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Design and production of conjugate vaccines against S. Paratyphi A using an o-linked glycosylation system *in vivo*

Hengliang Wang[1], **Jun Wu**[1] and **Ming Zeng**[2]
[1]Beijing Institute of Biotechnology, China
[2]National Institutes for Food and Drug Control, China

Enteric fever, mainly caused by *Salmonella enterica* serovar Paratyphi A, remains a common and serious infectious disease worldwide. As yet, there are no licensed vaccines against S. Paratyphi A. Biosynthesis of conjugate vaccines has become a promising approach against bacterial infection. However, the popular biosynthetic strategy using N-linked glycosylation systems does not recognize the specialized O-polysaccharide structure of S. Paratyphi A. Here, we describe an O-linked glycosylation approach, the only currently available glycosylation system suitable for an S. Paratyphi A conjugate vaccine. We successfully generated a recombinant S. Paratyphi A strain with a longer O-polysaccharide chain and transformed the O-linked glycosylation system into the strain. Thus, we avoided the need for construction of an O-polysaccharide expression vector. *In vivo* assays indicated that this conjugate vaccine could evoke IgG1 antibody to O-antigen of S. Paratyphi A strain CMCC 50973 and elicit bactericidal activity against S. Paratyphi A strain CMCC 50973 and five other epidemic strains. Furthermore, we replaced the peptides after the glycosylation site (Ser) with an antigenic peptide (P2). The results showed that the anti-lipopolysaccharide antibody titer, bactericidal activity of serum and protective effect during animal challenge could be improved, indicating a potential strategy for further vaccine design. Our system provides an easier and more economical method for the production of S. Paratyphi A conjugate vaccines. Modification of the glycosylation site sequon provides a potential approach for the development of next-generation precise conjugate vaccines.

Biography

Hengliang Wang has his expertise in research on pathogenic mechanism and gene-engineering vaccines of bacterial pathogens. He and his collaborators developed a novel synthetic biology strategy to produce bio conjugate vaccines using an O-linked protein glycosylation system. This system was proved to function in many gram-negative pathogens.

wanghl@bmi.ac.cn

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