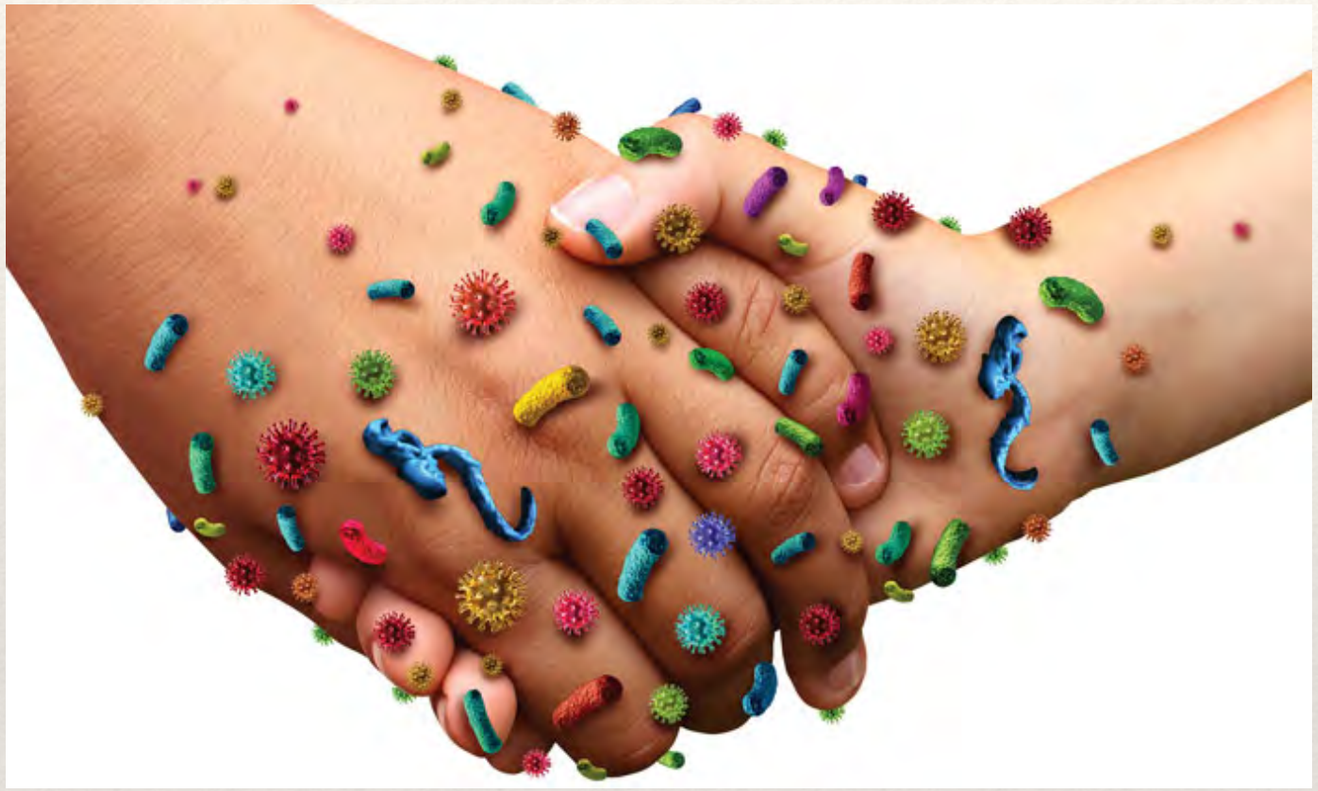
A Bacterial Protein as a Potential Therapeutic for *Clostridioides difficile* Infection



Prameet M. Sheth MSc. PhD. D(ABMM), F(CCM)
The Jay and Kendal Patry Clinical Chair in Genomics
Chief, Division of Microbiology
Kingston Health Sciences Centre

Associate Professor,
Gastrointestinal Disease Research Unit (GIDRU)
Department of Pathology and Molecular Medicine
Department of Biosciences and Molecular Sciences
Queen's University, Kingston - ON K7L 2V7

Hosted by Paul Webber
paul@webbertraining.com

Learning Objectives

- Understand the Pathophysiology of *Clostridioides difficile (C.diff)* infection.
- Examine the evidence for bacteria based therapies for *C. diff.*
- Summarize the discovery of a bacteria derived protein that protects mice from *C.diff* disease.

The Sheth Lab Group

Colleagues and Collaborators

Dr. Henry Wong
Dr. Calvin Sjaarda
Dr. Chris Lohans
Dr. Steven Smith

Technicians

Ms. Shu-Mei He
Hang Li

Undergraduate Students

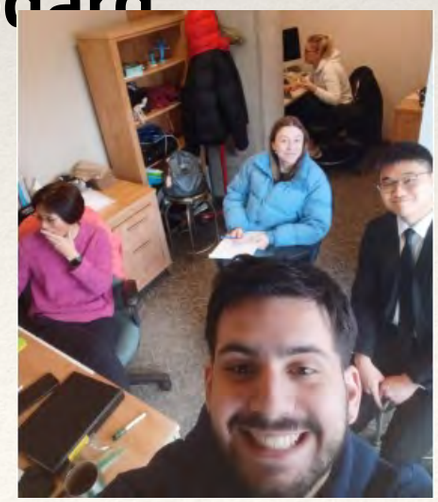
Nicole Major
Jad Tirani
Vivian Johanson-Bennet
Maja Jacobsen
Luka Parikh
Ava Woodard

Doctoral Students

Dr. Katya Douchant
Kyla Tozer
Hannah Wood

Masters Students

Jill Greenlaw
Victoria Mallett
Sarah Hopkins



Disclosures

- Serve on the scientific advisory board of a company developing Microbiome based Therapies called Tailored Therapeutics.

- Recipient of a US Patent for HtrA for use as a therapeutic for toxin producing bacteria.

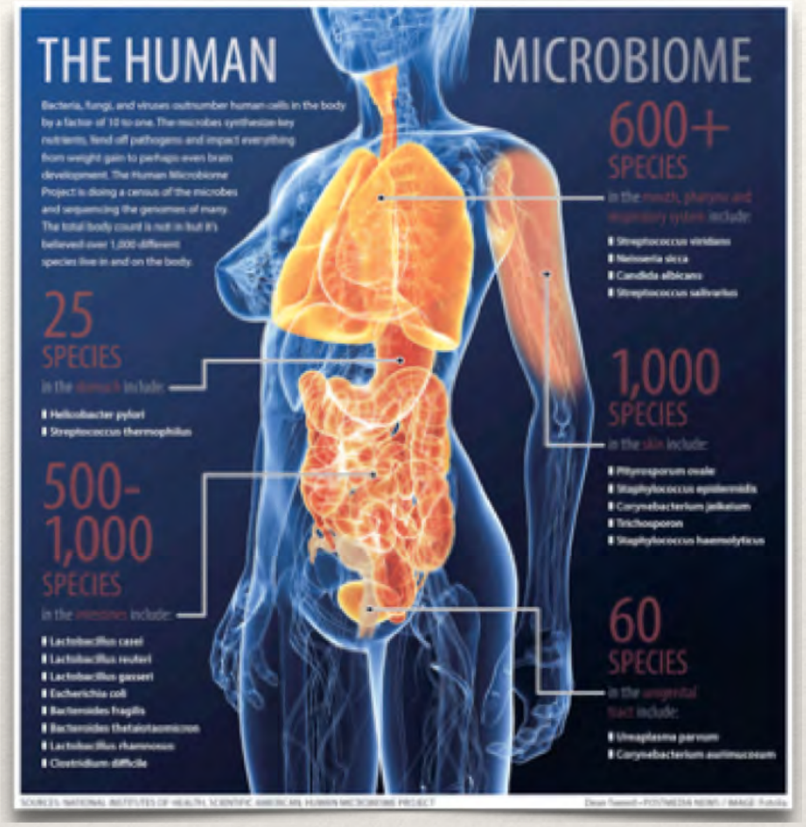
- Serve as the CEO for Monarch Informatics - a Health Informatics company in Ontario, Canada.

- Served as a consultant for GSK and BioMerieux inc.

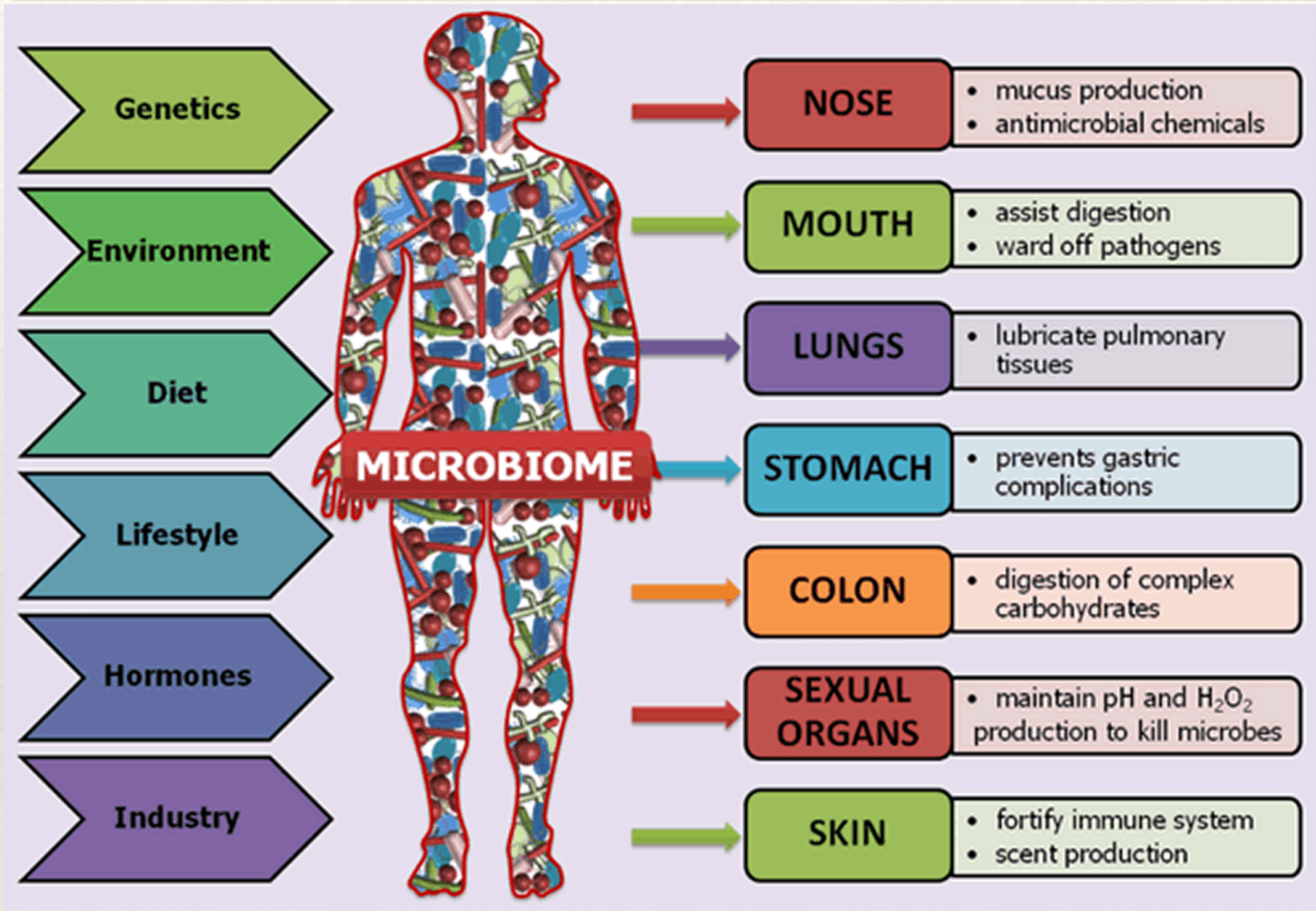
- Recipient of Research Grants from the CIHR, NSERC, The Gates Foundation, The NIH, The South Eastern Academic Medical Organization and The Weston Foundation.

The Human Microbiota

- The Human Body is home to trillions of bacteria.
- Over a 1000+ species of bacteria call our bodies home. They live in/on our bodies. 1000:1 proportion of anaerobes to aerobes.
- These organisms are referred to as “normal flora”.
- This represents a complete shift in the way we think about the interactions between us (human hosts) and the bacteria that inhabit us.
- Aggregate of all the species is called the microbiota, the collective genes of all the organisms is referred to as the microbiome.



A Fragile Relationship: Gut Microbes and the Host

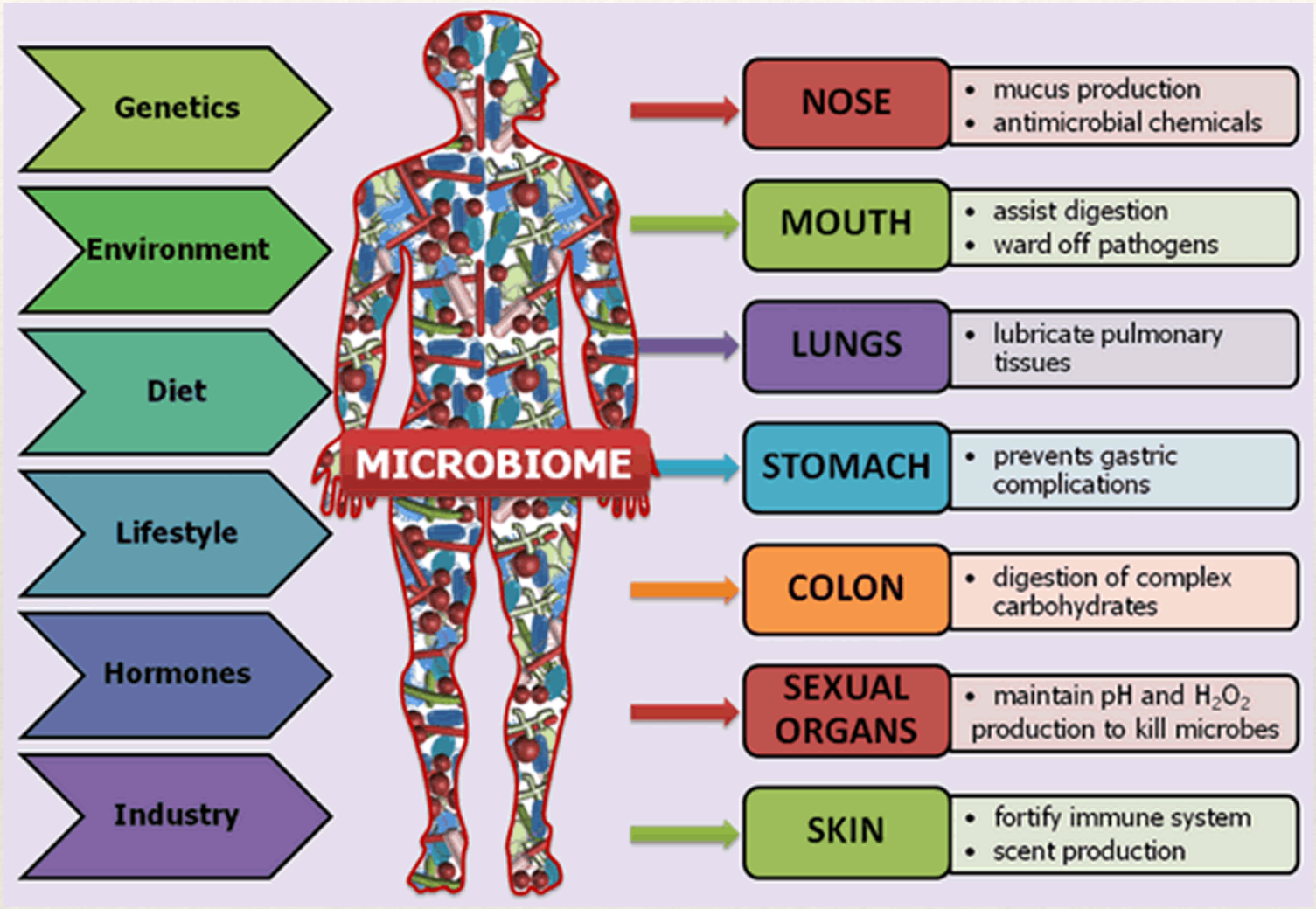


- A delicate balance of bacteria.

