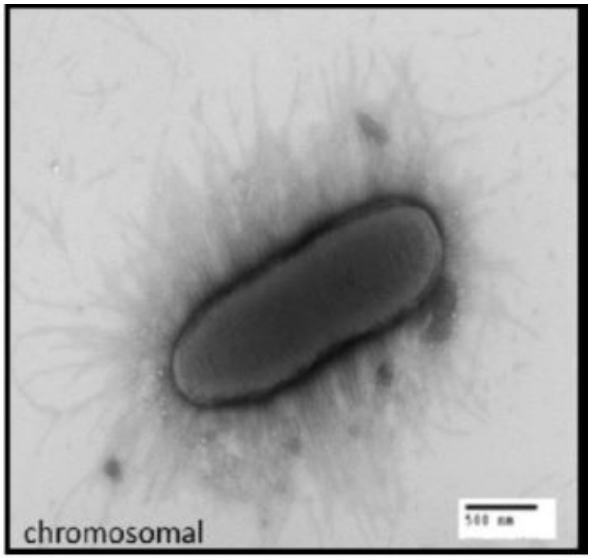
TECHNOLOGY

Optimized Shigella-ETEC Vaccine with Broad-Spectrum Protection

OVERVIEW

UMB's optimized *Shigella*-ETEC vaccine is designed to provide enhanced & essential protection against the clinically important species & serotypes of *Shigella* and Enterotoxigenic Escherichia coli (ETEC), the major causes of dehydrating diarrheal illness among children under 5 years old in low to middle-income countries, as well as leading causes of travelers' diarrhea. These pathogens are typically contracted from contaminated food or drinking water, and together caused ~ 20% of all diarrheal disease deaths (> 260,000) in 2016 (Kahlil et al. 2018 The Lancet). Both pathogens are also designated serious threats by the CDC due to increasing multidrug resistance leading to fewer options for therapeutic intervention. ***UMB's optimized multivalent vaccine strategy combines 5 to 6 strains of live attenuated Shigella, representing the prevalent species and serotypes found in clinical isolates, and with each Shigella strain engineered to express key ETEC antigens***. Engineered deletions in guaBA biosynthetic pathway genes and genes encoding enterotoxins have previously resulted in safe and effective *Shigella* and *Shigella*-ETEC candidate vaccines (DeLaine et al. 2016; & Kotloff et al. 2007 Hum Vaccin). ***Dr. Barry & collaborators have advanced the lead component of their multivalent vaccine "CVD 1208S-122" to a Phase 1 clinical trial***. CVD 1208S-122 is live, attenuated *S*. flexneri 2a expressing ETEC antigens CFA/I and LT (see Fig). ***Another advanced component of UMB's vaccine is plasmid-stabilized S. sonnei strain "CVD 1233-SP"*** *(expressing ETEC antigens),* ***which is proven protective against challenge in a guinea pig model*** *(Pilla et al. 2021).*

UMB's vaccine design is informed by our team's seasoned clinical vaccine development experience, and by global epidemiological data from the "Global Enteric Multicenter Study" (GEMS), a 2011 – 2014 consortium led by UMB's Center for Vaccine Development. The GEMS was the most comprehensive study of childhood diarrheal diseases ever conducted in developing country settings (> 22,500 children). Several *Shigella* serotypes were found to be of clinical significance, including the lesser-known *S*. flexneri 1b and 7a (Livio et al. 2014). ***Inclusion of these serotypes in our multivalent vaccine is predicted to expand coverage of all Shigella to ~90%***. The GEMS also revealed a previously under-recognized 'minor' fimbrial antigen from ETEC ("CS14") as significant in children with moderate-to-severe diarrhea. ***Inclusion of CS14 in our vaccine is predicted to expand the breadth of ETEC coverage from 64% to 84%*** (Vidal et al. 2019)



Transmission electron microscopy of CVD 1208S-122 following staining. CFA/I fimbriae emanating from the bacterium are readily visualized.

APPLICATIONS

A broad-spectrum *Shigella*-ETEC vaccine is expected to be a significant market opportunity, given the high unmet global need amid the current lack of a commercial vaccine, as well as the prevalent disease incidence among travelers. Another candidate *Shigella*-ETEC vaccine, composed of a single vector strain, published Phase 1 clinical results in 2022 (“ShigETEC”, Eveliqure). It’s anticipated that UMB’s broad-spectrum vaccine will provide significantly enhanced protection over other vaccines.

ADVANTAGES

- Rational design
- Broad-spectrum protection
- Clinical-stage development

STAGE OF DEVELOPMENT

A Phase 1 clinical trial (UMB-sponsored, with NIH funding) is enrolling patients (**NCT04634513**) to test the lead component of our multivalent *Shigella*-ETEC vaccine, “CVD 1208S-122. The other components of UMB’s multivalent vaccine have been fully characterized and two have been tested in a guinea pig model, with promising safety & immunogenicity.

LICENSING POTENTIAL

Available for licensing and collaborative R&D

CONTACT INFO

Office of Technology Transfer
620 W Lexington St., 4th Floor
Baltimore, MD 21201
Email: ott@umaryland.edu
Phone: (410) 706-2380

Additional Information

INSTITUTION

University of Maryland, Baltimore

PATENT STATUS

U.S. Patent # 11,471,520 (issued 2022)and Multiple patents pending (WO 2019/195437)

LICENSE STATUS

Available for partnering

CATEGORIES

- Vaccines

INVESTIGATOR(S)

Eileen M. Barry & Myron M. Levine

ATTACHMENTS

- Download UMB Market Summary (EB-2018-077; APR 2022).pdf

EXTERNAL RESOURCES

- Pilla et al. Pathogens 2021
- Vidal et al. PLoS Negl Trop Dis. 2019
- DeLaine et al. Pathog Dis. 2016
- Livio et al. Clin Infect Dis. 2014

EB-2018-077