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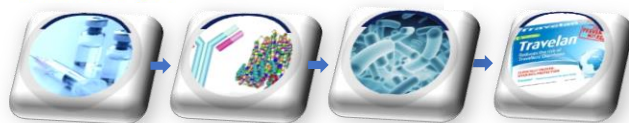
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The Problem:

- Infectious diarrhea is one of the most common illnesses reported by travelers and among deployed US troops in developing countries.
- Travelers' diarrhea (TD) is often acquired via ingestion of contaminated food and water. TD is predominantly bacterial, most common etiologic enterotoxigenic *E. coli* (ETEC), enteroaggregative *E. coli*, *Campylobacter*, *Shigella*, and *Salmonella* species.
- The morbidity associated with diarrheal illness can result in lost duty days, decreased performance and reduced operational readiness.

The Solution:

Immuron Technology Platform:



- **STEP 1** Development of Highly Specific Vaccines
- **STEP 2** Isolation of Hyperimmune antibody-rich bovine colostrum
- **STEP 3** Oral Antimicrobials without drawbacks of antibiotics
- **FINAL PRODUCT** Toxin Neutralization & Clearance of Targeted Gut Pathogens
- Travelan® is a hyperimmune bovine colostrum produced by immunization of cows during gestation with a vaccine derived from 13 ETEC strains known to cause TD.
- Travelan® is a pasteurized, lactose-reduced, low-fat, high-protein powder which contains over 80% proteins of which approximately 35% to 45% are antibodies.
- Travelan® is a listed medicine on the Australian Register for Therapeutic goods (TGA) indicated to reduce the risk of TD (AUST L 106709).
- Travelan® is marketed in Canada as a natural health product (NPN 80046016) indicated to reduce the risk of TD
- Travelan® is currently sold in the U.S. as a dietary supplement for digestive tract protection.

Travelan® is clinically proven to reduce the risk of Travelers' diarrhea by up to 90%:

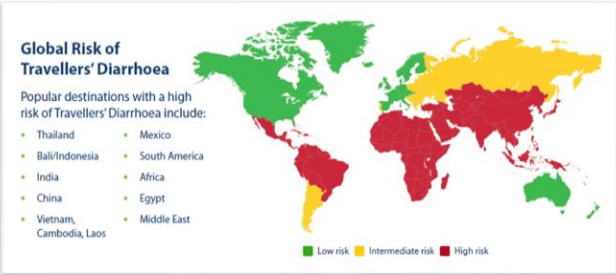
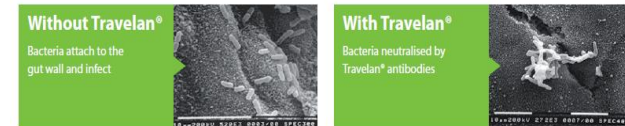
- Two separate randomized, double-blind placebo-controlled clinical trials involving 90 healthy volunteers investigated different Travelan® formulations to protect against diarrhea following oral challenge with ETEC (O78/H10407 strain).
- Results showed up to 90.9% protection against infection with ETEC (p<0.001)
- Travelan® reduced the symptoms of gastrointestinal symptoms such as abdominal cramps and stomach pain (p<0.05)



Otto W et al., *Scand. J. Gastroenterol.* (2011); 46 (7-8) 862-8.

Mode of Action:

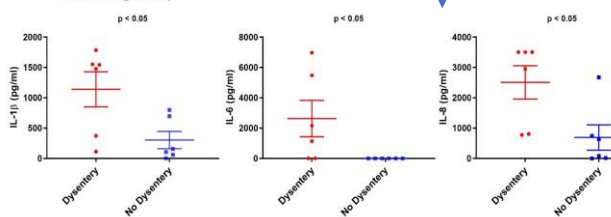
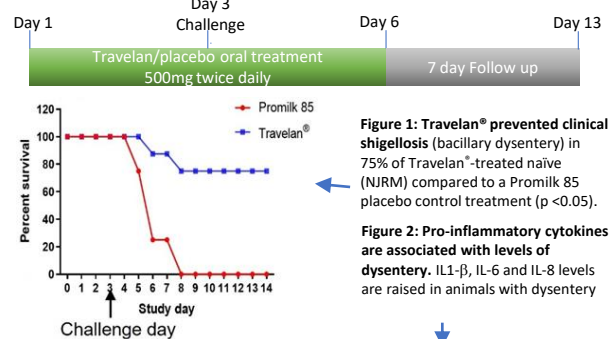
The antibodies in Travelan® bind to *E. coli* and other Travelers' diarrhea-causing bacteria in the gastrointestinal tract preventing them from attaching to the intestinal wall and thereby neutralizing their ability to cause diarrhea and its associated symptoms.



DuPont HL., 2005. *Nature Clinical Practice Gastroenterology & Hepatology* 2, 191-198

Therapeutic potential of Travelan® against Shigella infection:

Study design: 8 juvenile rhesus macaques (NCRM) received Travelan® and 4 received placebo. All animals were challenged with *Shigella flexneri* 2a



Travelan® is cross-reactive with other gram-negative bacteria:

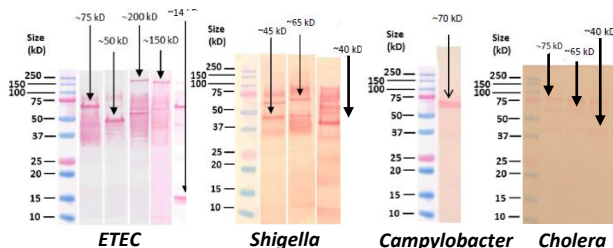
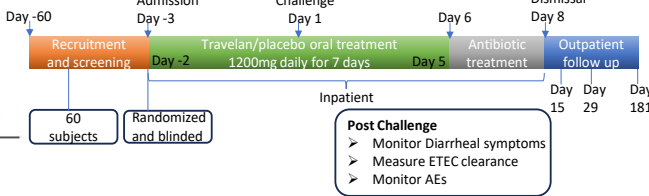


Figure 3: Whole cell lysates sourced from SE Asia probed with Travelan®. Example immunoblots from the field isolates for each species. Major immunoreactive bands are marked with an arrow. No immunoreactivity was observed for blots probed with skim milk.

Randomized double-blind phase 2 clinical study:

A controlled human infection model (CHIM) with a dosing schedule better suited to the military is in progress to assess the efficacy of Travelan® against moderate-to-severe diarrhea following challenge with ETEC strain H10407.



Summary:

- Travelan® is cross-reactive with ETEC strains not present in the bovine vaccine
- Travelan® demonstrated wide immunoreactivity with over 200 field isolates of gram-negative bacteria
- Travelan® was 75% effective in preventing shigellosis in a non-human primate model
- A phase 2 clinical study is currently in progress to evaluate dosing schedule more suited to the military
- Immuron is currently pursuing an FDA pathway in the U.S. to register Travelan® for prevention of Travelers' diarrhea in the U.S.

These findings provide implications for protection of the war fighter in the field and the potential for long-term protection and treatment for endemic populations in an outbreak of diarrheal-pathogens.

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