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Siderophore Receptor Protein from Klebsiella pneumoniae as a Promising Immunogen for Serotype-Independent Therapeutic Lead Development

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Abstract : Klebsiella pneumoniae causes a wide range of infections, including urinary tract infections, sepsis, bacteremia, pneumonia, and liver abscesses. The emergence of multi-drug resistance in this bacterium led to a major setback for clinical management. WHO also endorsed a need for finding alternative therapy to antibiotics for the treatment of these infections. Development of vaccines and passive antibody therapy has been proven as a potent alternative to antibiotics in the case of MDR, XDR, and PDR Klebsiella infections. Siderophore receptors have been demonstrated to be overexpressed for the internalization of iron siderophore complexes during infections in most Gram-negative bacteria. For the present study, immune response to siderophore receptors to establish this protein as a potential immunogen for the development of therapeutic leads was explored. Clinical strains of Klebsiella pneumoniae were grown in iron-deficient conditions, and the iron-regulated outer membrane proteins were extracted and characterized through mass spectrometry for specific identification. The gene for identified protein was cloned in pET- 28a vector and expressed in E. coli. The native protein and the recombinant protein were isolated and purified and used as antigens for the generation of immune response in BALB/c mice. The native protein of Klebsiella pneumoniae grown in iron-deficient conditions was identified as FepA (Ferrienterobactin receptor) and other siderophore receptors. This 80 kDa protein generated an immune response in BALB/c mice. The antiserum from mice after subsequent booster doses was collected and showed binding with FepA protein in western blot and phagocytic uptake of the K. pneumoniae in the presence antiserum from immunized mice also observed from the animal studies after bacterial challenge post immunisation in mice have shown bacterial clearance. The antiserum from mice showed binding and clearance of the Klebsiella pneumoniae bacteria in vitro and in vivo. These antigens used for generating an active immune response in mice can further be used for therapeutic monoclonal antibody development against Klebsiella pneumoniae infections.

Keywords : antiserum, FepA, Klebsiella pneumoniae, multi drug resistance, siderophore receptor
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