Pre-erythrocytic vaccines
for malaria elimination

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Recent progress in reducing malaria

Malaria elimination needs a wide range of strategies.

Need Malaria Vaccines!

Global

Africa (< 5y)

Africa (≥ 5y)

Other (≥ 5y)

Other (< 5y)

Leading Malaria Vaccine Candidate

RTS,S/AS01 Malaria Vaccine Phase 3 trial at 11 sites


Design:
1) 6,537 infants (6-12wk)
8,923 children (5-17mo)
2) Vaccination: 0, 1, 2mo
Efficacy against Clinical Malaria:
   Infants 27%
   Children 46%

Final results (Lancet. 2015 Apr 24)

Design:
1) 6,537 infants 8,922 children
2) Vaccination: 0, 1, 2mo, ± Boost at 20mo
3) Follow-up to: 38mo (infants)
   48mo (children)
Efficacy against Clinical Malaria:
   Infants 26% (Boost) 18% (No boost)
   Children 36% (Boost) 28% (No boost)
**Landmark Goal:**

By 2015, develop and license a first-generation malaria vaccine with $\geq 50\%$ efficacy and lasts $\geq 1$ year.

**Strategic Goals towards malaria eradication:**

By 2030, license vaccines targeting *Plasmodium falciparum* and *P. vivax* that encompass the following 2 objectives:

1. Malaria vaccines with $\geq 75\%$ efficacy against clinical malaria
2. Malaria vaccines that reduce transmission of the parasite

**Priority research areas:**

1. DEVELOP immunological assays
2. STANDARDIZE clinical trial
3. USE state-of-the-art approaches to identify novel potential candidate vaccine targets
4. CONFIRM mechanisms of protection, using controlled human malaria infection models

(http://www.who.int/immunization/topics/malaria/vaccine_roadmap/TRM_update_nov13.pdf)
Current Malaria Vaccine Candidates

Transmission-blocking vaccines (SSM-VIMT)
Pfs25, Pfs230

VIMT
1) Pre-erythrocytic
2) SSM-VIMT

Pre-erythrocytic Vaccines
CSP(RTS,S)

SSM-VIMT:
Sexual, Sporogenic, Mosquito-stage Vaccines Interrupting Malaria Transmission
Need more vaccines!
Post-genome novel candidate discovery
**E. coli** is NOT the optimal recombinant protein synthesis system for malaria proteins

![PlasmoDB logo](image)

**WHY malaria parasite proteins are difficult to produce?**
1. Codon bias (AT content: Pf 76%), Repeat sequences
2. Folding (eukaryotic) and often multiple disulfide bonds
3. No-glycosylation machinery

<table>
<thead>
<tr>
<th>Methods</th>
<th>Proteins expressed</th>
<th>Soluble</th>
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<tbody>
<tr>
<td><em>E. coli</em> cell</td>
<td>39 / 292 (13 %)</td>
<td>N.D.</td>
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<td>(Aguiar et al., Genome Res., 2004)</td>
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1. Eukaryotic (co-translational folding)
2. Negligible inhibitor contamination
3. No-glycosylation machinery

(Endo & Sawasaki. Curr Opin Biotech, 2006)
**WGCFS** is the **optimal** recombinant protein synthesis system for malaria proteins

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<td><strong>WGCFS</strong></td>
<td>478 / 567 (84%)</td>
<td>71% (&gt;50% of the protein soluble)</td>
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Pre-erythrocytic vaccine candidate discovery

Wheat germ

Protemist® DT II
Smal scale
~80 µg/well

Check:
1) Solubility, 2) Yield, 3) Purity

Wheat

Target Gene Selection

Protemist® XE
Large scale
10 mg/run

Check:
1) Solubility, 2) Yield, 3) Purity

mvi PATH
Malaria Vaccine Initiative

Functional assay

Antibody

Selection

Pre-erythrocytic vaccine candidates