Poster #2044 – Saturday, June 22th

Optimization of an Adjuvant-Only Vaccine as a Horizontal Infection-Prevention Strategy

Jun Yan[1], Travis B. Nielsen[1,2], Brian M. Luna[1,2], Peggy Lu[1], Brad Spellberg[1,2,3]

[1]Department of Molecular Microbiology & Immunology, Keck School of Medicine at the University of Southern California (USC), Los Angeles, CA; [2]ExBaq, LLC, Bethesda, MD; [3]Division of Infectious Diseases, LAC+USC Medical Center, Los Angeles, CA

Correspondence: Jun Yan, 323-865-3669
1441 Eastlake Ave, NTT 6419, Los Angeles, CA 90033
junyan@usc.edu

USC University of Southern California Keck School of Medicine

ExBaq

LAC+USC MEDICAL CENTER

Abstract

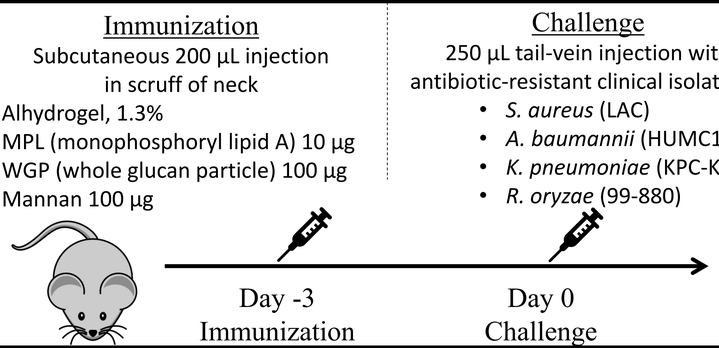
Background: Traditional vaccines protect vertically against pathogen-specific infections - a much narrower approach than horizontal, pathogen-agnostic approaches. Development of a broad-spectrum vaccine that protects against drug-resistant healthcare-associated infections (HAIs) would greatly improve healthcare. We previously reported that a unique combination of three-adjuvant provides short- to intermediate-term protection against Gram-negative and -positive bacterial infection, without the use of protein antigens. We now report dose optimization and effects of a fourth adjuvant (mannan).

Methods: We immunized mice subcutaneously with placebo or a combination of different adjuvants (aluminum hydroxide, monophosphoryl lipid A, whole glucan particles, and/or mannan). Three days after the immunization, mice were challenged with a lethal intravenous infection of *Acinetobacter baumannii*, *Klebsiella pneumoniae, Staphylococcus aureus,* or *Rhizopus oryzae*

Results: Lowering the dose of the triple-adjuvant regimen (aluminum hydroxide, monophosphoryl lipid A, whole glucan particles) conferred partial protection against bloodstream infections caused by XDR strains of *A. baumannii.* When mannan was added to the low-dose triple-adjuvant regimen, the quadruple-adjuvant combination provided protection similar to the high-dose triple-adjuvant regimen. In addition, Alhydrogel, MPL, and mannan provided similar if not better protection compared to the quadruple-adjuvant combination against bloodstream infections caused by *S. aureus* and even neutropenic mice from disseminated mucormycosis.

Conclusion: These data strongly encourage the translation of an adjuvant-only vaccine as a horizontal infection-prevention strategy for patients at risk of HAIs.

Methods



Results

A. baumannii IV in C3H

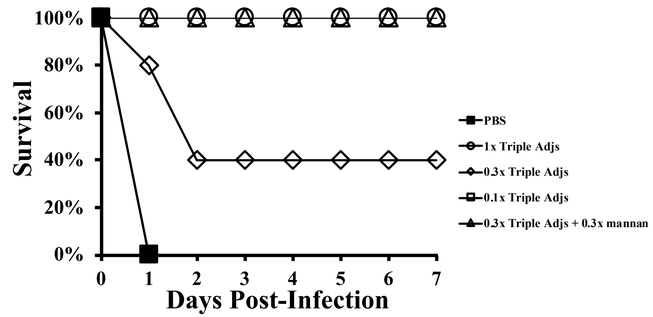


Figure 1. Comparing adjuvants with vs without mannan, including mannan improved survival of mice immunized with a lower dose of adjuvants when challenged with HUMC1 (an antibiotic-resistant clinical isolate of *A. baumannii*).

