, such as stability under tropical conditions and access for patients living in poverty. In endemic areas people often travel long distances to get to clinics and require medicines that can work quickly with only a few inexpensive doses and don’t require follow-up visits.

By leveraging our expertise in medicinal chemistry, we focus on developing small molecule-based medicines that can meet these requirements while maintaining the best possible safety and efficacy.

Fighting Neglected, Infectious Diseases

NITD is a public-private partnership between Novartis and the Singapore Economic Development Board, and is part of NIBR. NITD is dependent on the early formation of partnerships on a global scale. This is important from early research activities such as target identification and high-throughput screening through later stages of the drug development process. Partnerships are also necessary for successful outreach to patients, and to make affordable treatments available to developing countries.

NITD offers exceptional teaching and training opportunities for post-doctoral fellows and graduate students coming from all over the world, mostly from developing countries.
Malaria

Each year malaria kills more than 660,000 people, most of whom are African children. While current therapies are effective against the most common forms of malaria, recent publications suggest that the efficacy of the artemisinin-derivatives has been compromised in parts of South-East Asia. In addition, these therapies are only effective against the acute blood stages of the disease, thus leaving some patients at risk of relapse after initial treatment. Relapse prevention is especially important for Plasmodium vivax, which can form hypnozoites, dormant parasites that can persist in the liver for up to two years before reinitiating a blood-stage infection.

To address this unmet global health need, NITD has led the formation of a research consortium that brings together cutting-edge drug discovery at Novartis with world-class malaria biology expertise. Novartis currently has two drug candidates in development. Both KAE609 and KAF156 are new classes of anti-malarial compounds that treat malaria in different ways from current therapies, important to combat emerging drug resistance.

Novartis has also identified PI4K as a new drug target with potential to prevent, block and treat malaria.

Dengue Fever

Dengue and Dengue Haemorrhagic Fever (DHF) are caused by four closely related viral strains. The virus is transmitted to humans through the bites of infected mosquitoes. Infection with one of the viral strains does not guarantee immunity from the other three. The global prevalence of dengue has risen dramatically, and the disease is now endemic in more than 100 countries in Africa, the Americas, and the Eastern Mediterranean region. The most serious outbreaks are found in Southeast Asia and the Western Pacific.

• About 2.5 billion people, or 40 percent of the world’s population, lives in areas where there is a risk of dengue transmission
• A certain small percentage of the infected patients develop life-threatening hemorrhagic fever and shock syndrome that can lead to death

• Over the past four decades, dengue disease has become recognized as the world’s most important mosquito-borne viral disease

The NITD dengue team has worked with many of Singapore’s local and international collaborators to establish novel research tools and approaches, such as characterizing novel targets to enable drug discovery, establishing dengue pre-clinical models for antiviral testing, defining structure and function of dengue viral proteins, and developing screening assays that have been used to identify several candidate compounds in the fight against dengue.

Human African Trypanosomiasis (HAT)

HAT, also known as African sleeping sickness, is a parasitic disease caused by the parasite Trypanosoma brucei. These parasites are transmitted by the bite of the tsetse fly. The disease is endemic in 36 sub-Saharan African countries. In 2013 there were 6,400 new cases of the disease reported. HAT manifests itself in two stages: the bloodstream (stage I); if untreated, the parasites eventually cross into the Central Nervous System (CNS – stage II) causing severe neurologic disturbances which could eventually cause death. Currently the recommended treatment for stage II HAT is to combine seven days eflornithine (two infusions/day) and ten days oral nifurtimox (NECT). The administration of this treatment is challenging as it requires an infusion which is extremely complex to administer in resource-poor settings.

NITD focused its drug discovery research on HAT since May 2012, in order to provide short course (~three days), safe, effective, cheap orally administered drugs to replace first-line treatments against HAT which would improve and simplify current case management. We have undertaken the largest ever compound screen (~2.2 million) against Tb. brucei and identified a large and diverse set of HAT active compounds. Our “hit to lead” activities have resulted in identification of 3–5 novel lead-like scaffolds having different modes of action and complete to partial cure in mouse models of stage I HAT.