- The gut microbiota is stable, but is strongly influenced by age, diet, environment, xenobiotics that can result in dramatic changes in populations of the GI tract.

Tiffany et al, Gastroinstestinal and Liver Physiology 2019

A Fragile Relationship: Gut Microbes and the Host

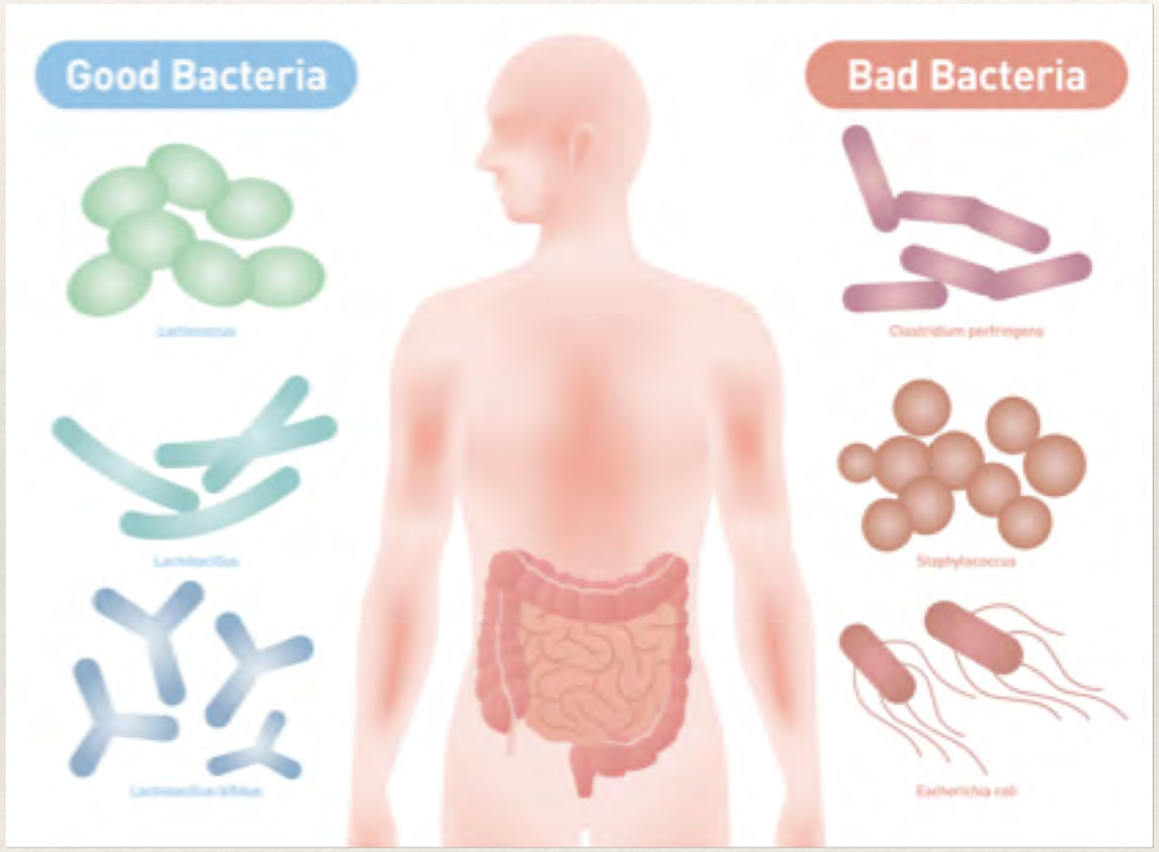


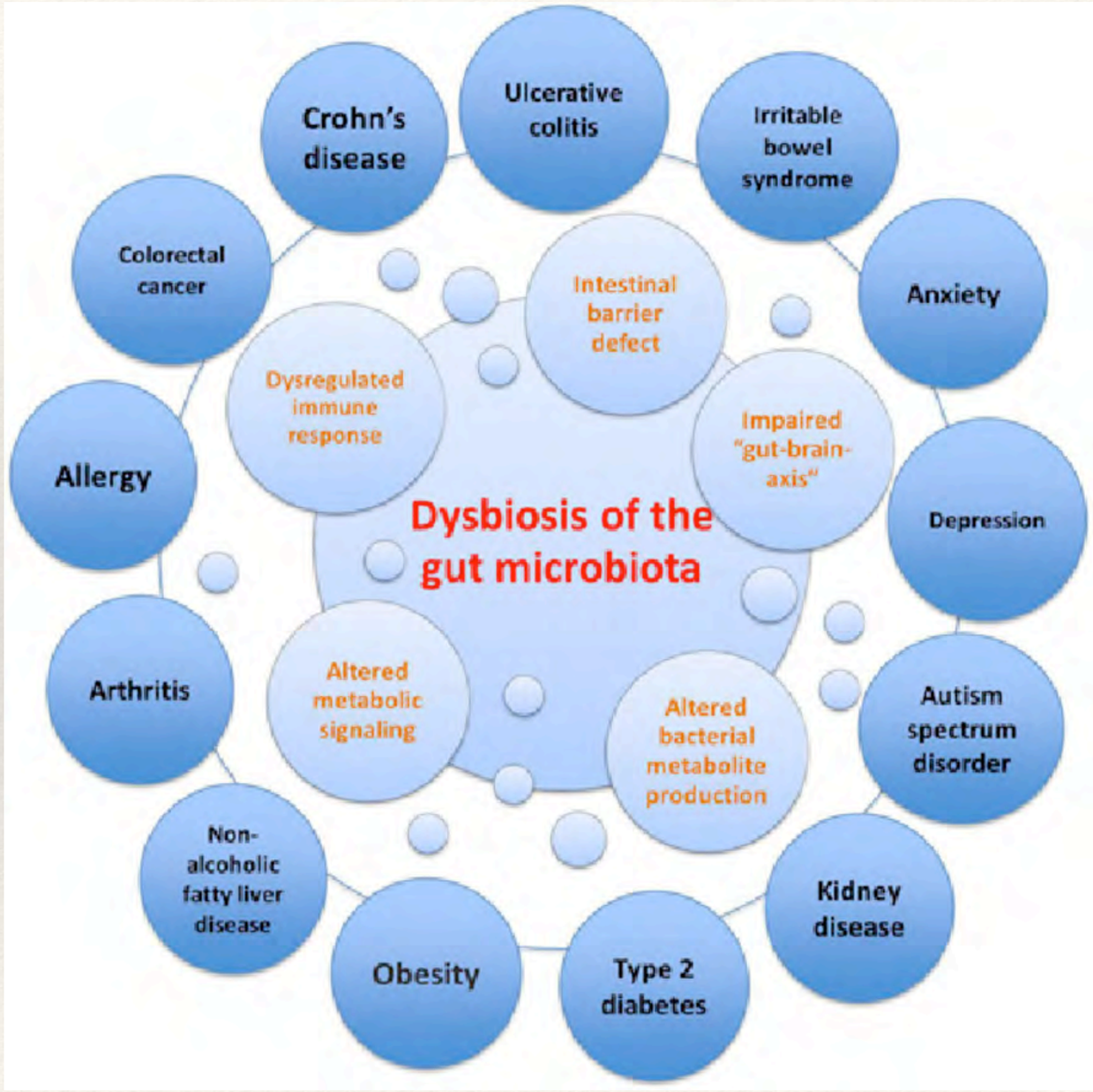
- A delicate balance of bacteria.

- The gut microbiota is stable, but is strongly influenced by age, diet, environment, xenobiotics that can result in dramatic changes in populations of the GI tract.

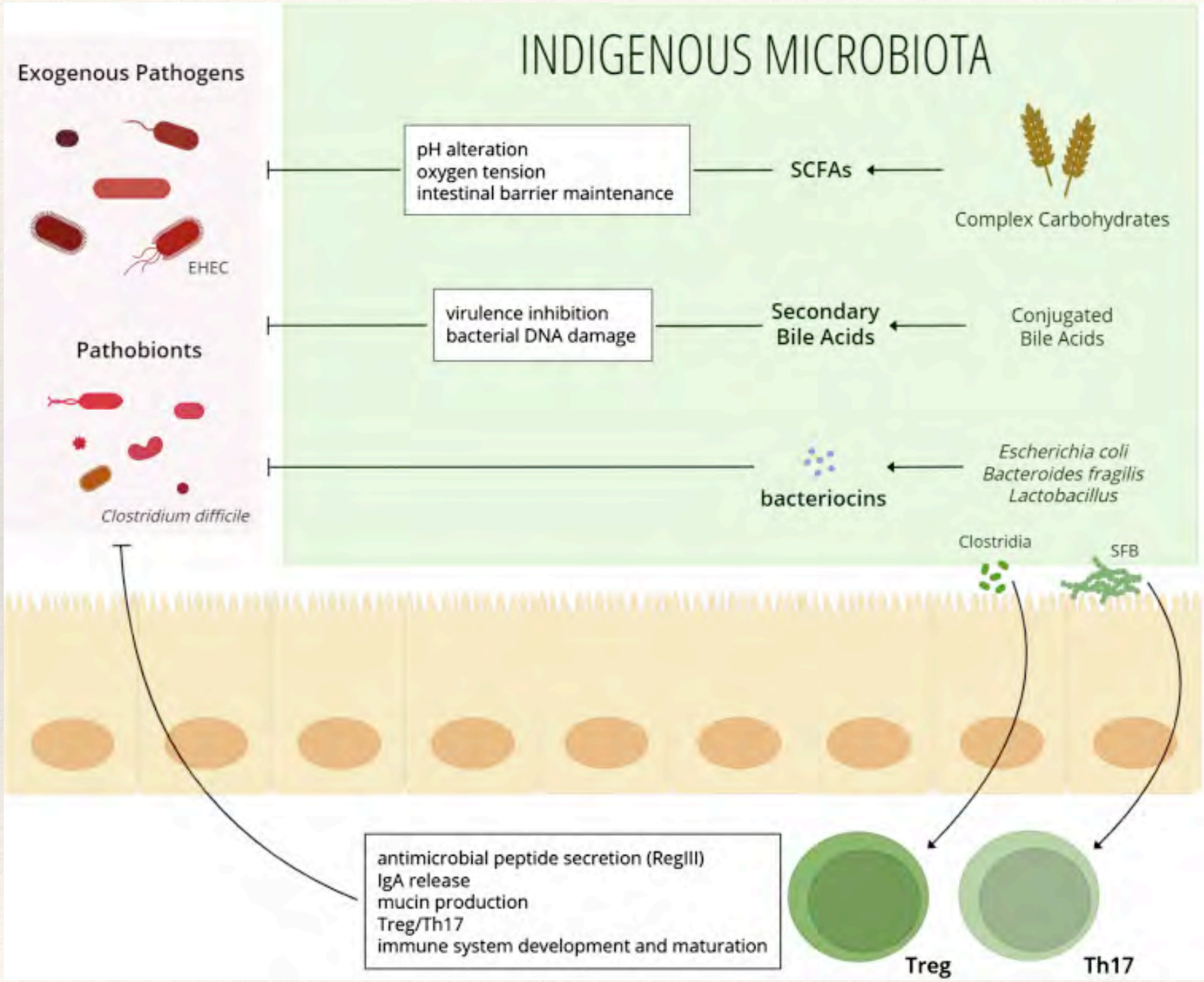
Tiffany et al, Gastroinstestinal and Liver Physiology 2019

A Fragile Relationship: Gut Microbes and the Host





Pathogen Resistance and the Microbiome

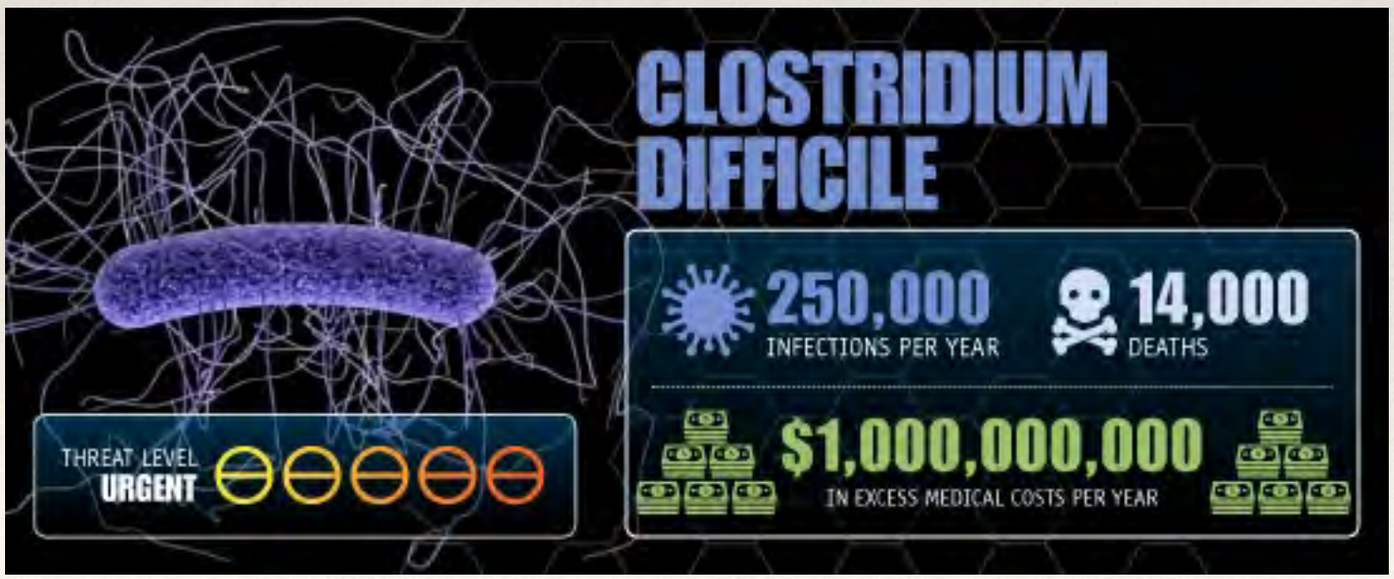


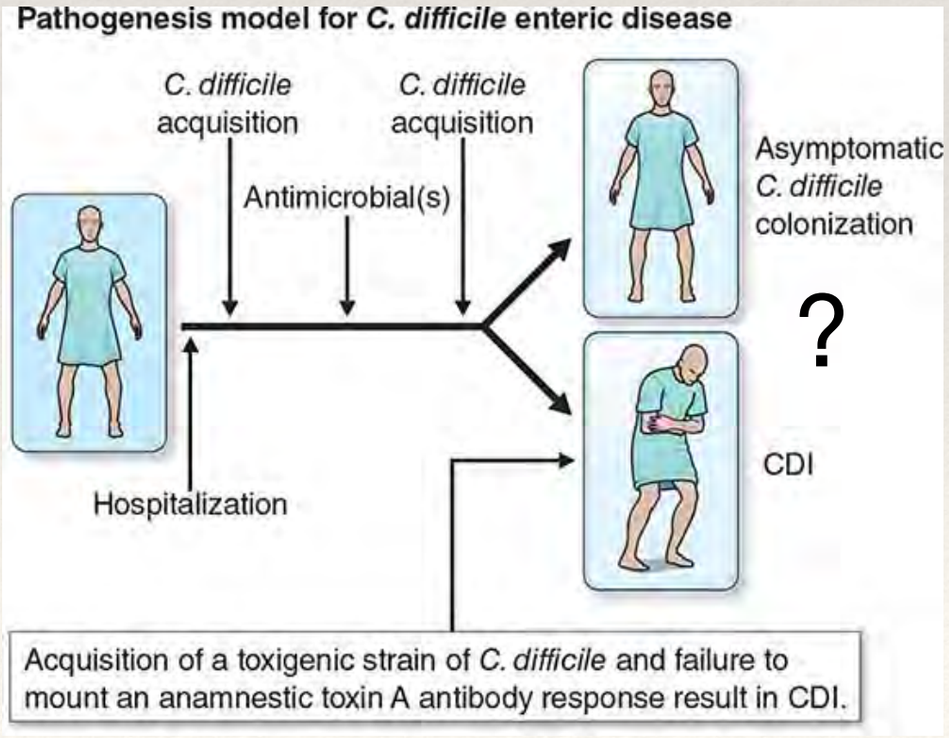
- One of the functions the microbiota performs is prevents the colonization of "pathogens".
- However, even after colonization the factors that result in clinical disease remain unclear.