K. pneumoniae IV in C3H

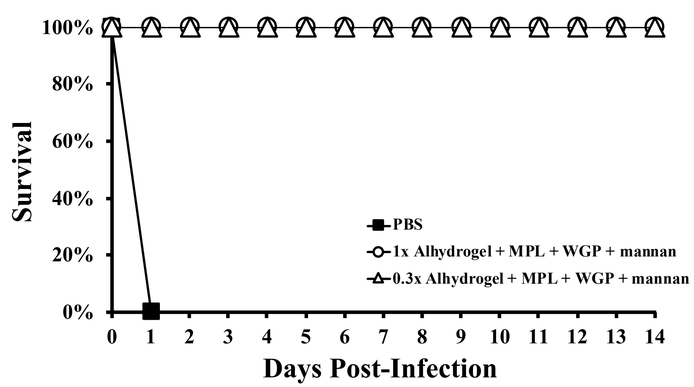


Figure 2. Mice were immunized with the combination of quadruple adjuvants and then infected 3 days later with the Gram-negative bacterium *K. pneumoniae* (strain KPC-KP1).

R. oryzae IV in BALB/c

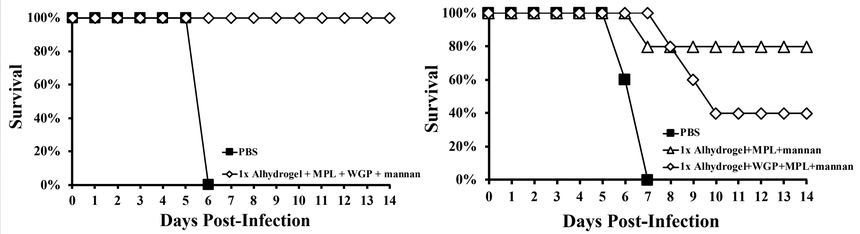


Figure 3. Neutrophil-depleted mice were immunized with various adjuvant groups and then infected 3 days later with the fungus *R. oryzae* (stain 99-880) at either **A)** 1.2E3 or **B)** 2.9E3 spores/mouse.

S. aureus IV in BALB/c

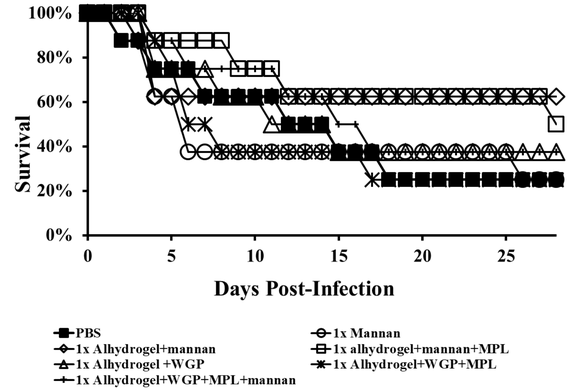


Figure 4. Mice were immunized with the quadruple adjuvants and then infected 3 days later with the Gram-positive bacterium *S. aureus* (stain LAC).

Conclusions and Future Directions

- Immunization with only adjuvants protected different strains of mice against a variety of pathogens from different kingdoms.
- Mannan, when used in conjunction with the three other adjuvants, provided additional protection and a low-dose quadruple-adjuvant combination resulted in similar protection as compared to a high-dose triple-adjuvant regimen.
- These data strongly encourage the translation of these adjuvants as a horizontal infection-prevention strategy for patients at risk of HAIs.
- In the future, we plan to study the mechanism of protection and further optimize dosing.