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Identification of fully human monoclonal antibodies against the adhesin domain of colonizing factor antigen I of Escherichia coli

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Abstract:

Enterotoxigenic Escherichia coli (ETEC) causes significant diarrheal illness in infants in the developing world and travelers to endemic countries including military personnel. Infection of the host involves bacterial colonization of the small intestinal epithelium and toxin secretion leading to watery diarrhea. CFA/I is the most common colonizing factor antigens expressed on the surface of ETEC isolates. The CFA/I adhesin, CfaE, appears to be required for ETEC binding to human intestinal cells for colonization. Human antibodies against the binding domain of CfaE have potential to block colonization of ETEC and serve as a potent immunoprophylactic therapeutic for ETEC-related diarrhea.

In the current study, we generated a panel of fully human monoclonal antibodies (HuMabs) against the adhesin domain of CfaE using mice transgenic for human immunoglobulin genes and identified lead antibodies utilizing a series of in vitro assays. Mice were immunized with the N-terminal binding domain of CfaE fused to maltose binding protein. Over thirty unique IgG1 HuMabs were identified with binding activity to recombinant CfaE. These antibodies were tested for inhibition of hemagglutination of type A human erythrocytes by ETEC. Two lead HuMabs, 837-6 and 840-53, inhibited hemagglutination at low concentrations (<1 nM). Both antibodies also blocked the binding of ETEC with intestinal epithelial cells. Biacore analysis revealed an affinity of less than 2 nM with distinct epitopes of CfaE. Our analysis suggests that CfaE specific HuMabs 837-6 and 840-53, as the first isolated fully human monoclonal antibodies against CfaE adhesion domain, could potentially be used in combination with heat labile toxin neutralizing antibodies to prevent traveler’s diarrhea.