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Editorial ***Open Access***

Scope of Development of Vaccine against Antibiotic Resistant *Klebsiella pneumoniae*: Current Perspective

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Klebsiella pneumoniae is a Gram-negative bacterium which is frequently found in hospital environments. *Klebsiella pneumoniae* isolates have emerged as a major cause of global community-acquired infections. *Klebsiella pneumoniae* is an important pathogen associated with nosocomial infection and has developed increasing resistance to antibiotics such as extended-spectrum β-lactams and carbapenem[1]. *Klebsiella pneumoniae* can invade tissues and cause pneumonia, sepsis, meningitis, liver abscesses, urinary infections, among many other diseases of high significance[2]. Klebsiella pneumoniae can also cause infections in the community; in particular, the emergence of hypervirulent multidrug-resistant strains (MDR) in the community, such as extended spectrum beta-lactamase (ESBL)-producing and *Klebsiella pneumoniae* carbapenemase (KPC), is cause of great concern worldwide[3]. Hyperproduction of polysaccharide capsule is the main virulence mechanism reported in *Klebsiella pneumoniae*, contributing to immune evasion and antimicrobial resistance[4-6]. Capsule production is strictly associated with community-acquired pneumonia and community-acquired urinary infections by *Klebsiella pneumoniae*[5]. In addition, biofilm formation is an important virulence trait in Klebsiella pneumoniae; it can occur in both biotic and abiotic surfaces, as well as within host cells, generating intracellular bacterial communities (IBCs). Biofilms display increased resistance to antibiotics and host immune defenses[6] and promote a favorable environment for horizontal gene transmission[7].

High antibiotic resistance is a hallmark in *Klebsiella pneumoniae* infections. In addition to intrinsic resistance to antibiotics, *Klebsiella pneumoniae* exhibits high levels of horizontal resistance transmission, mainly by conjugative plasmids, which allow the spread of resistance to other microorganisms, of clinical importance such as *Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter cloacae* and *Escherichia coli* members of the ESKAPE group[8]. Plasmid-associated carbapenemases, including KPC, NDM, IMP, VIM, and OXA-48 enzymes, are disseminated worldwide and cause high rates of morbidity and mortality, varying from 32% to 65% cases[9-11]. The combination of increased and widespread antibiotic resistance and the emergence of hypervirulent strains in community-acquired infections place *Klebsiella pneumoniae* as a pathogen of critical risk. According to a global report by the World Health Organization[12], the antimicrobial resistance of Klebsiella pneumoniae in severe healthcare-associated infections is around 50% worldwide. Despite the recent approval of new antimicrobial options to treat KPC-producing *Klebsiella pneumoniae* - especially ceftazidime-avibactam, a cephalosporin drug associated with a new beta-lactamase inhibitor avibactam-resistance associated with KPC-3 and porin mutations or multiple carbapenemases production has been reported[13-14]. Thus, there is an urgent need for effective strategies to prevent *Klebsiella pneumoniae* infections. Such formulations could prevent both nosocomial and community-acquired infections, especially those associated with hypervirulent strains. *Klebsiella pneumoniae* vaccines could target those at increased risk, including hospitalized patients, immunocompromised individuals, and newborns either directly or through maternal immunization. Vaccination is a promising approach to prevent *Klebsiella pneumoniae* infection; however, the high

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heterogeneity of strains is a limiting factor. The best antigenic target for an anti-Klebsiella vaccine should be expressed by all or most of strains[1].

Although serotypes K1 and K2 have been identified as the predominant capsular types associated with invasive infections, no *Klebsiella pneumoniae* vaccine is commercially available, probably due to immunogenicity loss in the traditional depolymerization method to obtain capsule polysaccharide (CPS) for the preparation of conjugated vaccine. In a study, it has successfully retained immunogenicity by using K1 (K1-ORF34) and K2 (K2-ORF16) CPS depolymerases that were identified from phages to cleave K1 and K2 CPSs into intact structural units of oligosaccharides with intact modifications[15]. Immunization experiments of mice showed both K1 and K2 CPS-conjugated vaccines induced anti-CPS antibodies with 128-fold and 64-fold increases of bactericidal activities, respectively, compare to mice without vaccinations[16].

The most frequently used animal model was BALB/c mice. Proteins, polysaccharides, and their combinations (conjugates) were the most common vaccine candidates used[17]. The amount of antigen, the route used for immunization, and the challenge strategy was varying in the studies and were chosen based on several factors such as the animal model, the type of antigen, and the schedule of immunization[18]. Almost all studies claimed that their vaccine was effective/protective, indicated by increasing survival rate, reducing organ bacterial load, and eliciting protective antibody and/or cytokine responses.

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