Ignacio et al, 2019 in the book Microbiome and Metabolome in Diagnosis, Therapy, and other Strategic Applications

Clostridioides (formerly *Clostridium*) *difficile*

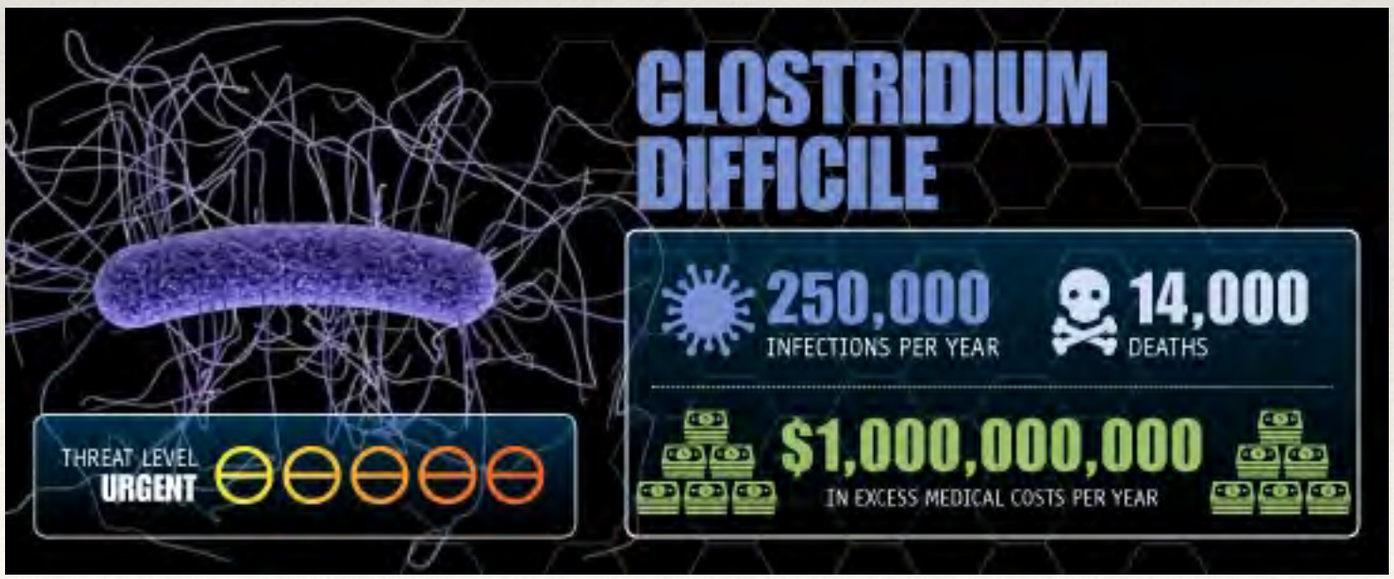
- *C. difficile* is the #1 cause of infectious diarrhea and infectious colitis in humans.
- An increase in the incidence, morbidity, and mortality of patients infected with *C. difficile* has been seen in recent decades
- The single largest risk factor for *C. difficile* disease is antibiotic use.

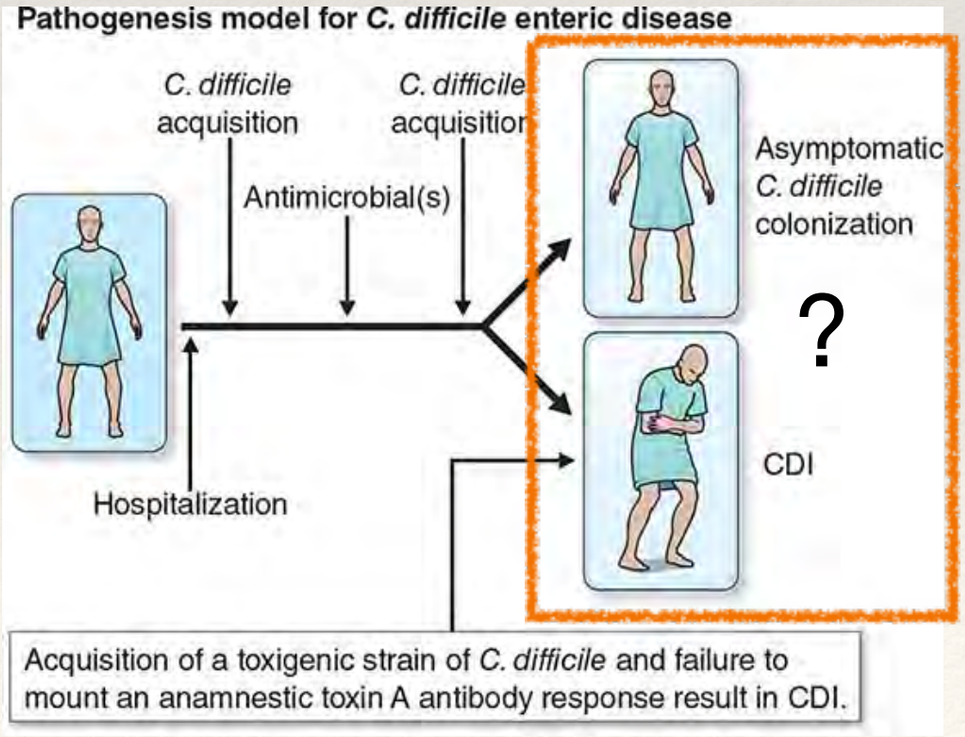




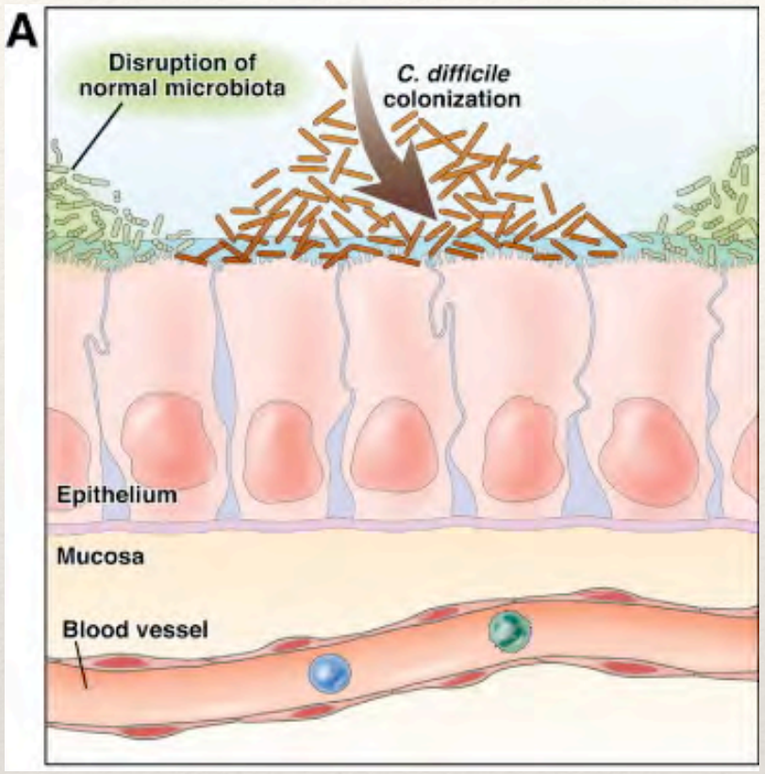
Clostridioides (formerly *Clostridium*) *difficile*

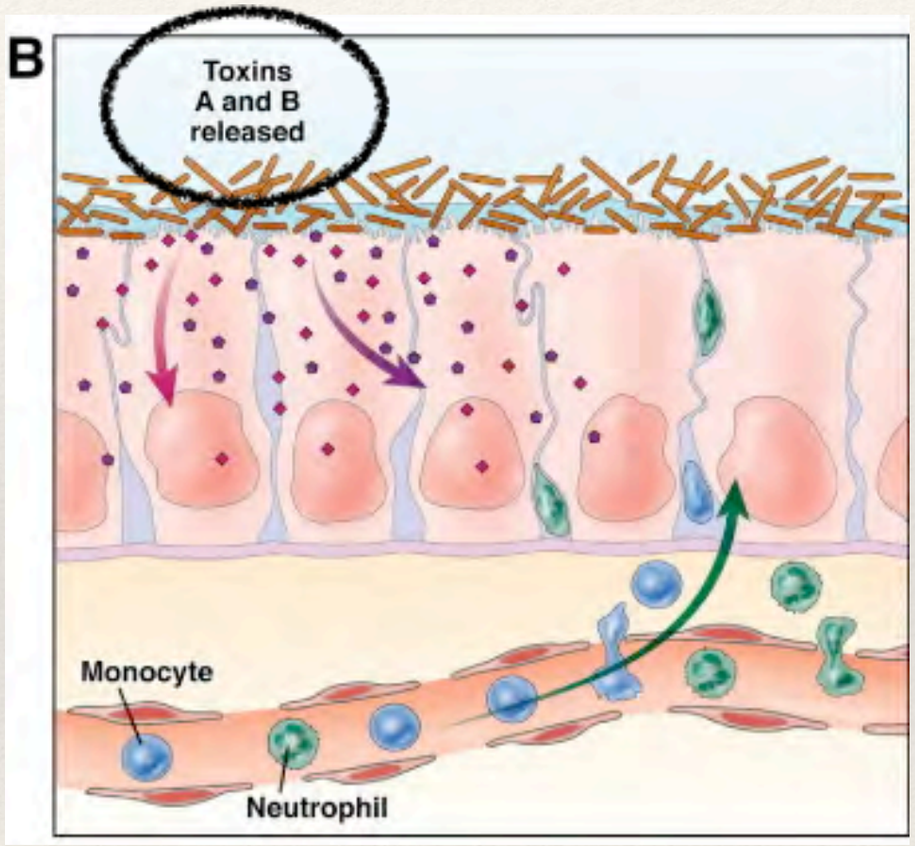
- *C. difficile* is the #1 cause of infectious diarrhea and infectious colitis in humans.
- An increase in the incidence, morbidity, and mortality of patients infected with *C. difficile* has been seen in recent decades
- The single largest risk factor for *C. difficile* disease is antibiotic use.





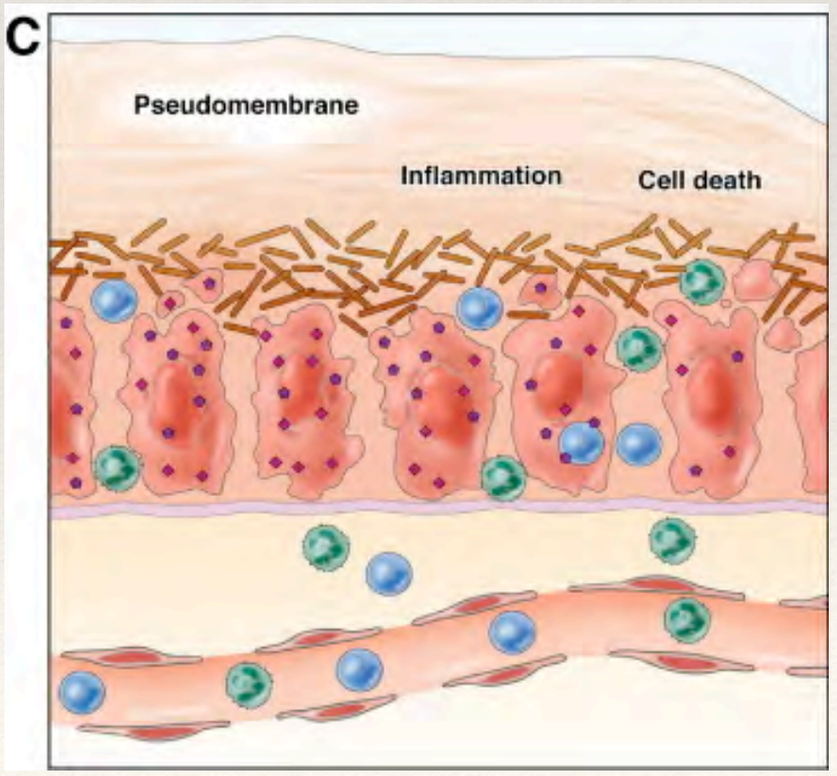
CD is a Toxin Mediated Disease.





