May 20th, 12:30 PM

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

Maja Sedic
University of Massachusetts Medical School

Danielle Wisheart
University of Massachusetts Medical School, danielle.wisheart@umassmed.edu

Monir Ejemel
University of Massachusetts Medical School, monir.ejemel@umassmed.edu

See next page for additional authors

Follow this and additional works at: http://escholarship.umassmed.edu/cts_retreat

Part of the Bacterial Infections and Mycoses Commons, Immunology of Infectious Disease Commons, and the Immunoprophylaxis and Therapy Commons

http://escholarship.umassmed.edu/cts_retreat/2016/posters/75

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Presenter Information
Maja Sedic, Danielle Wisheart, Monir Ejemel, Matteo Stoppato, Serena Giuntini, Eileen Barry, William D. Thomas, Mark S. Klempner, and Yan Wang

Keywords
Enterotoxigenic Escherichia coli, travelers, developing world, diarrheal illness

Creative Commons License
This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License.

This poster abstract is available at eScholarship@UMMS: http://escholarship.umassmed.edu/cts_retreat/2016/posters/75
Identification of fully human monoclonal antibodies against the adhesin domain of colonizing factor antigen I of *Escherichia coli*

Maja Sedic, PhD¹, Danielle Wisheart, BS¹, Monir Ejemel, BS¹, Matteo Stoppato, PhD¹, Serena Giuntini, PhD¹, Eileen M. Barry, PhD², William D. Thomas Jr., PhD¹, Mark S. Klempner, MD¹, Yang Wang, MD PhD¹*

¹ MassBiologics, University of Massachusetts Medical School, Boston, Massachusetts, USA
² University of Maryland Baltimore, Center for Vaccine Development, Baltimore, Maryland, USA

*Corresponding Author: Yang.Wang@umassmed.edu

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.