Trivalent subunit and Live-attenuated vaccines against pneumonic plague

Ashok K. Chopra, Ph.D., C.Sc.
John S. Dunn Distinguished Chair in Global Health & Director Center for Antibiotic Resistance and Microbiome
Dr. Leon Bromberg Distinguished Professor
Assistant Director, Graduate Program
Department of Microbiology & Immunology
Center for Biodefense & Emerging Infections and Tropical Diseases
Institute for Human Infections & Immunity
Institute for Translational Sciences
Senior Scientist, Sealy Center for Vaccine Development
Scientific Staff, Shriners Burns Institute

Jeanny Sealy Hospital

Old Red
M2B
Keiller-GNL complex
Galveston National Lab
Ad5-based trivalent subunit plague vaccine; Ad5-YFV (YscF, F1, and LcrV); CVI. 2016, 23: 586-600 (patent-claims allowed, March 2018)

Table 1. NHP (CM) immunization and challenge timeline (Prime-boost)

<table>
<thead>
<tr>
<th>Group (size)</th>
<th>Induction of preexisting anti-adenovirus immunity (Ad5-Empty) (Day 0)</th>
<th>Prime vaccination (rAd5-YFV) as mist (Day 30)</th>
<th>Boost with purified rYFV fusion protein (Day 42)</th>
<th>Aerosol Challenge (Day 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunized (4)</td>
<td>5 x 10^{10} v.p./250 µl Ad5-empty i.m. route</td>
<td>1 x 10^{11} v.p./500 µl rAd5-YFV i.n. route (250 µl per nostril)</td>
<td>50 µg of rYFV protein mixed with alhydrogel (250 µl) given by the i.m. route</td>
<td>WT CO92 (Dp: 1.32 to 8.08 x 10^7 CFU)</td>
</tr>
<tr>
<td>Control (4)</td>
<td>Saline (250 µl) i.m. route</td>
<td>Saline (500 µl) i.n. route (250 µl per nostril)</td>
<td>Saline (250 µl) i.m. route</td>
<td></td>
</tr>
</tbody>
</table>

Dp of 1.32 to 8.08 x 10^7 CFU WT CO92

Percent Survival

Days Post Infection

Control Immunized (Prime-Boost) Control

Immun. b/challenge Immun. a/challenge

Control

Lung

Pleura

Mediastinal LN

Prime boost
Immunity conferred by the LMA mutant to mice against plague

Tiner et al. Clin. Vaccine Immunol. 22; 1255-68
Protection of mice and rats from pneumonic plague after immunization with LMA or LMP vaccines-Submitted patent

Tiner et al. Npj Vaccines 1, Article #16020 (2016), doi:10.1038/npj Vaccines 2016.20

**Signature-Tagged Mutagenesis**

**Step 1** (Library Generation)

**Step 2** (Pooling)

**Step 3** (Fitness Challenge in Pneumonic Plague Model)

**Step 4** (Abundance Differential)


Total = 53 tags 5088 mutants
Funding: NIH; SBIR (phase I and II); NSF; American Water Works Association RF; Crohn’s & Colitis Foundation of America; American Heart Association; EPA; Companies (Pfizer, Protein Potential); Army; Texas Higher Education Coordinating Board