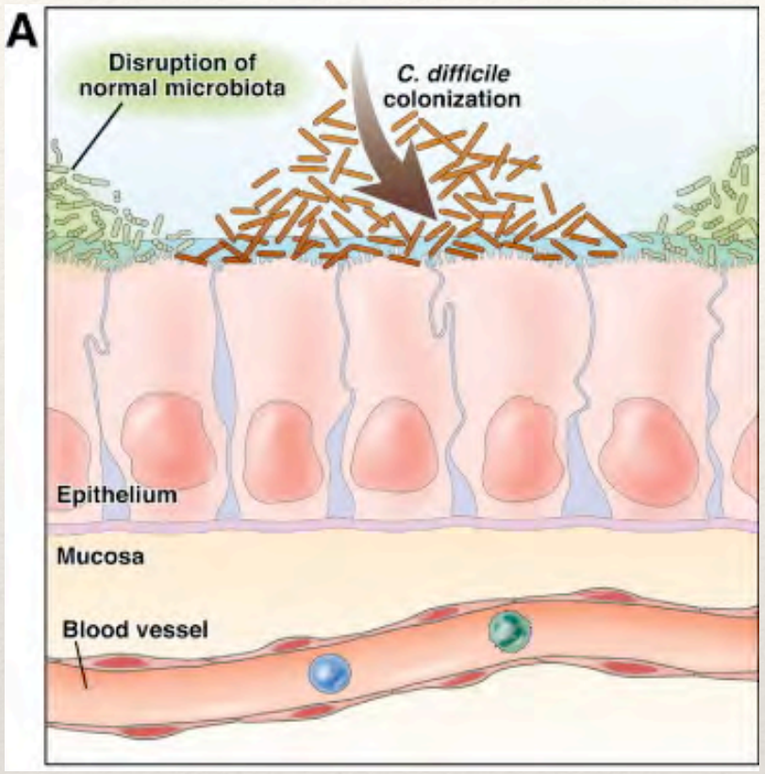
Toxin A - Enterotoxin
Toxin B - Cytotoxin

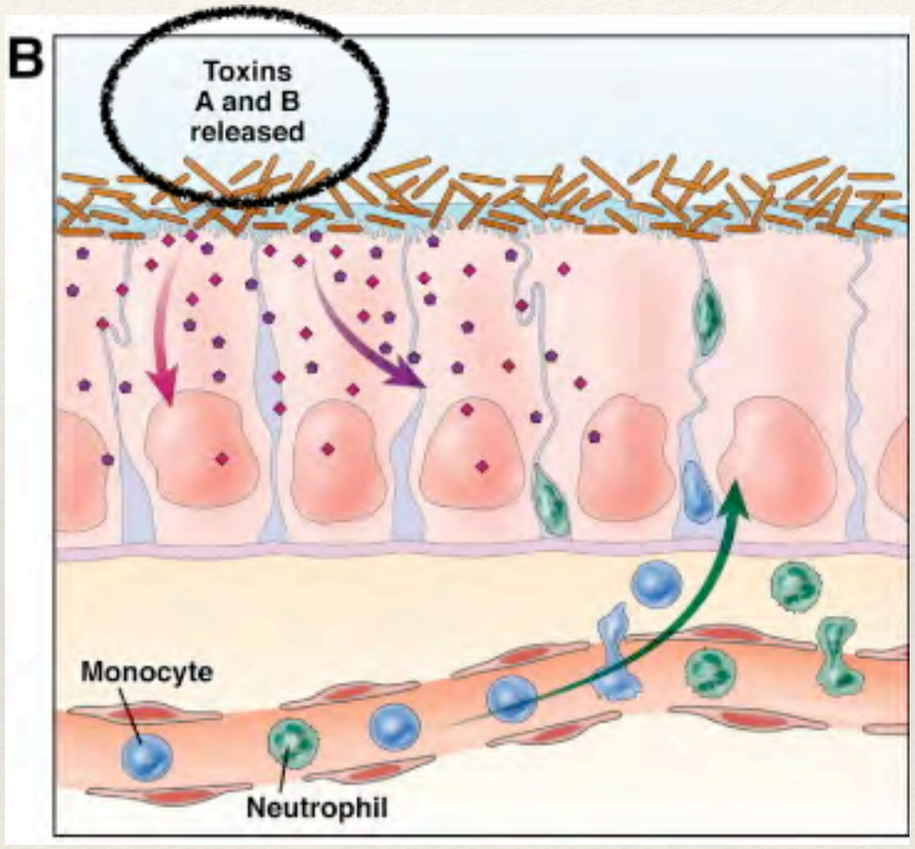
The toxins lead to cellular **cytoskeletal rearrangement** and **cell death**



McCollum et al, Clinical Gastroenterology and Hepatology 2012

CD is a Toxin Mediated Disease.

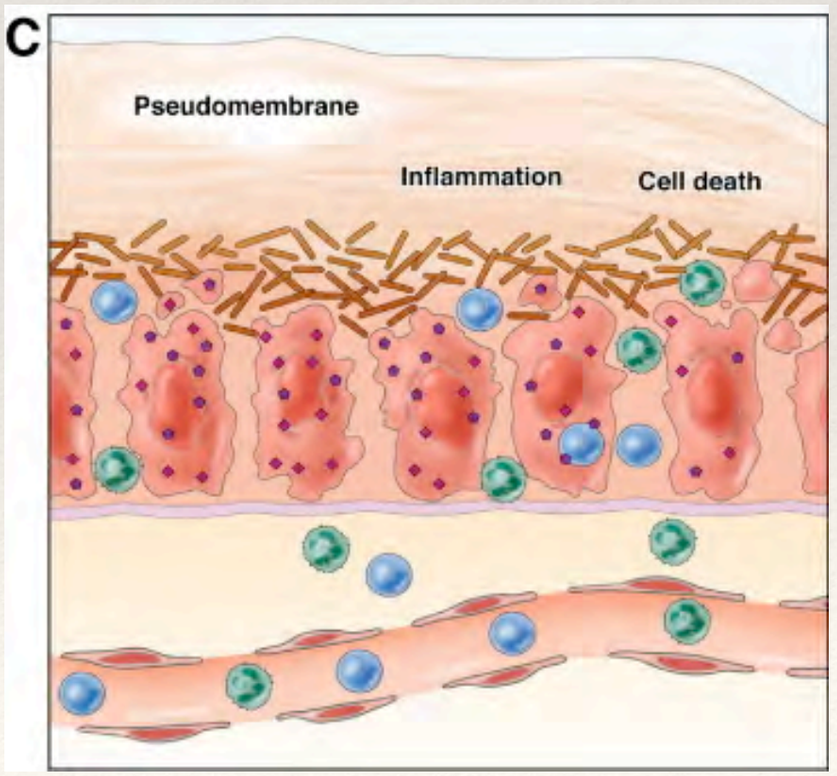




Toxin A - Enterotoxin
Toxin B - Cytotoxin

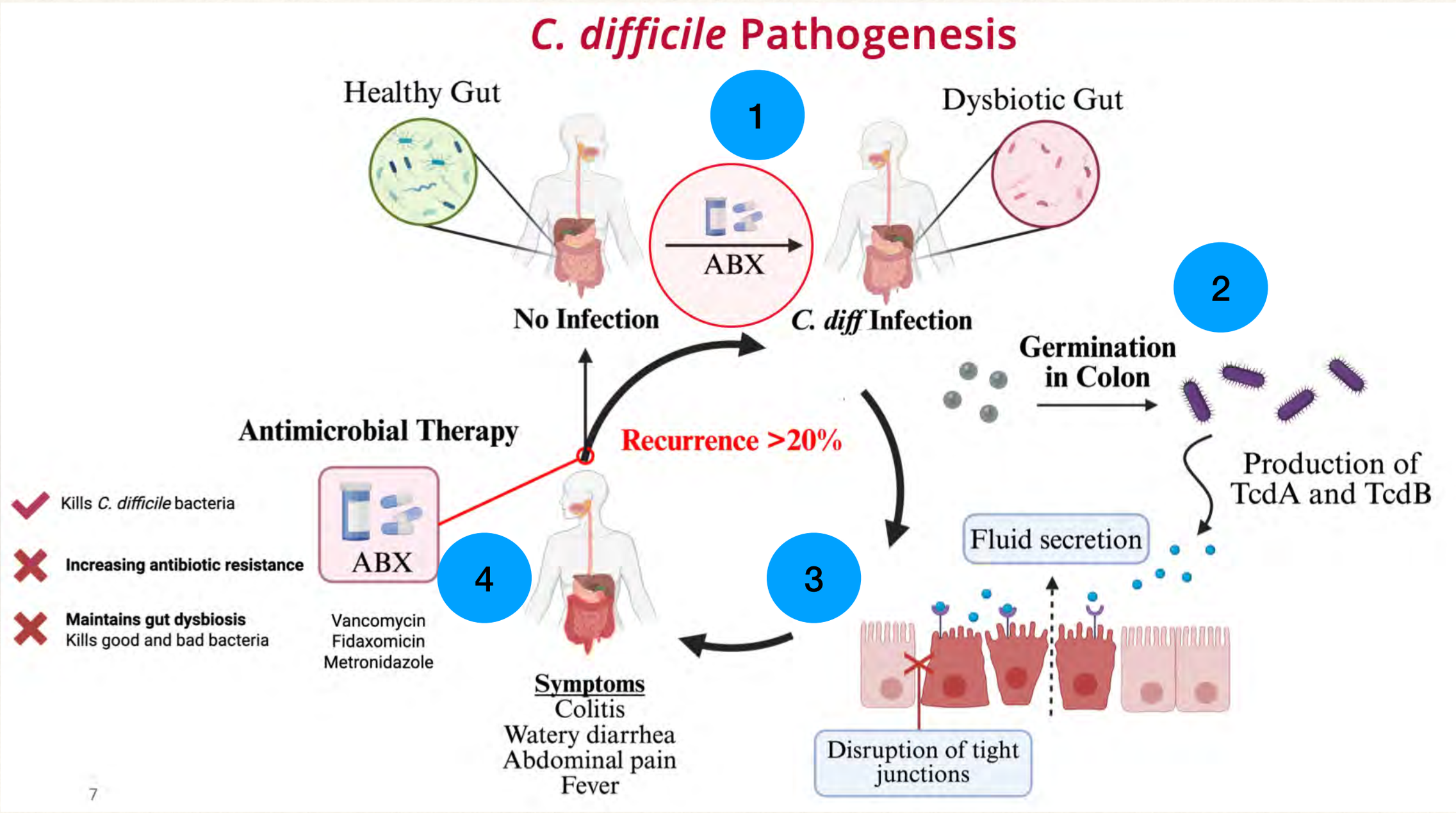
↓

The toxins lead to cellular **cytoskeletal rearrangement** and **cell death**

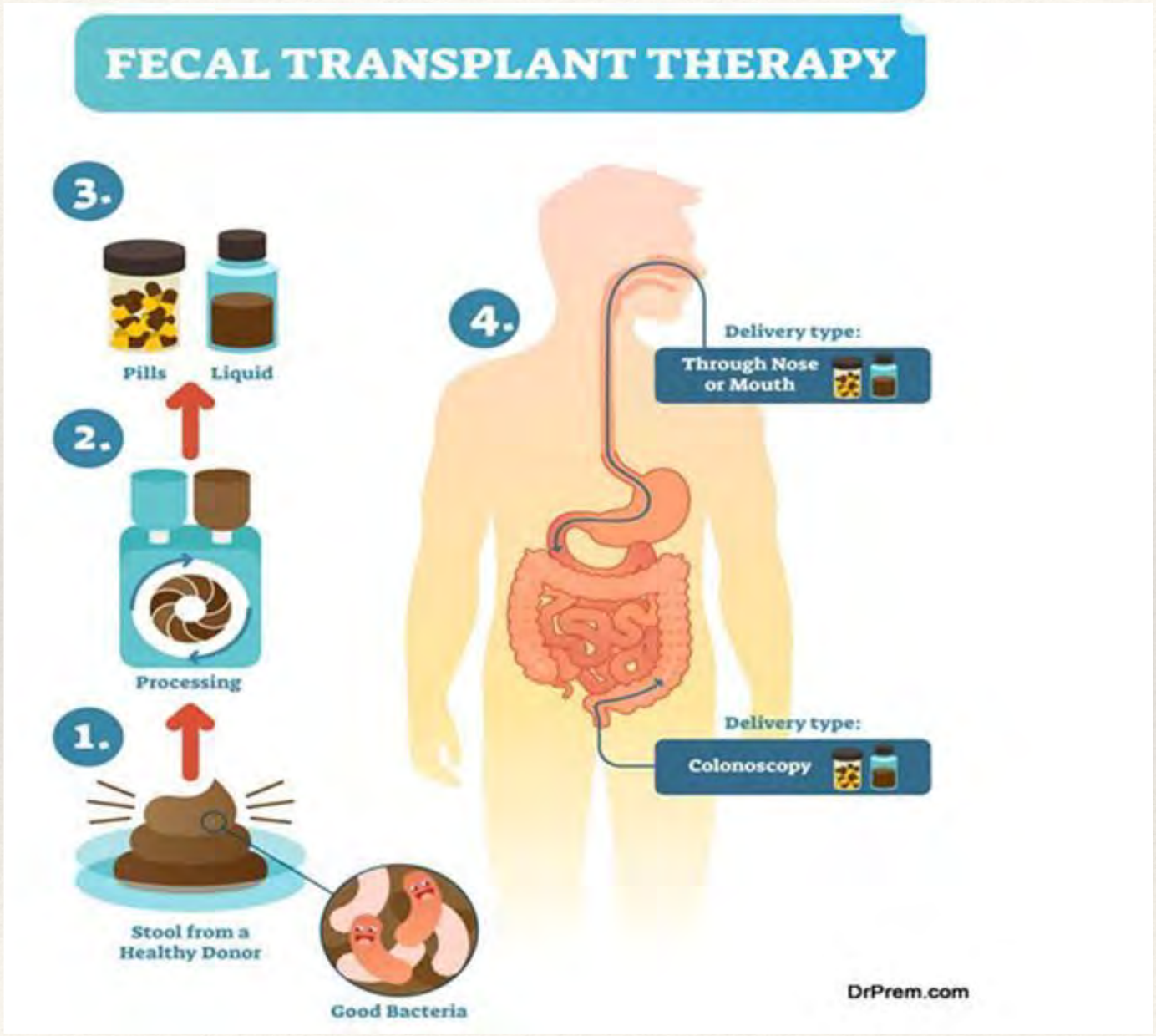


McCollum et al, Clinical Gastroenterology and Hepatology 2012

C. difficile Pathogenesis



Fecal Microbial Therapy (FMT).



- FMT's serve to "repopulate" the disturbed microbiota in C.diff patients.

Correcting the Microbiota with FMT's

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., et al.

January 31, 2013
N Engl J Med 2013; 368:407-415
DOI: 10.1056/NEJMoa1205037

32 References 1980 Citing Articles Letters 15 Comments

Abstract

BACKGROUND

Recurrent *Clostridium difficile* infection is difficult to treat, and failure rates for antibiotic therapy are high. We studied the effect of duodenal infusion of donor feces in patients with recurrent *C. difficile* infection.

METHODS

We randomly assigned patients to receive one of three therapies: an initial vancomycin regimen (500 mg orally four times per day for 4 days), followed by bowel lavage and subsequent infusion of a solution of donor feces through a nasoduodenal tube; a standard vancomycin regimen (500 mg orally four times per day for 14 days); or a standard vancomycin regimen with bowel lavage. The primary end point was the resolution of diarrhea associated with *C. difficile* infection without relapse after 10 weeks.

