Development of a non-invasion intranasal vaccine for *Klebsiella pneumoniae* urinary tract infection

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Background: Predicting which individuals will develop *Klebsiella pneumoniae* infections is challenging, making vaccine efficacy studies in large healthy populations difficult. Therefore, establishing a clinically relevant and feasible proof-of-concept model is essential. Given the high prevalence of *K. pneumoniae* in urinary tract infections (UTIs), particularly recurrent infections, this study aims to evaluate an OmpK36-based vaccine in an appropriate experimental model.

Methods: An intranasal and subcutaneous immunization model was employed to assess vaccine efficacy. Subcutaneous immunization with OmpK36, with or without adjuvant, was used to evaluate systemic immune responses. For intranasal delivery, OmpK36 was combined with the PELC adjuvant to enhance mucosal penetration and antigen uptake. Immune responses were assessed by measuring OmpK36-specific IgG in serum and IgA levels in serum and vaginal washes. Protective efficacy was further evaluated using a *K. pneumoniae* challenge in mice.

Results: Compared with control mice, subcutaneous immunization with OmpK36 significantly increased serum IgG levels and protection, indicating the induction of systemic immunity. Intranasal immunization with the PELC-OmpK36 formulation significantly enhanced IgA antibody titers in both serum and vaginal washes, suggesting effective mucosal immune activation. Upon *K. pneumoniae* challenge, non-immunized mice developed vaginal necrosis and inflammation, whereas mice immunized with PELC-OmpK36 showed no significant necrosis or severe inflammation.

Conclusions: Intranasal immunization with the PELC-OmpK36 formulation effectively induces both systemic and mucosal immune responses and provides protective immunity against *K. pneumoniae*-associated UTIs. This approach represents a promising non-invasive vaccination strategy for preventing recurrent infections.

