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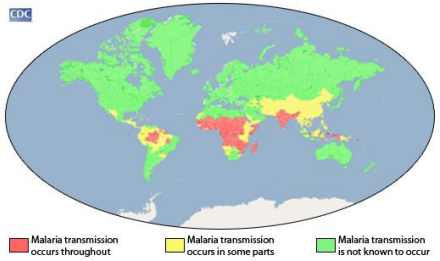
COLLEGE of PHARMACY

Background

Significance of malaria and the struggles of vaccination



- Mostly present in underdeveloped regions with warm climates.
- There is currently no effective malarial vaccine.
- In general, vaccination in these regions is poor due to a lack of necessary cold-chain conditions and trained professionals.

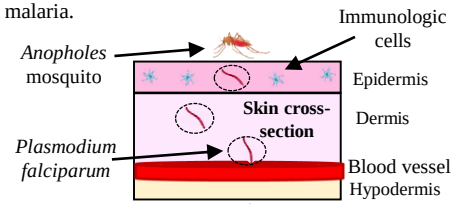
Courtesy: CDC

What is TRIO?

- TRIO is a salivary protein from the *Anopheles* mosquito, which itself is responsible for injecting parasitic *Plasmodium falciparum* into the bloodstream of a human host, inducing malarial infection. When TRIO peptides are expressed on the surface of Virus-Like Particles (VLPs), this creates a novel vaccination strategy against malaria.

TRIO peptides

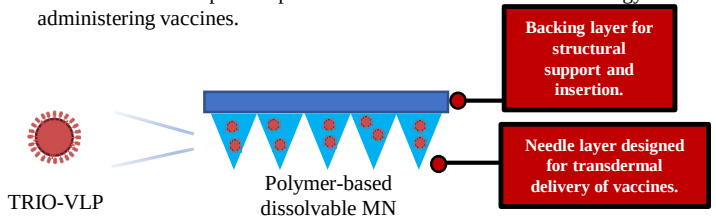
Surface expression of TRIO peptides on a VLP (TRIO-VLP)



Cross-section of skin showing injection of *P. falciparum* into the bloodstream

What are Microneedles (MN) and what are their benefits?

- MN are dissolvable patches placed on the skin as a needle-free strategy for administering vaccines.



Benefits of using MN:

Preliminary Data

Proof of concept with MN use: Antibody titers from mice immunized using MN loaded with CIS43 VLPs and MF59 adjuvant

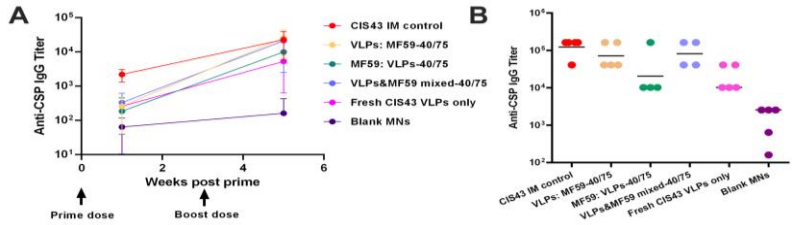
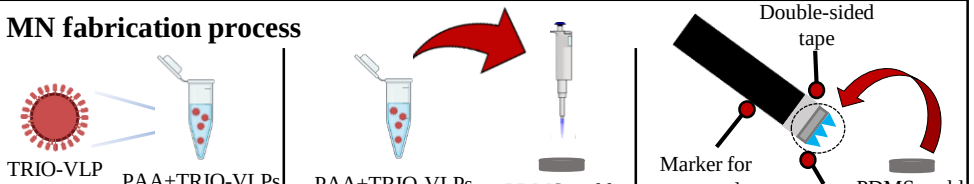


Figure 1. Immune response of stabilized MN with CIS43 VLPs + MF59 adjuvant:
The mMNs were kept for **three months at 40°C/ 75% relative humidity (RH)**. Figures **A** and **B** represent antibody titers in vaccinated mice 5 weeks and 11 months after the first vaccine dose, respectively. In this study, we also compared the immunogenicity of stabilized mMNs with control groups, including freshly-made mMNs, and vaccines administered intramuscularly and subcutaneously.

Methods

MN fabrication process



Stage 1: Creation of a stock solution using Poly(acrylic acid) (PAA) + TRIO-VLP

Stage 2: Pipetting the stock solution into a PDMS mold, which is then centrifuged

Stage 3: Removal of the MN from its mold following a 24-hour drying period in a desiccator

Results

Removal of a microneedle patch from its mold

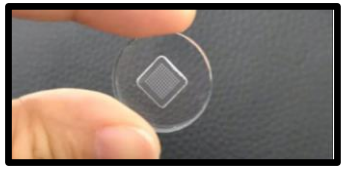


Figure 2. PDMS mold used in MN fabrication.
Courtesy: Micropoint Technologies Pte Ltd.

24-hour drying period

Figure 3. MN after removal from mold.

Results (cont.)

Characterizing needle sharpness

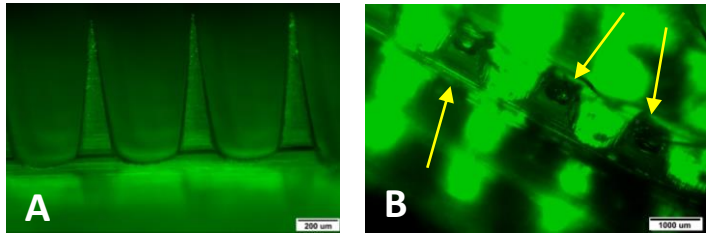


Figure 4. A) Fluorescent microscopy image of a MN pre-insertion. Needles appear sharp. B) Fluorescent microscopy image of a MN post-vaccination of mice with CIS43 VLPs and MF59 adjuvant (refer to Figure 1). Needles have dissolved (see arrows).

Needle penetration test

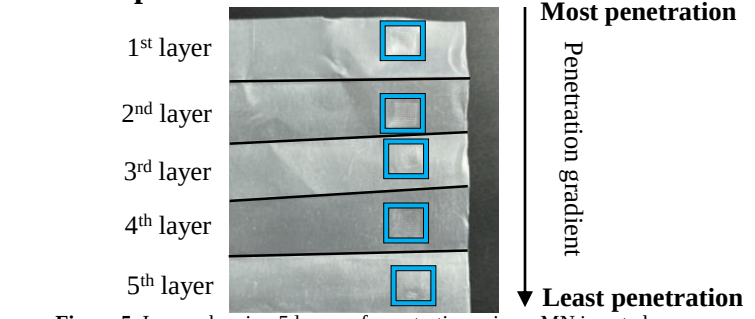


Figure 5. Image showing 5 layers of penetration using a MN inserted in parafilm. Boxes highlight region of penetration to show the depth gradient that is formed. Each parafilm layer is ~13mm in thickness.

Future Directions

- Penetration strength testing using a texture analyzer
- SDS-PAGE + Spectrophotometry for quantifying TRIO-VLPs in MN
- Long-term thermostability studies of MN
- Animal studies using TRIO-VLPs in MN

Acknowledgements

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