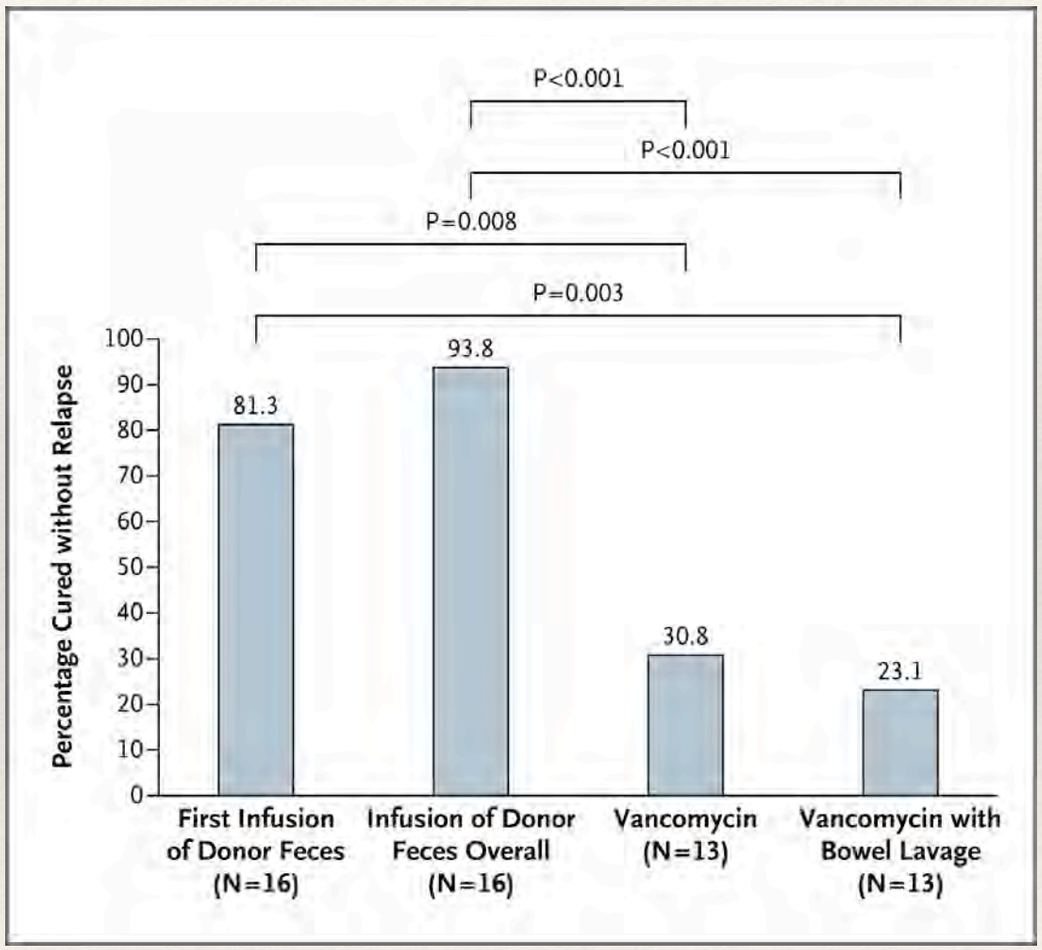
RESULTS

The study was stopped after an interim analysis. Of 16 patients in the infusion group, 13 (81%) had resolution of *C. difficile*–associated diarrhea after the first infusion. The 3 remaining patients received a second infusion with feces from a different donor, with resolution in 2 patients. Resolution of *C. difficile* infection occurred in 4 of 13 patients (31%) receiving vancomycin alone and in 3 of 13 patients (23%) receiving vancomycin

Related Articles

EDITORIAL JAN 31, 2013
Fecal Microbiota Transplantation — An O
Therapy Comes of Age
C.P. Kelly

CORRESPONDENCE MAY 30, 2013
Duodenal Infusion of Feces for Recurrent
Clostridium difficile



van Nood et al, NEJM 2013

Challenges with FMT : Donor Screening

Step 1

Inclusion criteria:

- Aged 25-60 years
- Be in good health and feeling well

In the past 3 months
- No use of antibiotics, antifungal or antiviral treatment.

In the past 6 months
- No high-risk behaviour
- No blood transfusions
- No acute bowel disease
- No travel in countries with high-risk of infectious diseases

Exclusion criteria:

- Any medical illnesses
- BMI < 18 kg/m² or > 28 kg/m²)
- Use of medication
- Allergic diseases
- Chronic diseases
- Gastrointestinal complaints*
- Depression**
- Previous gastrointestinal surgery (Except appendectomy)

Family history of
- Colorectal cancer, Inflammatory bowel diseases, or Celiac disease

Step 2

Blood screenings:

- Complete blood count
- C-reactive protein
- Electrolytes (potassium, sodium)
- Immunoglobulin G, A and M
- Pancreatic amylase
- Liver function (albumin, alanine aminotransferase, INR, bilirubin, alkaline phosphatase)

Serological parameters
- Cytomegalovirus (CMV)
- Epstein-Barr virus (EBV)
- Hepatitis B+C
- HIV
- Syphilis

Microbial screenings:

Enteropathogenic bacteria
- Enteropathogenic *E. coli*
- *Clostridium difficile*
- *Campylobacter jejuni*
- *Salmonella* and *Shigella* species
- *Yersinia Enterocolitica*

Virus
- Adenovirus
- Enterovirus
- Parechovirus

Multi-resistant bacteria
- ESBL-producing *Enterobacteriaceae*
- Carbapenem-resistant:
  - *Pseudomonas aeruginosa*
  - *Acinetobacter species*
  - *Enterobacteriaceae*
- Vancomycin-resistant *Enterococcus* species

Enteropathogenic parasites
- *Entamoeba dispar*
- *Entamoeba histolytica*
- *Cryptosporidium*
- *Giardia duodenalis*

Microscopy examination
- Worms, eggs and cysts of intestinal parasites

Also..We do not know HOW this works!!

Challenges with FMT's : Donor Screening

ORIGINAL RESEARCH

Challenges establishing a multi-purpose fecal microbiota transplantation stool donor program in Toronto, Canada

Susy S Hota MD, MSc[1,2], Isabella McNamara MPH[3], Robbie Jin BSc[3], Melissa Kissoon BSc[3], Satyender Singh PhD[1], Susan M Poutanen MD, MPH[2,3,4]

BACKGROUND: The success of fecal microbiota transplantation (FMT) programs depends on maintaining suitable stool donors. We describe challenges recruiting and retaining universal donors in the first 2 years of an FMT clinical and research program in Toronto and identify opportunities for improvement. **METHODS:** A four-stage screening process is used to identify suitable FMT donors in the Microbiota Therapeutics Outcomes Program. Donor screening follows Health Canada recommendations and excludes persons with history or risk for diseases associated with dysbiosis. Donors are rescreened microbiologically approximately every 1–3 months and answer ongoing health, exposure, and dietary questionnaires. **RESULTS:** In the first 2 years of our program, 5 of 322 (1.6%) prospective stool donors passed initial screening, and only 2 (0.6%) were retained. Most prospective donors were excluded on telephone screening, at which point high BMI, medication use, and family history of relevant illness were common exclusions. No candidate was excluded because of a concerning physical examination. Microbiologic reasons for donor exclusion included carriage of *Blastocystis hominis* ($n = 2$), *Helicobacter pylori* ($n = 2$), extended spectrum beta-lactamase producing organisms ($n = 1$), Shiga-toxin producing *Escherichia coli* ($n = 1$), and sapovirus ($n = 1$). Universal donors were lost temporarily because of travel, antibiotic exposures, and transient carriage of antibiotic-resistant organisms. **CONCLUSIONS:** Recruiting and retaining suitable donors for FMT is challenging because of rigorous exclusions and labour-intensive screening processes. We present considerations for efficiency in donor screening, including targeting recruitment populations, expanded website self-screening, eliminating physical examinations, and streamlining post-travel risk assessment.

KEYWORDS: donor program, fecal microbiota transplantation, recurrent *Clostridium difficile* infection

- Over a 2 year period Hota et al, screened 322 individuals as potential candidates for FMT's.
- 5/322 passed initial screens
- 2/322 were retained in the end.

Stool works….but so do stool filtrates….

> Gastroenterology. 2017 Mar;152(4):799-811.e7. doi: 10.1053/j.gastro.2016.11.010. Epub 2016 Nov 17.

Efficacy of Sterile Fecal Filtrate Transfer for Treating Patients With Clostridium difficile Infection

Stephan J Ott [1], Georg H Waetzig [2], Ateequr Rehman [3], Jacqueline Moltzau-Anderson [4], Richa Bharti [3], Juris A Grasis [5], Liam Cassidy [6], Andreas Tholey [6], Helmut Fickenscher [7], Dirk Seegert [2], Philip Rosenstiel [3], Stefan Schreiber [8]

Affiliations + expand

PMID: 27866880 DOI: 10.1053/j.gastro.2016.11.010

Free article

Abstract

Background & aims: Fecal microbiota transplantation (FMT) is a highly effective therapy for recurrent Clostridium difficile infection (CDI). However, transferring undefined living bacteria entails uncontrollable risks for infectious and metabolic or malignant diseases, particularly in immunocompromised patients. We investigated whether sterile fecal filtrates (containing bacterial debris, proteins, antimicrobial compounds, metabolic products, and oligonucleotides/DNA), rather than intact microorganisms, are effective in patients with CDI.

Methods: We performed a clinical case series to investigate the effects of fecal filtrate transfer (FFT) in 5 patients with symptomatic chronic-relapsing CDI at the Department of Internal Medicine I at the University Hospital Schleswig-Holstein (Kiel, Germany). Patients were followed up for at least 6 months and for up to 33 months. Stool was collected from 5 donors selected by the patients, and fully characterized according to FMT standards. Stool was sterile-filtered to remove small particles and bacteria; the filtrate was transferred to patients in a single administration via nasojejunal tube. Fecal samples were collected from patients before and at 1 week and 6 weeks after FFT. Microbiome, virome, and proteome profiles of donors and patients were compared.

Results: In all 5 patients, FFT restored normal stool habits and eliminated symptoms of CDI for a minimum period of 6 months. Proteome analyses of selected FFT filtrates showed no obvious protein candidates associated with therapeutic efficacy. 16S ribosomal RNA gene sequencing detected diverse bacterial DNA signatures in the filtrates. Analysis of virus-like particles from a filtrate found to reduce symptoms of CDI showed a complex signature of bacteriophages. Bacterial phylogeny and virome profile analyses of fecal samples from recipients indicated longitudinal

- Filtered stool (bacteria free) when used in rCDI led to symptom resolution for up to 6 months.
- “Proteome analysis showed no obvious candidates associated with therapeutic efficacy”

Ott et al, Gastroenterology 2017

Defined Microbial Community (DMC)

Methodology | Open Access | Published: 09 January 2013

Stool substitute transplant therapy for the eradication of *Clostridium difficile* infection: 'RePOOPulating' the gut

Elaine O Petrof, Gregory B Gloor, Stephen J Vanner, Scott J Weese, David Carter, Michelle C Daigneault, Eric M Brown, Kathleen Schroeter & Emma Allen-Vercoe

Microbiome **1**, Article number: 3 (2013) | Cite this article

142k Accesses | **497** Citations | **342** Altmetric | Metrics

Abstract

Background

Fecal bacteriotherapy ('stool transplant') can be effective in treating recurrent *Clostridium difficile* infection, but concerns of donor infection transmission and patient acceptance limit its use. Here we describe the use of a stool substitute preparation, made from purified intestinal bacterial cultures derived from a single healthy donor, to treat recurrent *C. difficile* infection that had failed repeated standard antibiotics. Thirty-three isolates were recovered from a healthy donor stool sample. Two patients who had failed at least three courses of metronidazole or vancomycin underwent colonoscopy and the mixture was infused throughout the right and mid colon. Pre-treatment and post-treatment stool samples were analyzed by 16 S rRNA gene sequencing using the Ion Torrent platform.

Results

Both patients were infected with the hyper virulent *C. difficile* strain, ribotype 078. Following stool substitute treatment, each patient reverted to their normal bowel pattern within 2 to 3 days and remained symptom-free at 6 months. The analysis demonstrated that rRNA sequences found in the stool substitute were rare in the pre-treatment stool samples but constituted over 25% of the sequences up to 6 months after treatment.

Conclusion

This proof-of-principle study demonstrates that a stool substitute mixture comprising a multi-species community of bacteria is capable of curing antibiotic-resistant *C. difficile* colitis. This benefit correlates with major changes in stool microbial profile and these changes reflect isolates from the synthetic mixture.

Trial registration

Clinical trial registration number: CinicalTrials.gov NCT01372943

Table 1 Composition of stool substitute (RePOOPulate)

From: Stool substitute transplant therapy for the eradication of *Clostridium difficile* infection: 'RePOOPulating' the gut

Closest species match, inferred by alignment of 16S rRNA sequence to GreenGenes database[a]	% identity to closest match	Relative abundance (by biomass) in RePOOPulate formulation
Acidaminococcus intestinalis	100	+++
Bacteroides ovatus	99.52	+
Bifidobacterium adolescentis (two different strains)	99.79	++
	99.79	++
Bifidobacterium longum (two different strains)	99.86	+++
	99.16	+++
Blautia producta	96.43	+
Clostridium cocleatum	91.92	+
Collinsella aerofaciens	98.73	+
Dorea longicatena (two different strains)	99.62	+
	99.60	+
Escherichia coli	99.80	+
Eubacterium desmolans	94.90	+
Eubacterium eligens	98.15	+++++
Eubacterium limosum	97.05	+
Eubacterium rectale (four different strains)	99.59	+++++
	99.60	+++++
	99.19	+++++
	99.53	+++++
Eubacterium ventriosum	100	++
Faecalibacterium prausnitzii	99.17	+++++
Lachnospira pectinoshiza	95.22	+
Lactobacillus casei/paracasei	99.47	+
Lactobacillus casei	99.74	+
Parabacteroides distasonis	99.45	++
Raoultella sp.	99.40	+
Roseburia faecalis	99.65	++
Roseburia intestinalis	100	++
Ruminococcus torques (two different strains)	99.15	+++
	99.29	+++
Ruminococcus obeum (two different strains)	94.89	+
	94.69	+
Streptococcus mitis[b]	99.79	+

****33 organisms DMC**

Defined Microbial Communities

Clinical Trial > N Engl J Med. 2022 Jan 20;386(3):220-229. doi: 10.1056/NEJMoa2106516.

SER-109, an Oral Microbiome Therapy for Recurrent *Clostridioides difficile* Infection

Paul Feuerstadt [1], Thomas J Louie [1], Bret Lashner [1], Elaine E L Wang [1], Liyang Diao [1], Jessica A Bryant [1], Matthew Sims [1], Colleen S Kraft [1], Stuart H Cohen [1], Charles S Berenson [1], Louis Y Korman [1], Christopher B Ford [1], Kevin D Litcofsky [1], Mary-Jane Lombardo [1], Jennifer R Wortman [1], Henry Wu [1], John G Auniņš [1], Christopher W J McChalicher [1], Jonathan A Winkler [1], Barbara H McGovern [1], Michele Trucksis [1], Matthew R Henn [1], Lisa von Moltke [1]

Affiliations + expand

PMID: 35045228 DOI: 10.1056/NEJMoa2106516

Abstract

Background: Current therapies for recurrent *Clostridioides difficile* infection do not address the disrupted microbiome, which supports *C. difficile* spore germination into toxin-producing bacteria. SER-109 is an investigational microbiome therapeutic composed of purified Firmicutes spores for the treatment of recurrent *C. difficile* infection.

~ $20,000 per person

- Phase 3 double blinded placebo controlled trial using SER-109 - a defined microbial community - bacterial spores isolated from healthy donor stool.
- *C. difficile* recurrence in patients given SER-109 (12%) vs. placebo (40%) - 8 weeks post treatment.
- But we still don't know how this all works…. **NO MECHANISM!**

We also have a Bacterial community

communications biology

Explore content ⌄ About the journal ⌄ Publish with us ⌄

nature › communications biology › articles › article

Article | Open access | Published: 27 January 2024

Defined microbial communities and their soluble products protect mice from *Clostridioides difficile* infection

Katya Douchant, Shu-Mei He, Curtis Noordhof, Jill Greenlaw, Sarah Vancuren, Kathleen Schroeter, Emma Allen-Vercoe, Calvin Sjaarda, Stephen J. Vanner, Elaine O. Petrof, Prameet M. Sheth ✉ & Mabel Guzman

Communications Biology **7**, Article number: 135 (2024) | Cite this article

4760 Accesses | **3** Citations | **2** Altmetric | Metrics

Abstract

Clostridioides difficile is the leading cause of antibiotic-associated infectious diarrhea. The development of *C.difficile* infection is tied to perturbations of the bacterial community in the gastrointestinal tract, called the gastrointestinal microbiota. Repairing the gastrointestinal microbiota by introducing lab-designed bacterial communities, or defined microbial communities, has recently shown promise as therapeutics against *C.difficile* infection, however, the mechanisms of action of defined microbial communities remain unclear. Using an antibiotic- *C.difficile* mouse model, we report the ability of an 18-member community and

We have our own Bacterial community that protected against *C.difficile*.

In our study we reported that soluble factors from the bacterial community was enough to protect against *C. difficile*

↓

Suggesting you don't need bacteria…just something they release…but What??