Fig. 1 Protocol of immunization

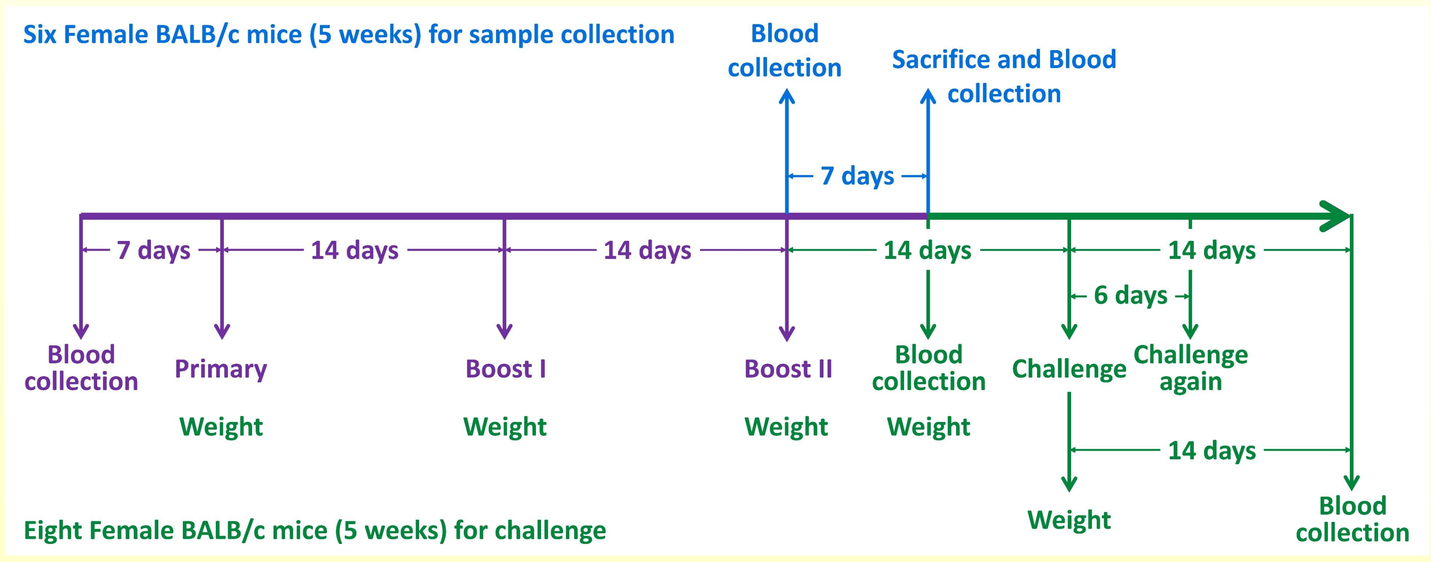
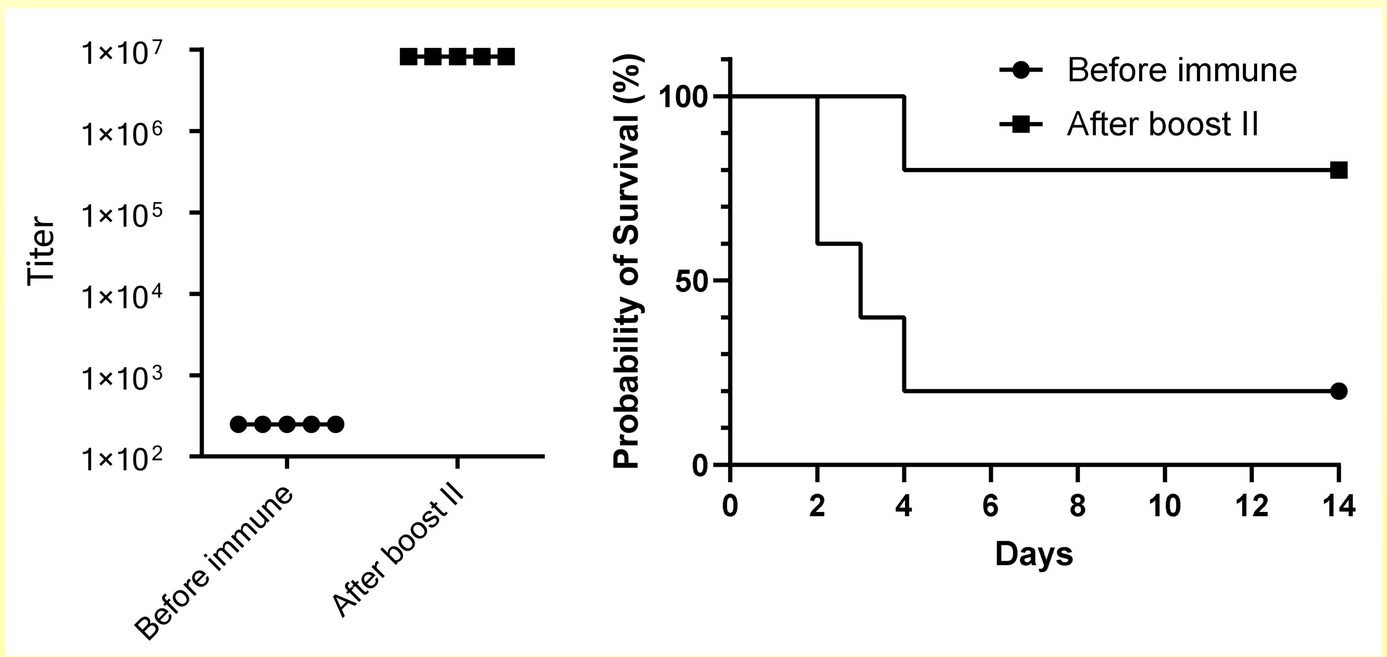


Table 1. Materials and dosage for immunization

Intranasal	Subcutaneous
10 % GPBS	rOmpK36
rOmpK36	
rOmpK36 + Flip	
rOmpK36 + PELC + CPG	

*PELC, Polymerized Emulsion with a Lipid and Carbomer.
*rOmpK36, 60 μg; PELC, 200 D.

