Laser Vaccine Adjuvant as a dose-sparing option for HPV vaccination

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Laser Adjuvant for HPV Vaccine

- Global Burden of Cervical Cancer
- HPV vaccination and challenges in resource-poor settings
- Laser as a novel approach in vaccination
- Next steps for Laser Adjuvant Technology
Cervical Cancer: Background

• Second most prevalent cancer in women
• In 2008, there were 530,000 new cases associated with 275,000 deaths (WHO)
• Over 85% of cases of cervical cancer were recorded in low-income countries
• In Africa, 75,000 new cases were recorded with 50,000 associated deaths (WHO)

Source:
• Cervical cancer is caused by HPV infection
• Most frequently type of HPV are 16 and 18 (70-80%) 
• Moreover, there is an increasing link between HPV infection and cancer of anogenital tract 
• Currently, there are two HPV vaccines e.g. Cervarix® and Gardasil®.
National HPV Vaccination Scheme

http://www.gavialliance.org/support/nvs/human-papillomavirus-vaccine-support/
Both Cervarix® and Gardasil® are administered by IM route and 3 doses over 6 months.

A pilot randomized study to assess immunogenicity, reactogenicity, safety and tolerability of two human papillomavirus vaccines administered intramuscularly and intradermally to females aged 18–26 years


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• Safety and effectiveness compared between ID administration with 20% dosage and full dose IM vaccine administration.
• All groups demonstrated seroconversion (HPV 16 and HPV18 antibody titre >= 1:320) after 2^{nd} vaccine dose.
• The main factor potentially limiting ID route is its greater reactogenicity.
Adjuvants and Dose-Sparing Technologies

- Modern vaccines tend to be highly targeted and less immunogenic
- Many licensed and candidate adjuvants have significant side effects which limit their usage
Examples of Current Adjuvants

- Alum (aluminum salts) has been the most widely used adjuvant for the past 80 years (HAV, HBV, DTaP, Hib) – local and systemic reactions
- AS03 (squalene based oil-in-water emulsion) for H5N1 – pH1N1 vaccine in Europe is linked to narcolepsy
- AS04 (Alum+monophosphoryl lipid A) for HPV (Cervarix®) – local and systemic reactions

Source:
Global Use of Medical LASERS
Advantages of Laser as a Vaccine Adjuvant

• Established medical approach
  – More than three decades of medical experience with lasers (LASIK, tattoo removal, hair removal, lipolysis)

• Less chance of local and systemic adverse reactions – laser does not persist in the body

• No need for chemical formulation with other drugs and cold chain storage
Laser Setup for Preclinical Studies at VIC

- Continuous wave (CW) and pulsed wave (PW) 1064 nm near-infrared (invisible, skin-color insensitive) laser
- PW 532 nm green (visible) laser
- No thermal skin damage was found at this dose
- Non-painful: final skin temperatures remained below thermal pain threshold of 41°C
Testing Near-infrared (NIR) Laser Adjuvant in a Mouse Model of Influenza Vaccination

Day 1
- Intradermal vaccination
  - Whole inactivated virus (Influenza A PR/8/34) 1 µg/mouse
  - No vaccine
  - Vaccine i.d. only
  - Vaccine i.d. + PW 532 nm laser
  - Vaccine i.d. + CW 1064 nm laser
  - Vaccine + Alum i.d.

Day 28
- Intranasal live viral challenge (Influenza A PR/8/34)

Day 28 ~ 42
- Monitoring survival

Day 28
- Blood drawing, sampling of spleen and lung
  - ELISA for anti-influenza antibody
  - ICS / flow cytometry on splenocytes
  - Viral titration in lung
NIR Laser Enhances the Humoral Immune Response to Influenza Vaccination
Flow cytometry analysis on splenocytes from post-challenge mice

**NIR Laser Enhances Vaccine Specific CD4+ T Cell Responses**

\[ T_{H1} \]

\[ T_{H2} \]

\[ P = 0.044 \]

\[ P = 0.003 \]

\[ P = 0.003 \]
NIR Laser Augments Vaccine Efficacy and Protection in Lethal Challenge Model

Survival time

Influenza viral titer in lung
1064 nm NIR Laser Treatment at Equivalent Doses to Mice is Tolerated and Painless in Humans

Human dosing: 3.7 W/cm², 120 seconds, 444 J/cm²
Mouse dosing: 5.0 W/cm², 60 seconds, 300 J/cm²
Potential Development in Laser Vaccine Adjuvant

A: The current benchtop testing system
B: A portable SemiNex laser
C: A potential clinically applicable light delivery system
Conclusions

- We would like to integrate the Laser adjuvant with a dose-sparing study in intradermal HPV vaccination.
- Laser offers the opportunity to reduce reactogenicity, increase vaccine specific immune responses and dose spare.
- Next steps include animal model studies, clinical trials, and development of portable and robust laser devices.
Next Steps With PRRR

• Step 1: test ID HPV vaccination with 20% dosage approach in animal model.
• Step 2: we proceed with LASER safety and efficacy trial in US and at site in Africa preferably Zambia
• Step 3: continue to develop simple LASER / Light Delivery device

• GOAL: To increase the uptake and reduce the cost of HPV vaccination by one third at least
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