State of available therapies

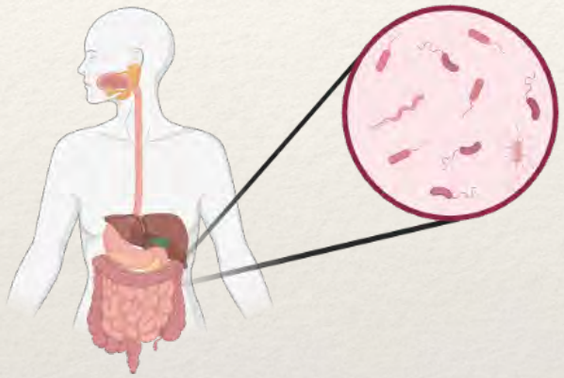
Antimicrobial Therapy

Vancomycin
Fidaxomicin
Metronidazole

Expensive

Increasing antibiotic resistance

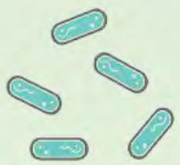
Maintains gut dysbiosis
- Kills good and bad bacteria



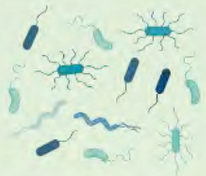
Increases the risk of recurrence and reinfection

Microbe-Based Therapies

Fecal Microbiota Transplant



Single Strain Probiotic



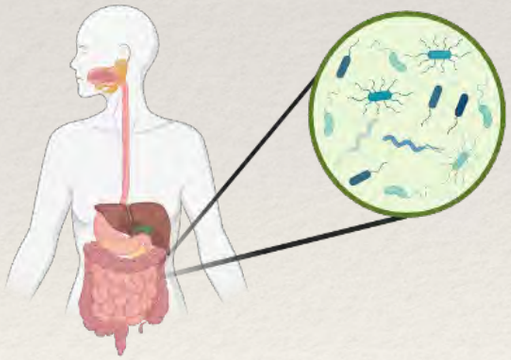
Multistrain Probiotic

Restores the GIM

Secretes antimicrobial substances

Reinforces the intestinal barrier

Interferes with *C. diff* colonization

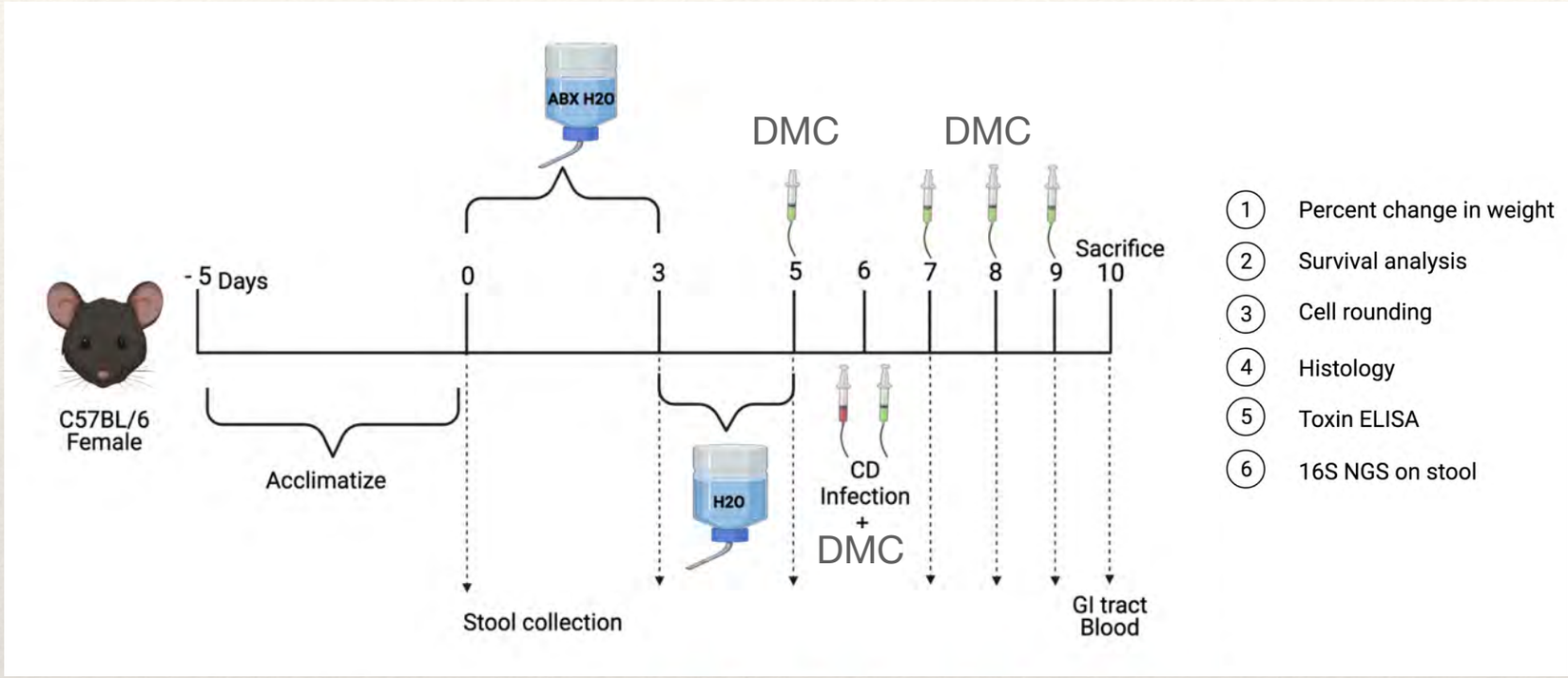


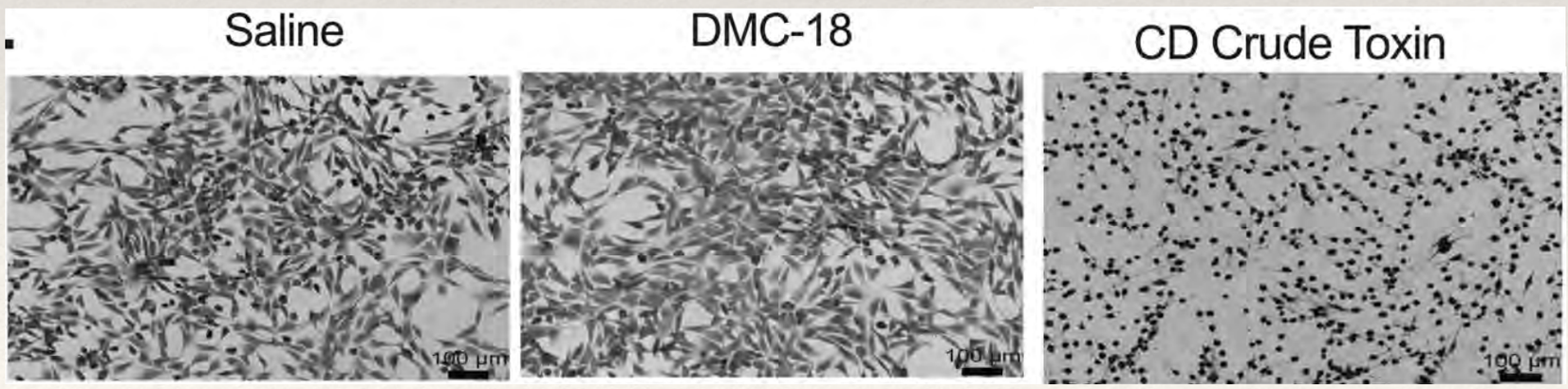
Lack of standardization
What is a "healthy" FMT donor?

High variability
What is inside an FMT
Between batches of probiotics

Unknown MOA

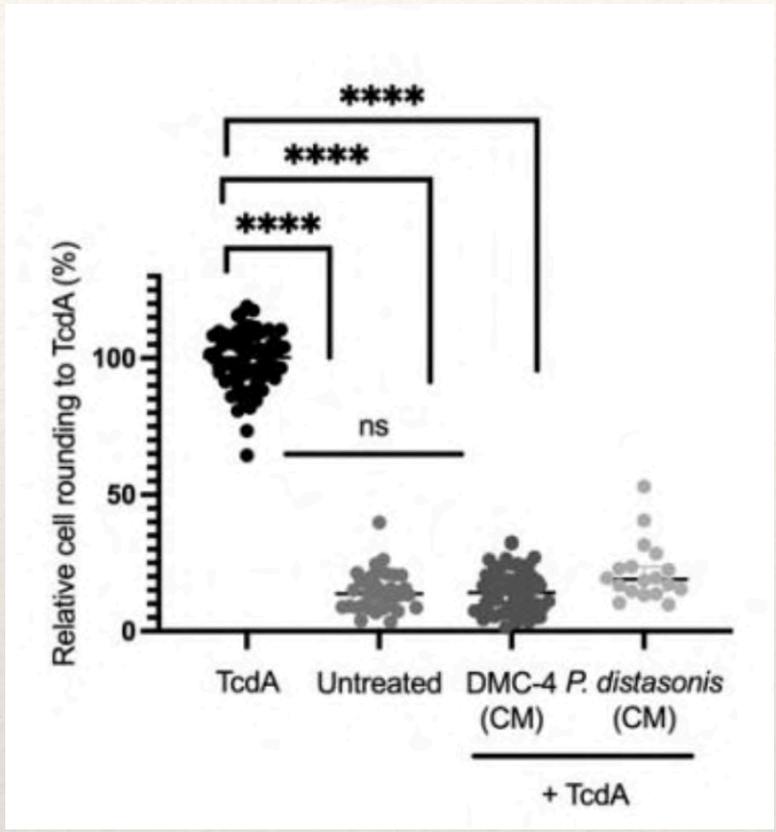
Methods used in the Lab



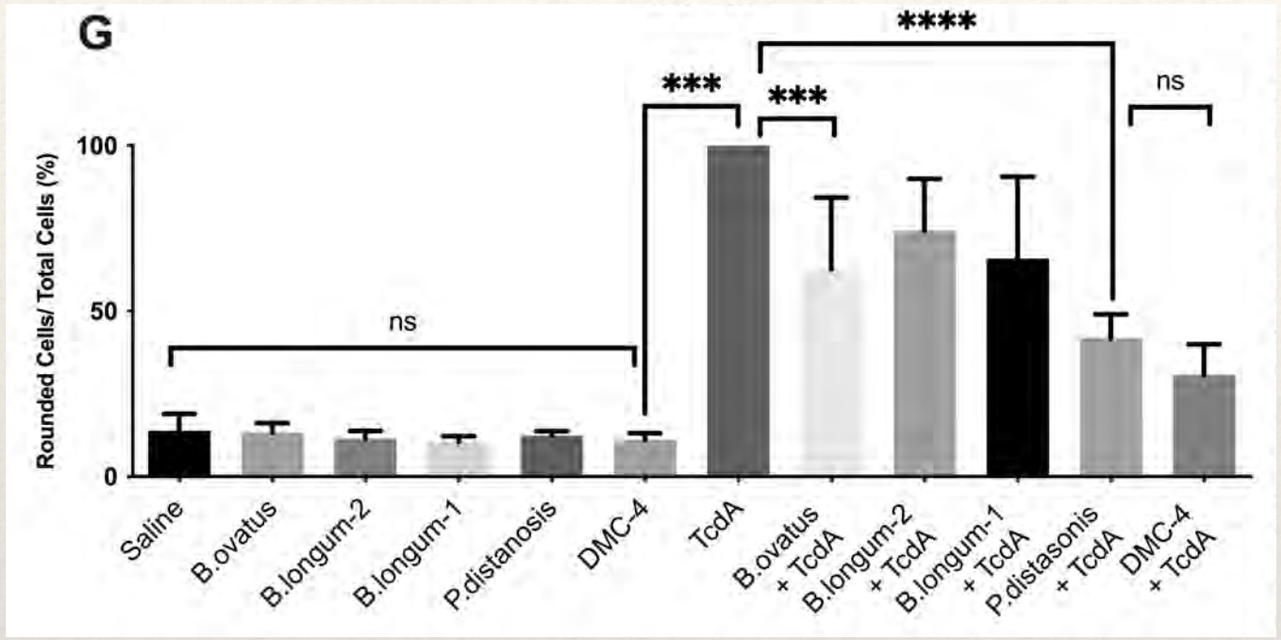


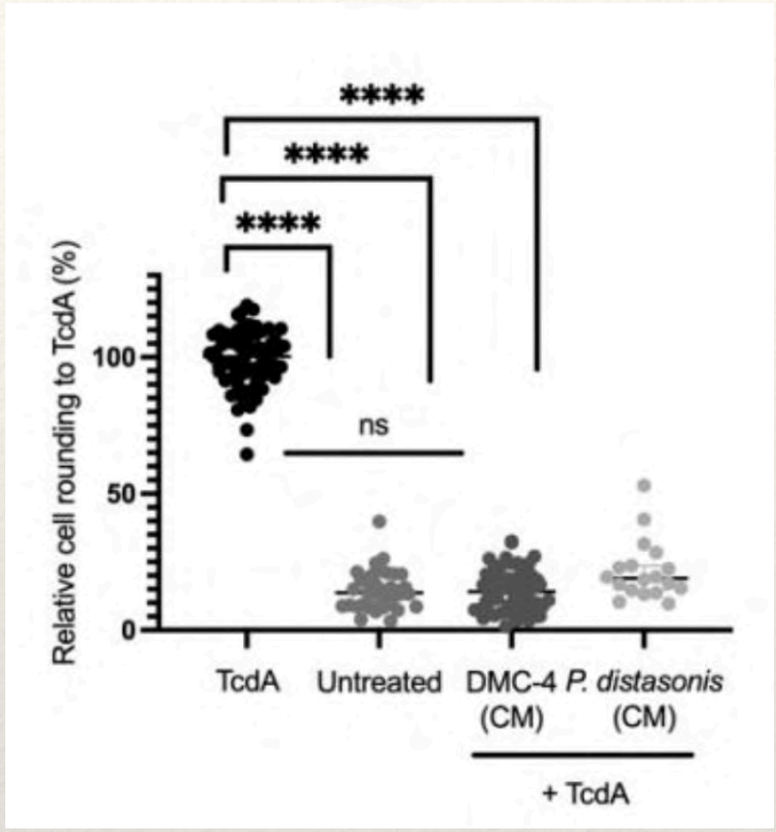
- Within 24/48 hours of infection the mice get sick with disease that is consistent with CD infection.
- Mice develop diarrhea, experience weight loss, reduced movement, hunched posture.
- Cell rounding assays allow us to determine *in vitro* toxin activity.

