A Vaccine to Block Malaria Transmission: Pfs230 Antigen Design and Display (T2016-207)

Ehime University Proteo-Science Center, Japan
Takafumi Tsuboi, Tomoko Ishino, Mayumi Tachibana, Eizo Takashima

PATH Malaria Vaccine Initiative, USA
C. Richter King (PI), Ashley J. Birkett, David C. Kaslow

NIH, Laboratory of Malaria and Vector Research, USA
Kazutoyo Miura, Carole A. Long

GHIT R&D FORUM, Dec. 8, 2017, Tokyo
1. Objective & Goals

Malaria transmission-blocking vaccine development

WHO Malaria Vaccine Technology ROADMAP (2013)
Strategic Goals towards malaria eradication

1. Protective efficacy >75% against clinical malaria
2. Vaccines that reduce transmission

No efficacious transmission-blocking vaccine (TBV) to date
Only Pfs25 & Pfs230 tested in humans

1. Pfs25 trial indicates immunogenicity in humans needs improvement.
2. New approaches to the discovery and optimization of Pfs230, as well as novel ways to augment the immune responses are needed.
2. Partnership

Why “EHIME : PATH MVI”?

EHIME U: TBV basic research with WGCFS

- Candidate Discovery of TBV Antigens
- Wheat Germ Expression System (WGCFS) express quality malaria proteins
- Immunologic Evaluation

PATH MVI: TBV development

- Candidate Optimization & Production
  - Partnerships & capacities for optimization & production in scalable system
  - Adjuvant and formulation
- Candidate Evaluation
  - LMVR/NIH Ref Lab functional assays (SMFA)
- Translational Development
  - Human challenge models
  - Regulatory pathway

EHIME U: TBV basic research with WGCFS

PATH MVI: TBV development

Why “EHIME : PATH MVI”?

EHIME U: TBV basic research with WGCFS

PATH MVI: TBV development
3. Activities (approach)

WGCF system to identify superior Pfs230 domains

Pfs230: Cysteine-rich very complex domains

Gerloff et al., PNAS, 2005

3,135 aa

Full-coverage construct design

(unpublished)
3. Activities to date (result 1)
Mouse antibodies recognize parasite Pfs230 proteins.

Mouse antibodies react specifically but differently against parasite Pfs230.

**Western blot**

<table>
<thead>
<tr>
<th>01</th>
<th>02</th>
<th>03</th>
<th>04</th>
<th>05</th>
<th>12</th>
<th>27</th>
</tr>
</thead>
</table>

**IFA**

01 02 03 04 05 12 27 Nve. Cntl.

(unpublished)
3. Activities to date (result 2)

Anti-Pfs230 antibodies block transmission

Mouse antibody differently reduce transmission of parasites to mosquitoes

Parasite No./mosquito

<table>
<thead>
<tr>
<th>150</th>
<th>100</th>
<th>50</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>4B7</td>
<td>Nve. Cntl.</td>
<td>TBV01</td>
<td>TBV02</td>
</tr>
<tr>
<td>TBV03</td>
<td>TBV04</td>
<td>TBV05</td>
<td>TBV12</td>
</tr>
<tr>
<td>TBV27</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pooled serum

LMVR/NIH
SMFA
Reference Center

(unpublished)
3. Activities in 2018

Ag production using scalable expression system with novel delivery platform

Leveraging existing MVI technology platforms

Select 5 potent Pfs230 domains (by Mar. 2018)

Multi-valent delivery
VLP (SpyCatcher)

LMVR/NIH SMFA Reference Center

Analytical Testing

Selection of Pfs230 vaccine candidate

Manufacturing & clinical studies (2019~)

**Multi-valent delivery**

- VLP (SpyCatcher)
- CoPoP
- Liposome
- CRM\textsubscript{197} conjugate

**Selection of Pfs230 vaccine candidate**
4. Lessons learned

- What lessons did project members take out of the project?
  1) Ehime U (Academia): Learned how to proceed basic science research towards product development such as malaria TBV.
  2) PATH MVI (PDP): PATH MVI benefits from expertise provided by Ehime U regarding the biology of Pfs230 and the expression of challenging proteins.

- How can these lessons be implemented in future projects?
  1) Ehime: Get ideas for the basic science research which will be useful for the future product development.
  2) PATH MVI: Continue to seek the best mix of partners with complementary experience for future projects.

- What could have been done to make the project better?
  Include additional partner with specific expertise in product development. (ie. adjuvant expert)
5. Comments

- Message to GHIT Fund and R&D experts

1) This type of partnership under GHIT Fund is very important for the effective product development towards malaria elimination.

2) GHIT funding allows us to pursue goals and objectives that are synergistic with our other funding. It maximizes the probability of success by enabling targeted translational research toward a malaria vaccine.

Thank you very much