Development and Evaluation of *S. epidermidis* DNA, mRNA and Protein Vaccines

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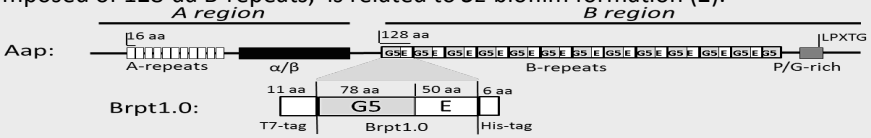
Introduction

- *S. epidermidis (SE)* represents one of the most prevalent causes of device-related hospital-acquired infections (1).
- Accumulation Associated Protein (Aap) of *S. epidermidis*, especially its B-region composed of 128-aa B-repeats, is related to *SE* biofilm formation (2).



- Antisera and mAbs against Aap are known to inhibit *SE* biofilm formation *in vitro* (3).

Materials and Methods

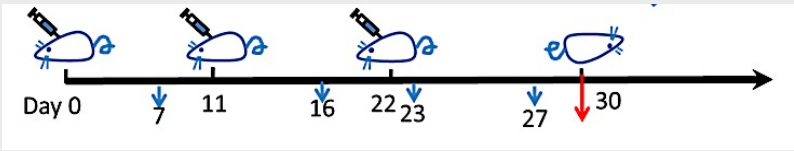
Vaccine Preparation

The gene fragment encoding a single B-repeat (128aa) of Aap was cloned into the plasmids pVAX1, pGEM4z-A64 and pET21, yielding pVAX/aapBrpt as the DNA vaccine; pGEM/aapBrpt, the precursor for the mRNA vaccine; and pET21/aapBrpt to express AapBrpt, as the protein vaccine.

Immunization

All C57BL/6J mice were *s.c.* immunized with either 25 μg DNA aapBrpt, 5 μg mRNA aapBrpt, or 100μg protein AapBrpt. Nucleic acid vaccines (DNAs and mRNAs) were delivered with or without *in vivo* JetPEI (Polyplus); protein vaccines were co-administrated with Freund's adjuvant. Ova albumen in DNA, mRNA or Protein forms were used as a negative control in each vaccine study.

Timeline



References

1. Otto M. 2009. *Staphylococcus epidermidis*--the "accidental" pathogen. Nat. Rev. Microbiol. 7:555–67.
2. Conrady DG, *et al*. 2013. Structural basis for Zn2+-dependent intercellular adhesion in staphylococcal biofilms. Proc. Natl. Acad. Sci. U. S. A. 110:E202–11.
3. Sun D, *et al.* 2005. Inhibition of Biofilm Formation by Monoclonal Antibodies against *Staphylococcus epidermidis* RP62A Accumulation- Associated Protein. Clin. Diagn. Lab. Immunol. 12:93–100.

Results

Significant AAP-specific IFNγ responses were induced in DNA- and mRNA-aapBrpt immunized mice. Both DNA vaccine **(Fig. 1)** and mRNA vaccine (**Fig. 2)** induced a significant Aap-specific IFNγ response in splenocytes. In addition, co-administration with *in vivo* JetPEI significantly enhanced this response. These results were consistent with the data obtained from flow cytometry analysis of Aap-activated CD4+IFNγ+ and CD8+ IFNγ+ splenocytes.

Fig. 1

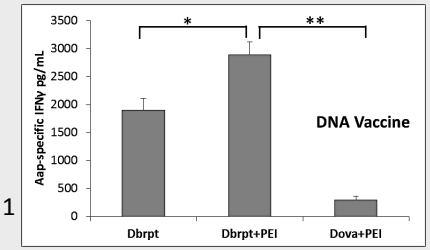
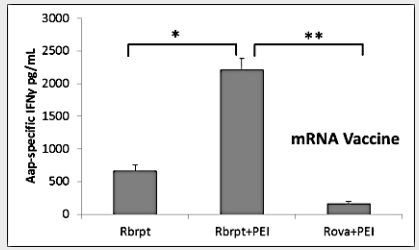


Fig. 2



Strong anti-*SE* antibody responses were developed in protein AapBrpt-immunized mice. Mice immunized with the AapBrpt protein vaccine developed a dramatically higher anti-*S. epidermidis* IgG antibody response compared to other groups of mice (**Fig. 3**).

Fig. 3

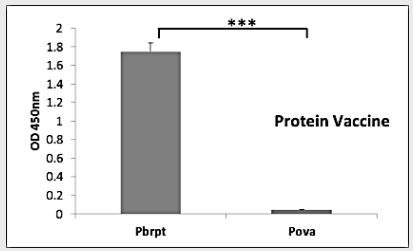
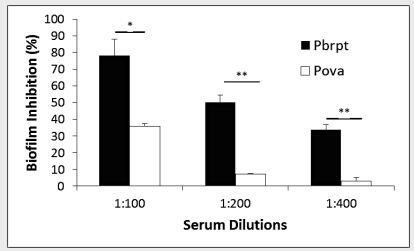


Fig. 4



Antisera induced by protein vaccine AapBrpt inhibited *S. epidermidis* RP62A biofilm formation *in vitro*. Biofilm inhibition assays further indicated that the high levels of antibodies induced by protein vaccine AapBrpt could inhibit *S. epidermidis* RP62A biofilm formation in a dose-dependent pattern (**Fig.4**).

Conclusions

- Our study validated the immunogenicity of three forms of *S. epidermidis* AapBrpt vaccines in mice.
- Our study demonstrated that while DNA/mRNA vaccines stimulated antigen-specific cellular immune responses, the protein vaccine developed stronger antibody responses against *S. epidermidis* biofilm formation.