Fig. 2. IgG titer and protection after subcutaneous OmpK36 immunization



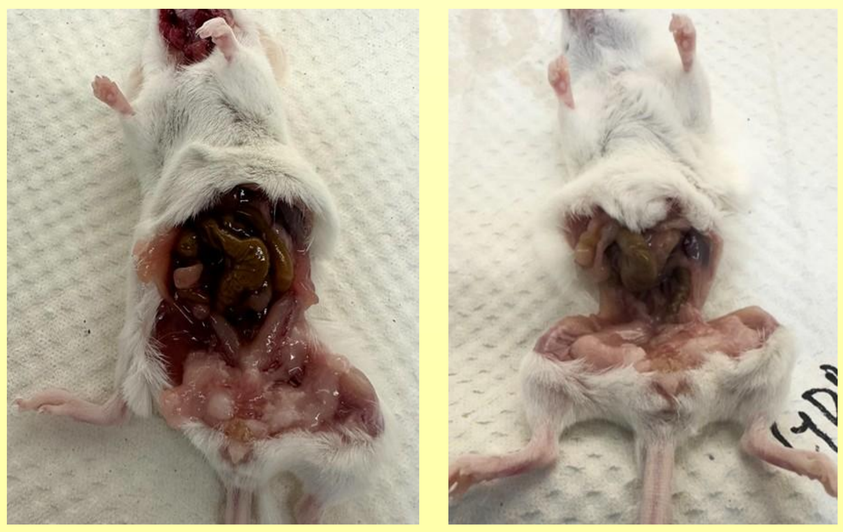


Fig. 3. IgG and IgA titers after intranasal OmpK36 immunization

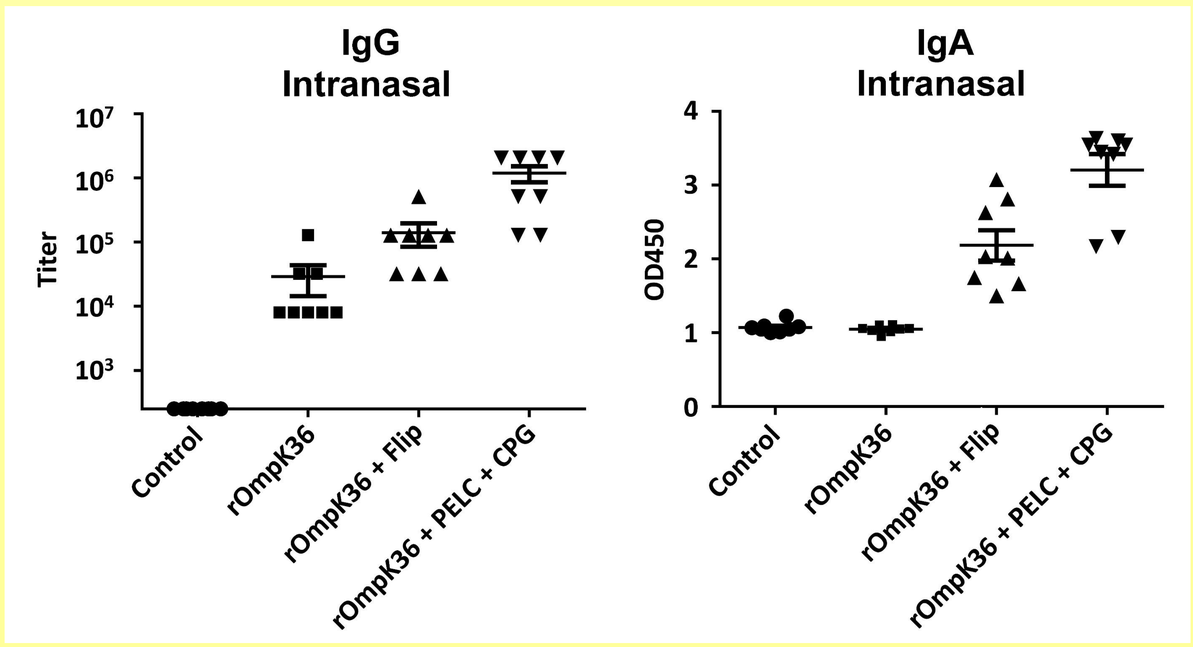


Fig. 4 Vaginal wash collection & pathology monitoring

Upon *K. pneumoniae* challenge, mice that were not immunized with OmpK36 exhibited a vaginal necrosis and inflammation, whereas those immunized with PELC-OmpK36 showed no substantial signs of necrosis or severe inflammation.