Soluble factor neutralized CD Toxin activity



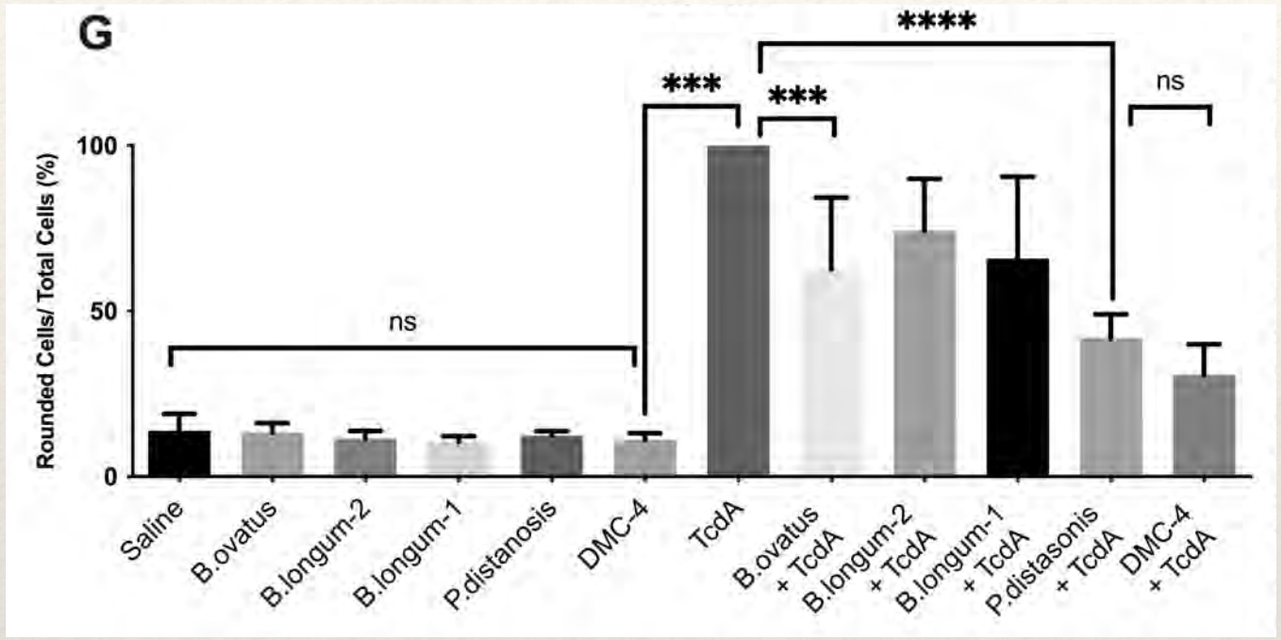
Soluble factor neutralized CD Toxin activity



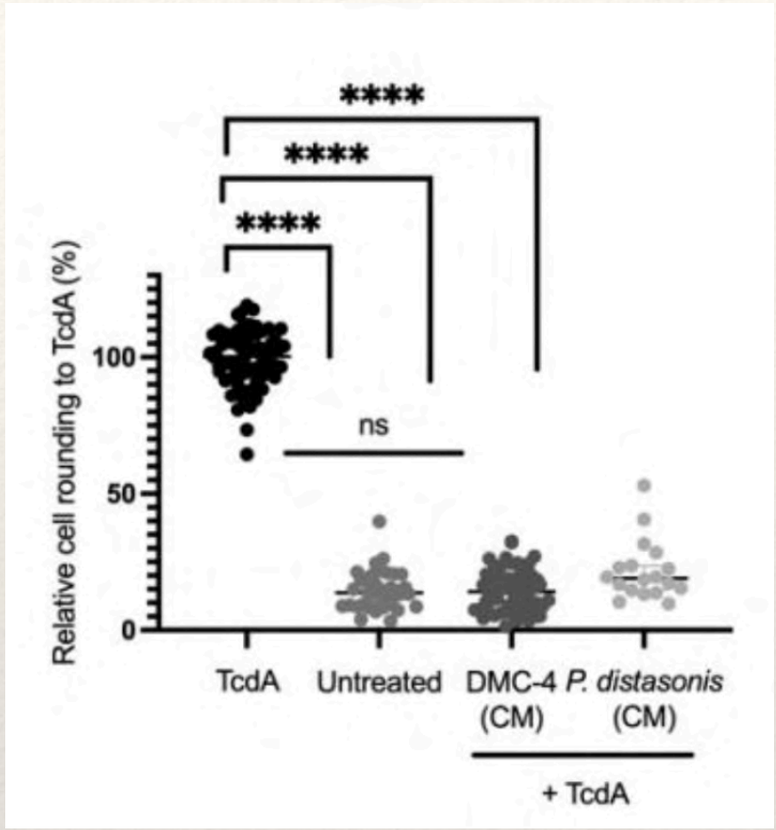


When the 4 bacteria were tested individually, *P. distasonis* neutralized toxin activity the most.

Soluble factor neutralized CD Toxin activity

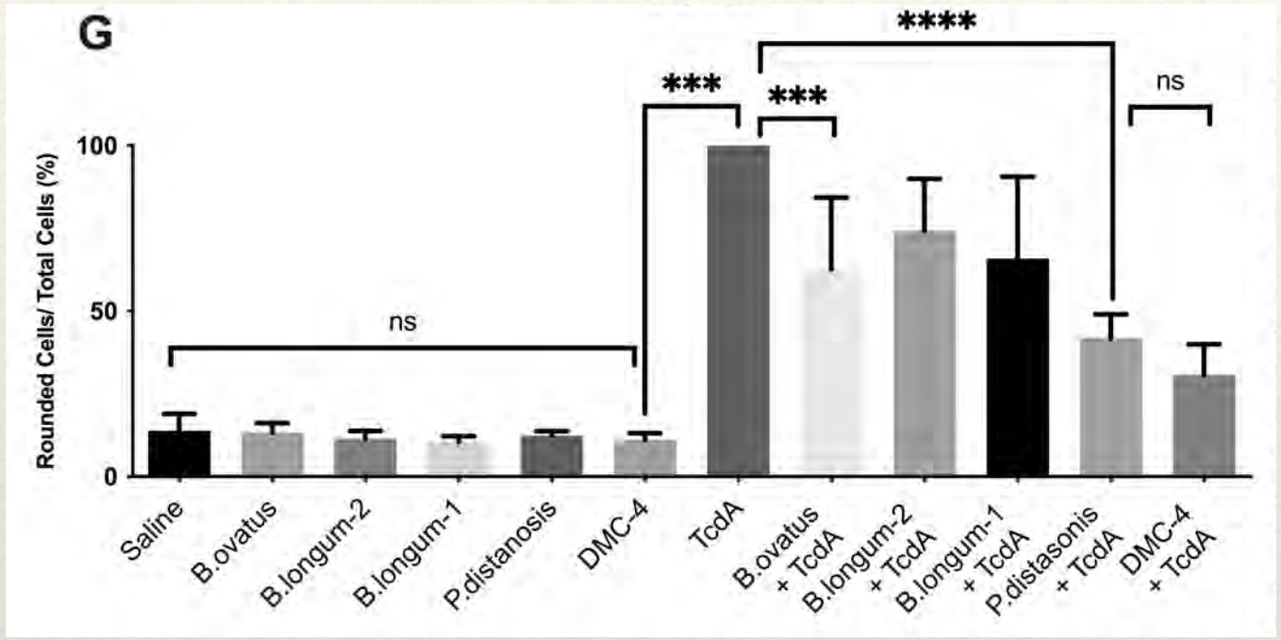


When the 4 bacteria were tested individually, *P. distasonis* neutralized toxin activity the most.

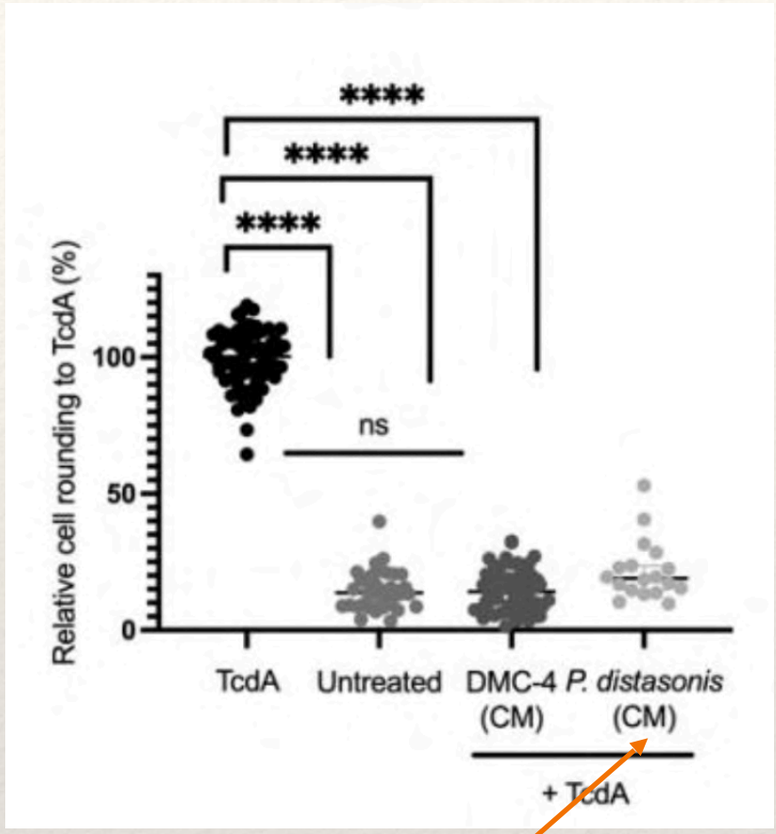


When we separated the bacteria from the media - the media was enough to neutralize toxins.

Soluble factor neutralized CD Toxin activity

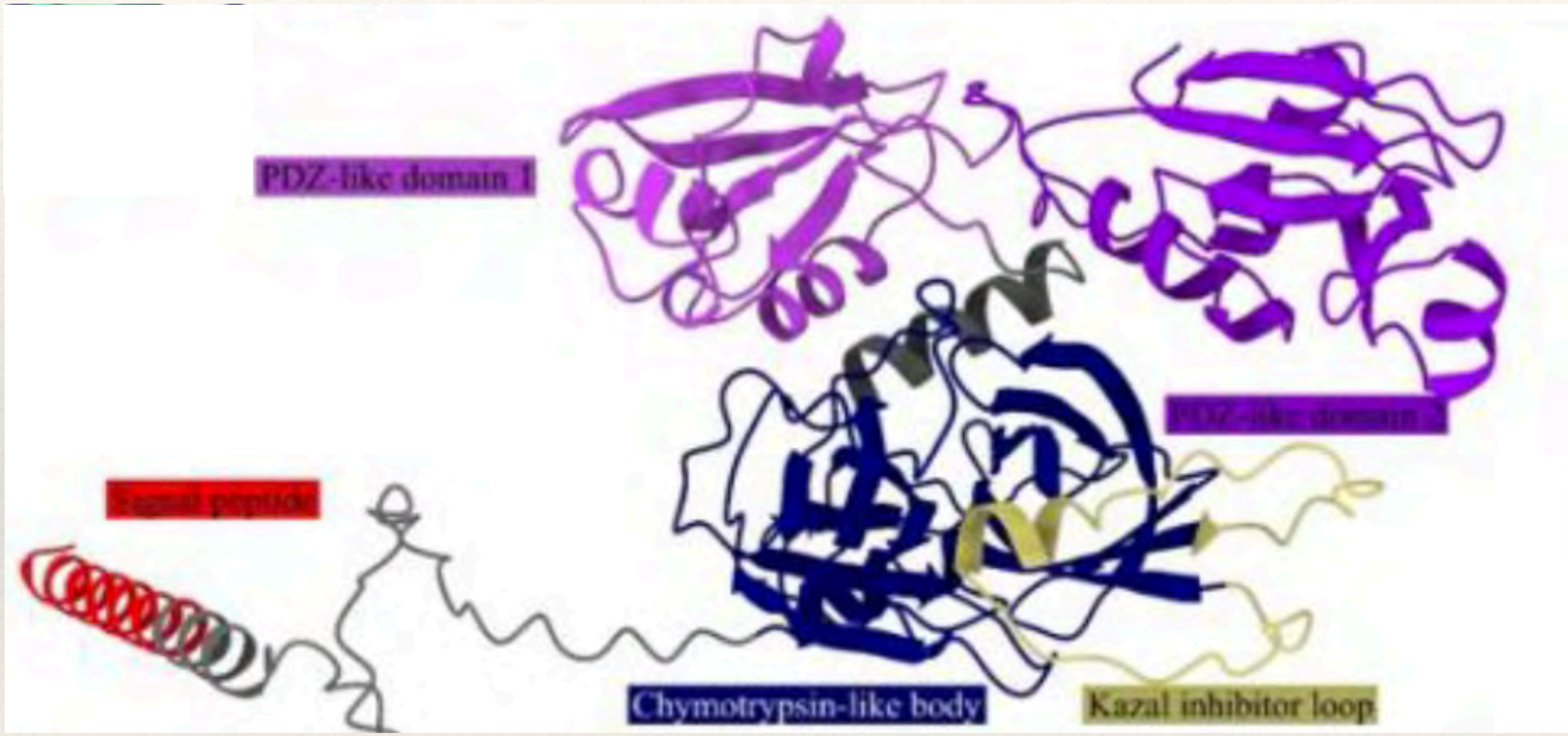


When the 4 bacteria were tested individually, *P. distasonis* neutralized toxin activity the most.



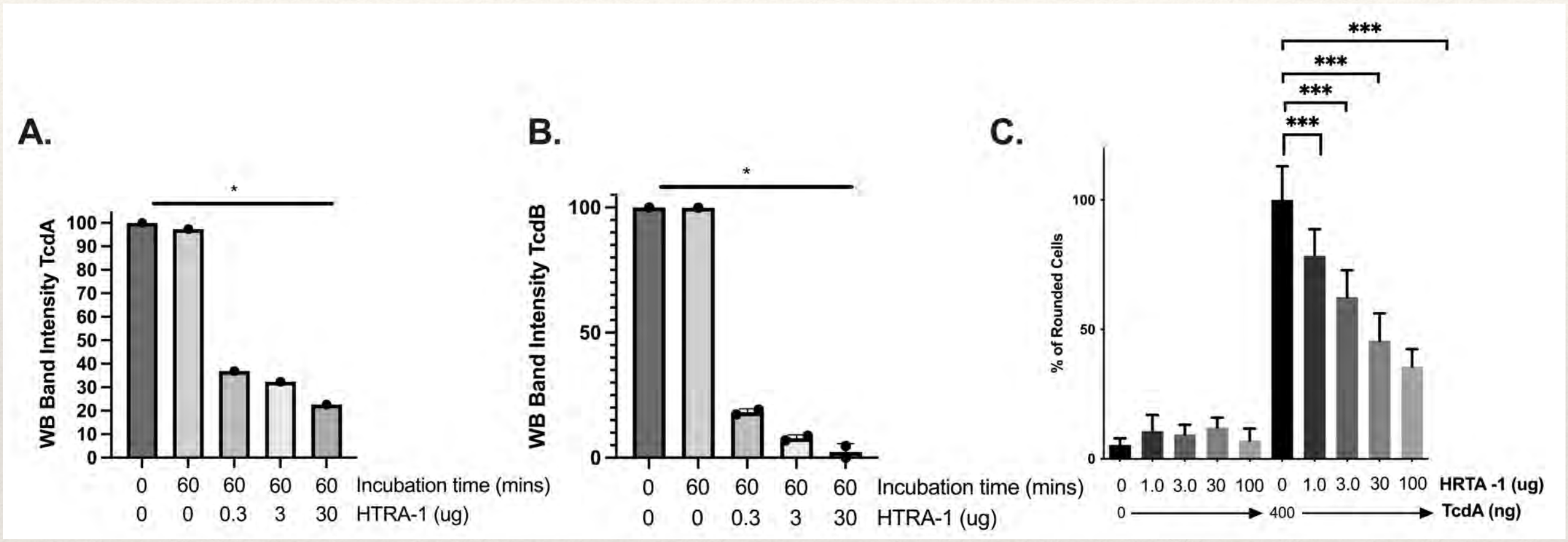
When we separated the bacteria from the media - the media was enough to neutralize toxins.

