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Multi-epitope fusion antigen (MEFA), novel technology for structural vaccinology

Weiping Zhang, **Rahul Nandre** and **Qiangde Duan**
Kansas State University, USA

Statement of the Problem: Vaccine development often encounters challenge of virulence heterogeneity. Enterotoxigenic *Escherichia coli* (ETEC) produce immunologically heterogeneous adhesins to attach to host receptors and two distinct enterotoxins to disrupt fluid homeostasis in small intestinal epithelial cells. ETEC bacteria are a leading cause of children's diarrhea and travelers' diarrhea. As an ETEC bacterium expressing one type of adhesins and either toxin can cause diarrhea, an effective vaccine must induce protective antibodies against most, if not all, of these adhesins and both toxins. However, conventional approaches are unsuccessful in developing a vaccine to induce broad anti-adhesin and antitoxin antibodies against ETEC diarrhea.

Methods & Materials: Aided with computational biology and structural biology, we developed a new structural vaccinology technology called MEFA, multiepitope fusion antigen. By *in vitro* predicting immunodominant B-cell epitopes from multiple virulence factors, we selected one virulence protein as the backbone and had its surface-exposed but less antigenic epitopes substituted with the most antigenic epitopes from each of the targeting virulence factors for a single immunogen. Applying this MEFA technology, we constructed two MEFAs to include antigenic elements from 7 or 9 ETEC heterogeneous adhesins, examined MEFA immunogenicity in mouse immunization, and assessed protection of MEFA-induced antibodies against ETEC bacterial adherence.

Findings: Two ETEC MEFAs, CFA MEFA and adhesin tip MEFA were constructed. The CFA MEFA carries epitopes from the major subunits of 7 most important ETEC adhesins (Fig 1), and the adhesin tip MEFA consists of epitopes from the tip subunits of 9 most prevalent adhesins. Mice immunized with either MEFA developed strong immune responses to each representing adhesin. Moreover, induced antibodies inhibited adherence from these adhesins.

Conclusion & Significance: This MEFA technology shows potential for developing broadly protective multivalent vaccines against ETEC diarrhea, and likely against other diseases caused by heterogeneous strains or pathogens.

Biography

Weiping Zhang is a Full Professor in the Diagnostic Medicine/Pathobiology department at Kansas State University. His research mainly focuses on enterotoxigenic *Escherichia coli* (ETEC) pathogenesis in diarrheal disease and vaccine development against ETEC associated diarrhea. His laboratory has applied the toxoid and toxoid fusion strategies and demonstrated for the first time that non-toxic STa molecules induced neutralizing anti-STa antibodies, and invented the MEFA technology to develop structure-based vaccines against heterogeneous ETEC adhesins.

wpzhang@vet.k-state.edu

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