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EDITORIAL

The contribution of capsule polysaccharide genes to virulence of *Klebsiella pneumoniae*

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Klebsiella pneumoniae is a Gram-negative, non-motile bacterium that is found in the environment, including in soil and surface water. *K. pneumoniae* readily colonizes human mucosal surfaces, such as those found in the gastrointestinal tract and oropharynx. *K. pneumoniae* can spread from colonizing sites to other tissues, leading to urinary tract infections, pneumonia, and other infections in humans.[1] Recently, concerns have arisen due to the emergence and dissemination of hypervirulent (HV) or antibiotic resistant strains.[2,3] To date, several *K. pneumoniae* virulence factors have been identified: the capsule, lipopolysaccharide, siderophores, and fimbriae (also known as pili).[1] Of these, the capsule, which is synthesized by gene products from the capsular polysaccharide synthesis (*cps*) locus, is the most thoroughly studied virulence factor for *K. pneumoniae*. In the bacterium, the capsule confers resistance against the bactericidal activity of antimicrobial peptides, complement, and phagocytes.[1] In addition, the capsule averts fulminant activation of the immune response.[4] Acapsular *K. pneumoniae* strains are markedly less virulent than isogenic encapsulated strains in mouse models,[5,6] and the strains that produce a capsule conferring a hypermucoviscous phenotype become HV.[7] Over 70 capsular serotypes have been reported for *K. pneumoniae*.[8] Among these, strains with the K1 and K2 capsular serotypes, which mainly cause liver abscess and belong to particular clones,[9,10] are known to be hypermucoviscous or HV.[7,11] In addition to K1 and K2, other serotypes have been described as HV, including K5, K16, K20, K54, and K57.[2] Although it is known that certain serotypes are more closely associated with human colonization or infection, the particular factors conferring their increased virulence are currently unclear.

In this issue of *Virulence*, Lin et al.[12] describe the contribution of genes located in the highly conserved region of the *cps* locus to the virulence of *K. pneumoniae*. In this study, Lin et al. identified a serotype K20 strain, which was isolated from a patient with a liver abscess, with high lethality in mice. The K20 strain belonged to ST268 based on multi-locus sequence typing analysis. Although the strain carried chromosomal and plasmid regulators of mucoid phenotype, c-*rmpA*, p-*rmpA*, and p-*rmpA2*, and several virulence determinants including aerobactin (*iucA*), yersiniabactin (*irp2*), salmochelin (*iroB*), enterobactin (*entB*), and iron-uptake system (*kfu*), it did not show a hypermucoviscous phenotype. The authors deleted 6 conserved genes (*galF, acidPPC, wzi, wza, wzb*, and *wzc*) from the *cps* locus of the K20 strain, and generated recombinants by complementation of the deleted mutants with genes from the K20 or K1 strains. They then characterized these mutations' effects on the bacterial virulence with respect to neutrophil phagocytosis, serum resistance, serum agglutination, and 50% lethal dose (LD_{50}) in mice.

Lin et al. determined that the 6 homologous genes from the *cps* locus could be categorized based on their effects on virulence.[12] While deletion of *galF* and *acidPPC* genes, which are driven by the P1 promoter,[13] had limited effect on virulence, the deletion of genes driven by the P2 promoter (*wzi, wza, wzb*, and *wzc*) exhibited moderate to high effects on virulence. The deletion mutants of the latter genes, which are responsible for surface assembly, CPS polymerization, and CPS production, also showed high susceptibility to neutrophilic phagocytosis and to serum. Thus, it appears that the homologous genes' influence on virulence differs according to their associated promoter or role in CPS biosynthesis. In contrast, creation of the *cps* gene recombinant mutants for the K1 or K20 strains did not impart consistent results. Recombinant mutants with the

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acidPPC gene from the K1 strain restored the virulence of the wild-type K20 strain in regards to serum killing, phagocytosis, and lethality in mice. However, mutants with *wzi, wza, wzb*, and *wzc* from the K1 strain exhibited inconsistent results in lethality, phagocytosis, and serum killing. For example, the recombinant with *wzi* of the K1 strain restored phagocytosis, but not serum killing and lethality, while the *wza* recombinant improved phagocytosis and serum resistance, but not lethality. Based on these observations, the authors conclude that the homologous genes for capsule biosynthesis in different serotypes of *K. pneumoniae* do not function in the same manner after gene switching.

This study by Lin et al. is significant for its characterization of the various effects that can be attributed to the homologous genes from different *K. pneumoniae* serotypes.[12] However, the study was limited in that it was based on a single strain of each serotype, and thus the relevance of this study's results in regards to other *K. pneumoniae* strains and serotypes must be explored. In addition, many studies indicate an association between *K. pneumoniae* serotypes and their severity of infection,[10,14,15] and between production of CPS and antibiotic resistance.[16] Further studies, including serotype switching, are warranted in order to more fully understand the effects of the K antigen or serotype on virulence and other features.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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