Tropical Medicine and Health: The Role of Science, Technology and Innovation in Thailand

Purpose: Consideration
Submitted by: Thailand
Tropical Medicine and Health: Role of STI in Thailand

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MOST
Ministry of Science and Technology of Thailand
Health Care

Disease Prevention:
Screening Tests
Vaccines

Rehabilitation:
Devices Assistive Technology

Health Promotion:
Food Supplements

Treatment and Care:
Drugs and Medical Devices
Simple Value Chain of Products/Services

- Raw Materials / Input
- Manufacturing Engineering & Packaging
- Marketing
- Utilization
Infectious & non-infectious diseases

Vaccine

Diagnostic tools

Drug

Med Tools & Device

Cell Bank

Gene Bank

Human Genome Bank (Digital Data)

In vitro and In vivo Research and Testing Center (I2RC)

High Throughput screening & testing

Big data / Data analytics

Center for Bio-Innovation and Engineering (OMICS center)

Center for Computational Science + Research and Development Center for Cyber-Physical System
Research on Diseases at BIOTEC

Infectious diseases
✓ • Malaria
✓ • TB
✓ • Dengue, ZIKA
  • Toxoplasmosis,
  • Trypanosomiasis
  • Leishmania

Non-infectious diseases
• Cancer
• DM
• Thalassemia
• Others

Drug
Vaccine
Diagnostics
Vector Control
Drug Screening & Development
Malaria is deadly!

- 216 million cases with 0.445 million death in 2016.
- *Plasmodium falciparum* is the most deadly species of 5 human malaria parasites.
- No effective vaccine available.
- *Anopheles* mosquito vectors developed resistance to insecticides.
- Resistance of the parasite to once effective anti-malarial drugs is increasing.

New antimalarial drugs are urgently needed.
## P218 – A New DHFR Inhibitor

*Primary target indication = chemoprotection*

<table>
<thead>
<tr>
<th><strong>Product vision</strong></th>
<th>Potential for Chemoprotection</th>
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</thead>
<tbody>
<tr>
<td><strong>MoA</strong></td>
<td><em>P. falciparum</em> dihydrofolate reductase (DHFR) inhibitor</td>
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</table>
| **Key features**   | - Clinically validated pathway  
                    - Activity against wild type, and antifolate resistance-conferring quadruple mutants |
| **Challenges**     | 10 fold difference between *P. falciparum* and *P. vivax* IC50 in ex-vivo field isolates |
| **Status**         | First in human study ongoing |
| **Next milestone** | Go/no go decision to initiate controlled human malaria infection cohort |
Novel Antimalarial ‘P218’ Targeting DHFR Enzyme

2002-2003

2008-2009

MMV
Medicines for Malaria Venture

NSTDA

2009

May 2014

Sep 2015

2017

1999

2003

Discovery

P218 preclinical

5-10 kg scale-up

P218 IND preclinical

P218 IND dossier

Phase I/IIA

First-in-Human

Human Challenge Model

- Recombinant DHFR enzyme
- Screen antifolates
- Molecular studies
- Drug design

- P218 lead candidate
- Preliminary preclinical studies

- Proposal request
- Begin preclinical studies for IND

- Collaborative Discovery program BIOTEC, LSHTM, Monash (MMV funded)

Expected completion of preclinical studies
MMV-supported projects

MMV support to projects may include financial, in-kind, and advisory activities.

Footnotes:
- Included in MMV portfolio after product approval and/or development, DNDi and partners completed development and registration of ASMQ and ASAQ.  
- Global Fund Expert Review Panel (DERP) reviewed product – permitted for time-limited procurement, while regulatory/WHO prequalification review is ongoing.  
- WHO Prequalified OR approved/positive opinion by regulatory bodies who are ICH members/observers.  
- Paediatric formulation.  * For children 13 – 60 months; ** For infants 3 – 12 months.

Brand names 1: Coartem® Dispersible; 2: Artesun®; 3: Eurartesim®; 4: Pyramax® tablets or granules; 5: ASAQ Winthrop®; 6: SPASQ-CA™
Footnotes: MMV-supported projects

Target Product Profiles and Target Candidate Profiles

MMV has defined Target Product Profiles and Target Candidate Profiles for medicines to support the eradication campaign.


Target Product Profiles
indicated by bars at the bottom of each compound box

- 3-day cure, artemisinin-based combination therapies
- Combinations aiming at a new single-exposure radical cure (SERC) TPP-1
- Severe malaria treatment and pre-referral intervention
- Intermittent /seasonal malaria chemoprevention
- Products targeting prevention of relapse for P. vivax
- Single-exposure chemoprotection (SEC) TPP-2

Target Candidate Profiles
activities for each individual molecule, indicated by symbols added to each compound in the translational portfolio

