Poster

Fighting against Klebsiella pneumoniae: vaccine for prevention of antibiotic resistant infections

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ABSTRACT

The World Health Organization recognises antimicrobial resistance (AMR) as one of the top 10 threats to human health. The pathogens commonly implicated in AMR infections are known as ESKAPE pathogens, where we find Klebsiella pneumoniae. It is a highly antibiotic-resistant opportunistic Enterobacteriaceae leading to a variety of diseases due to urinary-tract-infections, nosocomial, pneumonia, intra-abdominal infections and surgical wound infections that can potentially cause bacteremia and septicemia. Furthermore, it is the leading cause of neonatal sepsis worldwide.

Klebsiella pneumoniae is causing 650.000 deaths worldwide associated with antibiotic-resistance, focusing in neonates and elderly population affected by chronic diseases. Therefore, the focus of vaccine development has moved to preventing infections that occur throughout all life stages by bacterial vaccines. One of these is K-vax. It is a modified inactivated whole cell bacterial vaccine, under development by Vaxdyn.

In K-Vax, the major antigens leading to protective immunity are four full-length outer-membrane proteins (OMPs) expressed in a LPS-null inactivated Acinetobacter baumannii carrier cell. For vaccine approval by regulatory authorities, probing the mechanism of action of the vaccine and showing the contribution of the key antigens is essential.

In this work, first, we have analyzed the data presented previously by similar marketed vaccines to defend the mechanism of action before engaging in human clinical trials. Then, we have gathered the immunogenicity data available for K-Vax to present a proposal for mechanism of action. In particular, we have demonstrated that vaccination of animal models, including mice and rabbits, leads to a specific humoral response against K. pneumoniae OMPs. The antisera carries functional antibodies able to opsonize and promote killing of K. pneumoniae cells by complement or human phagocytes. The mechanism of action is effective against several K. pneumoniae clinical strains, including hypervirulent strains, showing the high strain coverage of the vaccine K-Vax.

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