POSTER ABSTRACTS

259. IgG mAbs against *Klebsiella pneumoniae* K1-CPS as a possible new therapeutic approach

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Background. *Klebsiella pneumoniae* (*Kp*) infections with hypervirulent (hvKp) serotypes are common in Asia and emerging in the US. Although these strains are usually sensitive to antibiotics they are highly invasive and can cause life-threatening infections including liver abscesses, pneumonia, meningitis and endophtalmitis in otherwise healthy patients. Also of concern is that ESBL and carbapenem resistance has already been noted in these strains in Asia. Most of these hvKp strains produce a hyperviscous capsular polysaccharide (CPS), which type as a K1 (50-80%) or K2 (20%) serotype. The goal was to generate monoclonal antibodies (mAb) against the K1 CPS that can be used as adjunctive therapy.

Methods. BALB/c mice were immunized with K1 CPS-conjugate to Protective Antigen of *Bacillus anthracis*. Spleen cells of mice with high IgG titers were fused to myeloma cells and hybridomes were isolated. Growth, agglutination, human serum resistance and mouse macrophage and human neutrophils phagocytosis assays were carried out with mAbs. Animal experiments were performed after intraperitoneal (i.p.) and intratracheal infections.

Results. CPS-PA conjugate successfully increased the IgG response in immunized BALB/c mice. Six distinct K1 specific IgG mAbs were isolated. Among them 4C5 (IgG1) and 19A10 (IgG3) were selected for further studies. Both mAbs were able to bind and agglutinate different clinical K1 strains. Both mAbs reduced *Kp* viability after 2h of co-incubation with the bacteria. Mabs significantly reduced the K1-*Kp* resistance to human serum. Both mAbs where opsonophagocytic 4C5 increased 100-fold phagocytosis of *Kp* by J744-macrophage cell line and also significantly increased phagocytosis of *Kp* by human neutrophils. 4C5 enhanced survival of mice injected with K1-*Kp* strains i.p. and i.t. and also decreased the bacterial cfu in liver, spleen and lung, respectively.

Conclusion. K1-CPS conjugation to PA was successfully employed to generate IgG response in mice. Both mAbs showed opsono-phagocytic characteristics and 4C5 also protected mice from 2 types of K1 infections. These results encourage efforts to develop these mAbs further for therapeutic use in humans, where they could be of great use especially if drug resistance continues to emerge in these hypervirulent K1 strains.

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