DEVELOPMENT OF A CHLAMYDIAL VACCINE FOR KOALAS

Peter Timms et al.
A sign showing a koala sitting on a pole with the words 'Vulnerable', 'Endangered', and 'Extinct' pointing in different directions. Above the sign, an excavator is digger in the background, indicating habitat destruction.
Keratoconjunctivitis
Reproductive tract disease
“Current” taxonomy for Chlamydiae

C. ibidis

C. gallinacea

C. avium

C. psittaci

C. abortus

C. pneumoniae

C. pecorum

C. muridarum

C. felis

C. caviae

C. trachomatis

C. suis
Goal: To develop a vaccine to protect koalas against *C. pecorum* infection and disease

- **Vaccine should result in;**
  - **Antibodies**
    - Specific & high titres
    - Neutralising
    - Present at mucosal sites
  - **T cell response**
    - Lymphocyte proliferation
    - Cytokines (interferon-gamma)
  - **Two types of vaccine**
    - Prophylactic
    - Therapeutic
Basic vaccine formulation

1. Chlamydial antigen
   1. Recombinant MOMP proteins
   2. Koala *C. pecorum* – 3 genotypes
2. Adjuvant
   1. Iscomatrix; Tri-adjuvant (VIDO)
3. Delivery: subcutaneous
4. Assessment
   1. Swab eyes and UGT and measure infection (qPCR) load
   2. Clinical disease
The “10-year” project

1. Can koalas produce an immune response to chlamydial antigens ✓
2. Is the vaccine safe to give to animals with current infection / disease ✓
3. Can a vaccine do something that natural infection is currently not doing ✓
4. Is there cross-strain immune recognition ✓ ?
5. Vaccination of male as well as female koalas ✓
6. Move from a multi-dose to a single dose vaccine ✓
7. Develop new koala immunological reagents ✓
8. Evaluate the vaccine under field conditions ✓
9. What is the basis of protection ?
10. Can you vaccinate against disease ?
Production of *in vitro* neutralising antibodies following vaccination
Production of a T cell response

![Graph showing production of T cell response for healthy and diseased conditions with vaccine and placebo groups.](image)
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First major field trial

- 60 free-ranging koalas; 30 Vaccine & 30 Control
- Vaccine
  - **Antigen:** Major Outer Membrane Protein (MOMP)
  - **Adjuvant:** Immune Stimulating Complex (ISC)
  - **Immunisation Schedule:** Days 0, 30 and 60
- Analysis
  - IgG antibody production; Cytokine production
  - *Chlamydia* infection load as determined by qPCR
  - Incidence of new disease
Chlamydia load decreases in vaccinated animals (ocular).

Unvaccinated

S1 Mdn of 39 [IQR = 20.3 – 76.4]
S2 Mdn 119.6 [IQR = 10.6 – 204.1]
Wilcoxon signed rank test

\[ z = -1.572, p = 0.116, r = 0.45 \]
Chlamydia load decreases in vaccinated animals (ocular).

<table>
<thead>
<tr>
<th></th>
<th>Vaccinated</th>
<th>Unvaccinated</th>
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<tbody>
<tr>
<td><strong>S1 Mdn</strong></td>
<td>13.9 [IQR = 10.7-48.2]</td>
<td>0 [IQR = 0-21.8]</td>
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<tr>
<td><strong>S2 Mdn</strong></td>
<td>0</td>
<td>119.6 [IQR = 10.6-204.1]</td>
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Wilcoxon signed rank test:
- **Vaccinated**
  - $z = -2.310$, $p = 0.021$, $r = 0.54$
- **Unvaccinated**
  - $z = -1.572$, $p = 0.116$, $r = 0.45$
Chlamydia load decreases in vaccinated animals (UGT).

**Vaccinated**

- S1 Median (Mdn) = 31.4 [IQR = 13.9 – 89.1]
- S2 Mdn = 0, [IQR = 0 -11.53]
- Wilcoxon signed rank test: \( z = -2.366, \ p = 0.018, \ r = -0.89 \)

**Unvaccinated**

- S1, Mdn = 57.9 [IQR = 41.6-131.2]
- S2, Mdn = 12.7 [IQR = 0 – 143.5]
- Wilcoxon signed rank test: \( z = -0.804, \ p = 0.422, \ r = -0.22 \)
Vaccinated animals do not progress to a diseased state. However, 11.5% of non-vaccinated animals developed the disease.
The “10-year” project

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In vitro neutralisation antibody levels
Mapping of the MOMP epitopes: PepScan technology
Absorption of sera against peptides and evaluation of remaining \emph{in vitro} neutralisation ability
Acknowledgements

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Key people

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- C Mangar