<table>
<thead>
<tr>
<th>Burrows et al., 2013</th>
<th>Burrows et al., 2017</th>
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<tbody>
<tr>
<td>Asexual blood stages</td>
<td>TCP-1.2</td>
</tr>
<tr>
<td></td>
<td>TCP-1</td>
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<tr>
<td>Relapse prevention</td>
<td>TCP-3a</td>
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<td></td>
<td>TCP-3</td>
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<tr>
<td>Transmission reduction</td>
<td>TCP-3b</td>
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<td></td>
<td>TCP-5,6</td>
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<tr>
<td>Chemoprotection</td>
<td>TCP-4</td>
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April 2018
Other Drug Discovery and Medical Research activities on infectious diseases at BIOTEC
Insect Fungi

Metarhizium anisopliae

Beauveria bassiana

BBR & MBB

TBRC & BCC
Natural product library: > 700 cpds; New structure: > 546 cpds
Publication: > 120 papers

Ganoderma austral
BCC 22314

GA001

pleosporin A
*Tetrahedron Lett.* 2014, 55, 469-471 (Cover Article)

anti-malaria IC₅₀ 1.6 µg/mL

cytotoxicity (vero) IC₅₀ >50 µg/mL
Commercialized natural products

- *Xylaria* sp. BCC 1067 (Xylariaceae) - depudecin
  - Sigma-Aldrich product number: D 5816
- *Verticillium hemipterigenum* BCC 237 (Invertebrate Pathogenic Fungus) - ascochlorin
  - Sigma-Aldrich product number: SML0104
- Basidiomycetes - panepoxydine
  - Sigma-Aldrich product number: SM0726

**New compounds for each category:**
- Insect fungi: 135 new cpds
- Marine fungi: 32 new cpds
- Endophytic fungi: 78 new cpds
- Basidiomycetes: 147 new cpds
- Actinomycetes: 48 new cpds
- Others: 109 new cpds
Mosquitos Platform for Disease and Vector Controls

Prevent the spread of Dengue Fever

SPECIAL ALERT: The Truth About the Zika Virus

MPMB/MMU & SMBR
Dengue Research

‘DENGUE RESEARCH’

New Biomarker/NS1-virus rep/viral assembly-capsid-packaging/Ab-DENV (MRC-NSTDA)

SPECIAL ALERT: The Truth About the Zika Virus

DENV-ZIKA
(Serological Cross-Reaction)
Now approach: HTP reverse genetics

Theme of Research

ONE: Pathogenesis
Virus factors
Heat factors

TWO: Vaccines
Conventional vaccines
New approached vaccines

THREE: Diagnostics
NS1: ELISA (serotyping), POC
New prognostic tests

FOUR: Clinical & translational research
Clinical specimens collection & diagnostics management

FIVE: Others
Other emerging diseases
Plurius Technologies
- Gene editing
- Antibody production
- Bioinformatics
- Epidemiology

DNA
LAV
VLP
Subunit E protein

Anti-dengue drug

SMBR/BIOTEC
ECDD คืออะไร?

ECDD คือ Excellent Center for Drug Discovery ซึ่งเป็นศูนย์กลางการวิจัยในด้านการพัฒนา葇าตัวช่วยในการเรียนรู้ สำหรับการบริการที่มีคุณภาพตามเกณฑ์ในระดับสากล ศูนย์นี้จะทำการพัฒนาการวิจัยเพื่อให้การผลิตสมุนไพรที่มีคุณภาพสูงขึ้น และการใช้ยาที่มีประสิทธิภาพสูงขึ้น การตั้งศูนย์นี้เพื่อเป็นการช่วยในการสร้างการพัฒนาการถึงการผลิตสมุนไพรที่มีคุณภาพสูงขึ้น และการใช้ยาที่มีประสิทธิภาพสูงขึ้น

กระบวนการค้นหาด้ายยา

1. Target Identification
2. Library Screening
3. Lead Optimization
4. Pre-Clinical Trial
5. Clinical Trial

ศูนย์ ECDD ตั้งอยู่ที่มหาวิทยาลัยบูรพา จังหวัดนนทบุรี ติดต่อได้ที่ 02-559-5500

ECDD@mahidol.ac.th
http://ecdd.ac.mahidol.ac.th
ECDD : Cell-Based Bioassay Screening Platform to Determine Activity Potency and Cytotoxicity Testing

Technology Features and Specifications, Competitive Advantage over the existing technology
- ECDD is equipped with high throughput and high content screening automation which provides the cutting-edge technology to the research community
- Increase accuracy and reduce variability of compound addition through the use of automation
- ECDD is capable of storing more than 100,000 compounds
- We accept synthetic compounds, purified natural compounds, fractionation and crude extracts to be deposited at ECDD

Potential Application
- ECDD have screened about 3,500 compounds from natural resources with biological activities to prevent and treat diseases such as diabetes mellitus, hypertension, obesity, diarrhea etc.
- ECDD acquires panels of cancer cell lines for 2D and 3D (cancer spheroids and organoids) development into novel anti-cancer drugs
- In the initial screening we test against colon cancer, breast cancer and lung cancer
- In the future, cancer screening platforms will developed directly from patient specimens

Customer Benefit
ECDD provides a broad range of high-throughput screening and assay development and fully-integrated services from initial discoveries to be applicable for
- Functional foods
- Food innovation
- Health supplements
- Investigational new drug.
Acknowledgements

- NSTDA: BIOTEC
- TCELS
- Other agencies in MOST