Agenda

NITD history

NITD resources

NITD Achievements
  Training
  Novartis ambassador for SE Asia and global public health
  Malaria
  Dengue
  Human African Trypanosomiasis

Conclusions
The Novartis Institute for Tropical Diseases aims to discover novel treatments and prevention methods for major tropical diseases.

In those developing countries where diseases are endemic, the Novartis Group intends to make treatments readily available and without profit.

The discovery technology is state-of-the-art and the scope of activities range from target discovery through to screen development and compound optimization.

The Institute is looking to recruit the best scientists in the world, and as a major center of excellence, will offer exceptional teaching and training opportunities for post-doctoral fellows and graduate students.
Criteria for the choice of location of Research Centers

- Access to talent
- Superior research environment: basic sciences and research hospitals, biotech
- Proximity to patients and their treating doctors
- Public support for biomedical sciences and political stability
- Acceptable animal experimentation laws
- Acceptable regulation for scientific research (stem cells etc)
- Good commercial and regulatory environment for the pharmaceutical industry
- Good Intellectual Property protection
Why Singapore?

- Modern drug discovery needs close proximity to patients and their treating doctors (tissues, disease knowledge)
- Modern drug discovery needs access to multidisciplinary scientific talent
- Singapore is close to countries where Dengue and TB are endemic.
- Singapore has established a high quality scientific environment
Singapore as a R&D site

Excellent outreach to Asia

- Proximity to patients and their treating doctors
  - Singapore is within a few miles of patient populations and treats them in its hospitals
  - 3 billion people with 7 hours flight radius
Discovery and early development of small molecules up to Proof-of-Concept in man for novel treatments for tropical diseases (malaria, dengue fever, tuberculosis until 2012 and human african trypanosomiasis)

The institute in numbers
- 2003 operations started
- 105 full time employees
- 18 nationalities
- 2 positive POCs/PhIII
Funding Landscape - SGD

External funding constituting 30%~40% of total funding

2003-2012
NVS-57% vs SEDB-36% vs Others-7%

2012 : Expiring of first SEDB RISC 10-year grant

2013-2015
NVS-71% vs SEDB-13% vs Others-16%
Funding Landscape - USD

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NITD budget 2015

Source of funding

Fund Size - SGD mio

- Third party funding, 10.7
- Novartis, 21.8

Total fund size (2015) – SGD32.5 mio
% of external funding – 33%

Wellcome Trust: 25 mio $ over >5 years, Malaria and HAT

Third Party Funding
- Singapore Economic Development Board
- Wellcome Trust
- Medicines for Malaria Venture
Research Environment: NITD collaborations in Singapore and East Asia
NITD as part of the Novartis Research family and as academic partner

Strong collaborative culture with academia

Connected to more than 6,000 NIBR scientists globally

Access to deep expertise and resources in all aspects of the drug discovery process
  - Compounds archives
  - Preclinical and development expertise (e.g. Safety and Developability assessment)
  - Target class know-how
  - Infectious diseases
Additional: Cost competitiveness

- Lower cost of operating research in Singapore as compared to other Novartis sites in Europe or the United States

<table>
<thead>
<tr>
<th>Site</th>
<th>Cost per FTE (kUSD) *</th>
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<tbody>
<tr>
<td>NITD</td>
<td>204</td>
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<tr>
<td>GNF</td>
<td>227</td>
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<td>Basel</td>
<td>278</td>
</tr>
<tr>
<td>Cambridge</td>
<td>317</td>
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* Based on LE3 2010
Training next generation scientists

Trained over 100 students and postdocs about 40 from the developing world
## List of all NITD symposiums

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Topic</th>
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<tbody>
<tr>
<td>2005</td>
<td>Bagamoyo, Tanzania</td>
<td>TB</td>
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<td>2006</td>
<td>St. Petersburg, Russia</td>
<td>TB</td>
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<td>2007</td>
<td>Masan, South Korea</td>
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<td>2008</td>
<td>Maputo, Mozambique</td>
<td>TB</td>
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<td>2009</td>
<td>Manila, Philippines</td>
<td>Dengue</td>
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<tr>
<td>2010</td>
<td>Yaoundé, Cameroun</td>
<td>TB</td>
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<tr>
<td>2012</td>
<td>Sao Paulo, Brazil</td>
<td>Dengue</td>
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<tr>
<td>2013</td>
<td>Cape Town South Africa</td>
<td>TB</td>
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</tbody>
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Malaria: medical Need
Growing resistance concerns demand NCEs

Use of artemisinin-monotherapies may have fostered beginning of drug resistance

Legend
- Introduced
- First case of resistance

Quinine
- Introduced: 1632
- First case of resistance: 1910

Chloroquine
- Introduced: 1934
- First case of resistance: 1957

Proguanil
- Introduced: 1948
- First case of resistance: 1949

Sulfadoxine-Pyrimethamine
- Introduced: 1967
- First case of resistance: 1967

Mefloquine
- Introduced: 1977
- First case of resistance: 1982

Atovaquone
- Introduced: 1996
- First case of resistance: 1996

Artemisinin
- (herbal)
- Introduced: 1972
- First case of resistance: ?

[Diagram showing the timeline of drug introduction and resistance of Malaria medications]
Malaria: the urgency of countering drug resistance

Artemisinin resistance is spreading in the greater Mekong sub-region

Dengue
An emerging global disease

IF THEY BREED,
YOU WILL BLEED.

STOP DENGUE. ACT NOW!
HOTLINE: 1800-X-DENGUE / 1800-333-7777

plh singapore 19.9.2015
Dengue Hemorrhagic Fever

Siripen Kalayanaroonj, M.D.

Queen Sirikit National Institute of Child Health (Children’s hospital) Bangkok, Thailand
HUMAN AFRICAN TRYPANOSOMIASIS
Human African Trypanosomiasis

Discovering novel, effective, safe and affordable oral therapy

- Disease caused by kinetoplastids Trypanosoma brucei gambiense and Trypanosoma brucei rhodesiense through the bite of infected tsetse flies
- Disease is endemic in 36 sub-Saharan African countries and the prevalence is estimated at ~ 300,000 mortality with estimated mortality estimated at 10 to 30,000 deaths per year

- HAT pathophysiology
  - 2 forms of disease, chronic with T. b. gambiense (anthroponotic) and acute with T. b. rhodesiense (zoonotic)
  - Disease manifests itself in 2 stages. Parasites first reside in the bloodstream (stage 1); they eventually cross into the CNS leading to stage 2 disease causing severe neurologic disturbances and death if not treated.

- Current therapies are inadequate
  - Melarsoprol kills 10% of patients die due to severe toxicity, Pentamidine and Suramine are only efficacious against 1st stage of disease
  - Recommended treatment for stage 2 patient is combining eflornithine and nifurtimox (NECT). WHO questioned the sustainability of NECT administration in the long-term because of high-cost and complexity of treatment administration.

- Target Product Profile
  - Cheap, safe, effective, and oral stage 1 / 2 treatment
Conclusions

- NITD has contributed two breakthrough first in class malaria compounds into the Novartis pipeline.

- NITD has been an antenna to understand the scientific and medical environment in SE Asia outside China and Japan.

- NITD and its initiatives have been an invaluable ambassador for Novartis businesses and a door opener to governments and regulatory authorities in the region.

- NITD Symposia have helped capacity building in developing countries, Africa, SE Asia, S Aerica and established Novartis as a key contributor to the needs of neglected patients.

- NITD has trained more than 100 scientists from the developing world.

- NITD is key element of Novartis’ global strategy.