Introducing HtrA



High temperature Requirement Protein (HtrA)

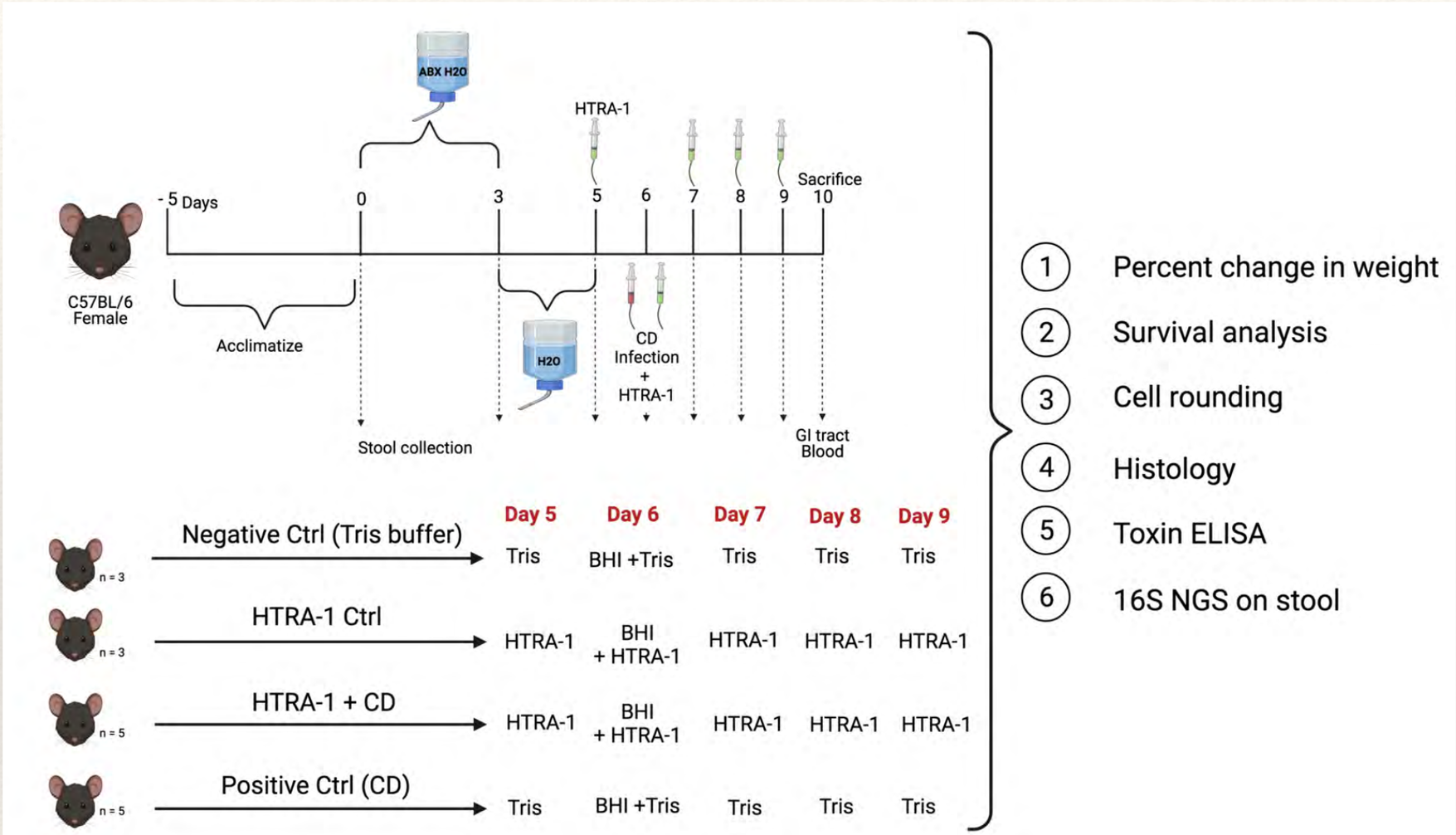
HtrA neutralized CD toxins (dose dependent)



HTRA degraded both CD toxins in vitro in a concentration dependent manner over 60 mins of time

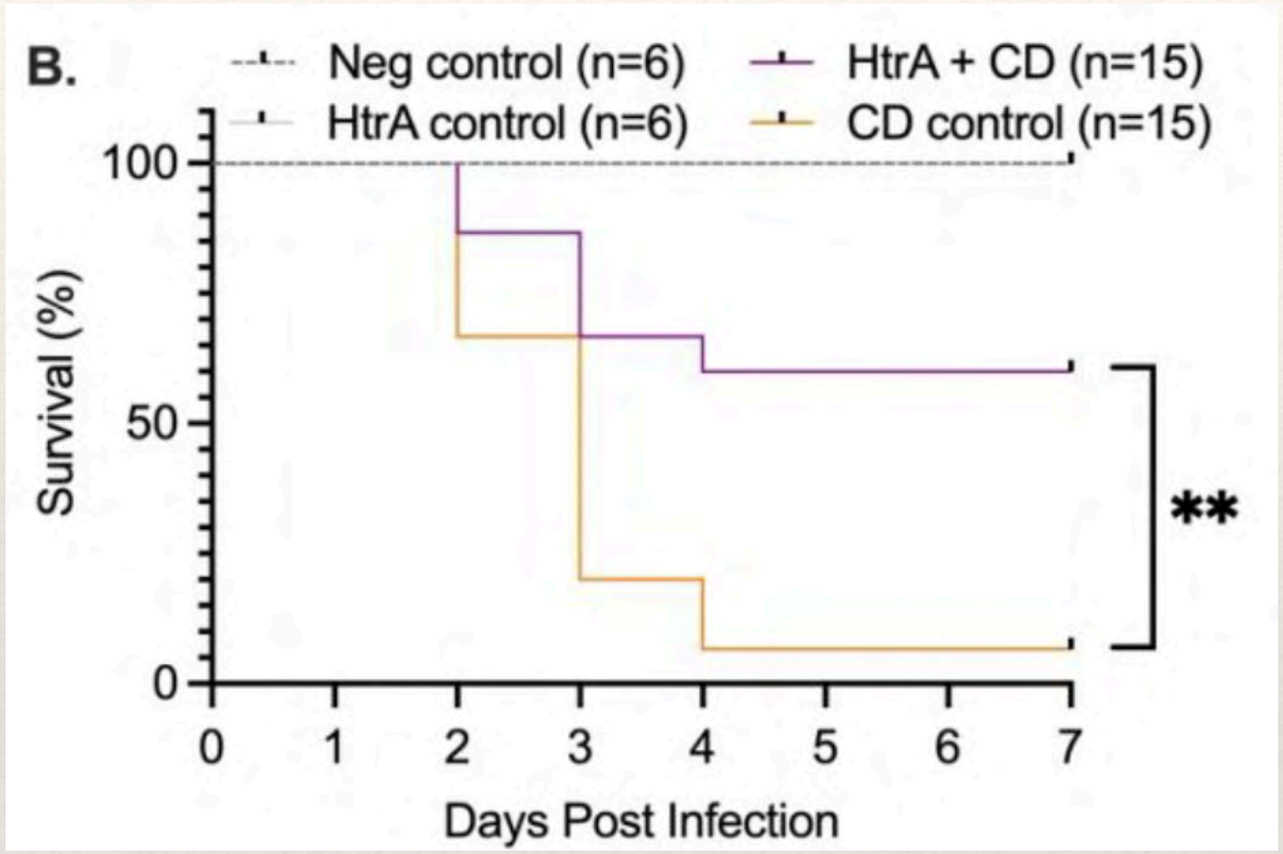
Protected cells from rounding *(in vitro)*

So does it work in an animal model?

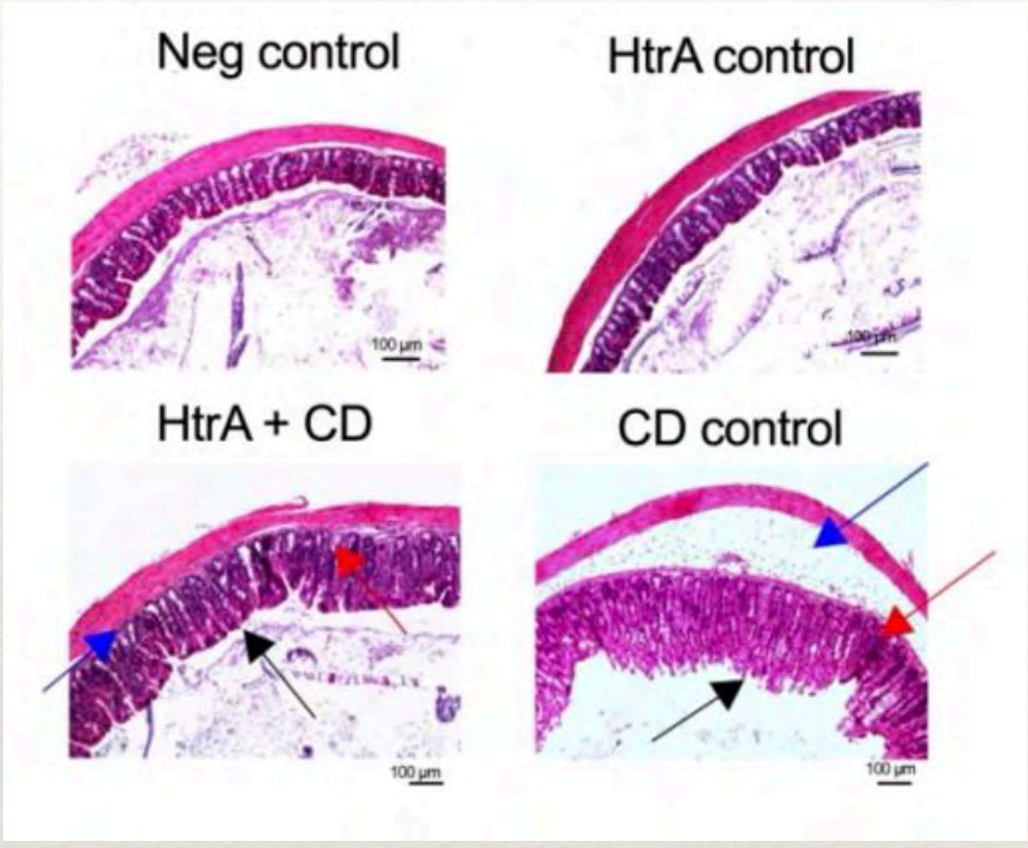


Our mouse model was based on oral administration….the big question is will HtrA survive the stomach acid??

HtrA protected Mice from *C.diff*

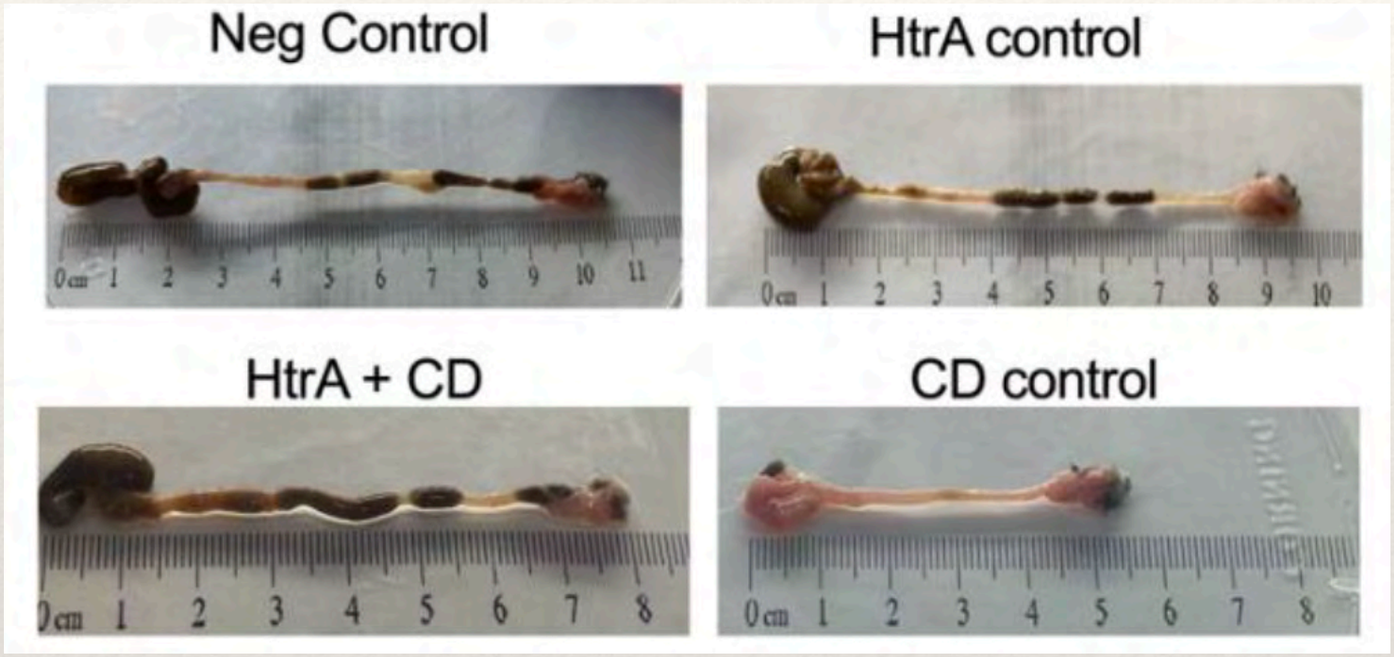


Protected Mice from C.diff mediated death (9-fold increase)

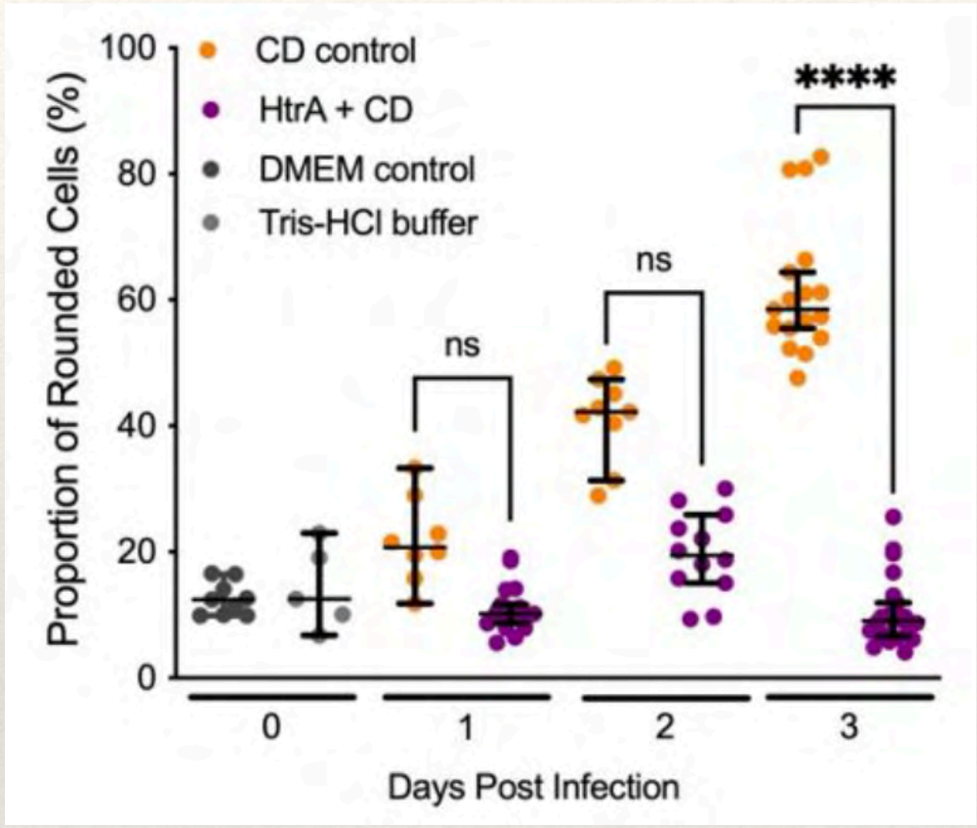


HtrA prevented *C.diff* mediated inflammation in the colon.

HtrA protected Mice from *C.diff*

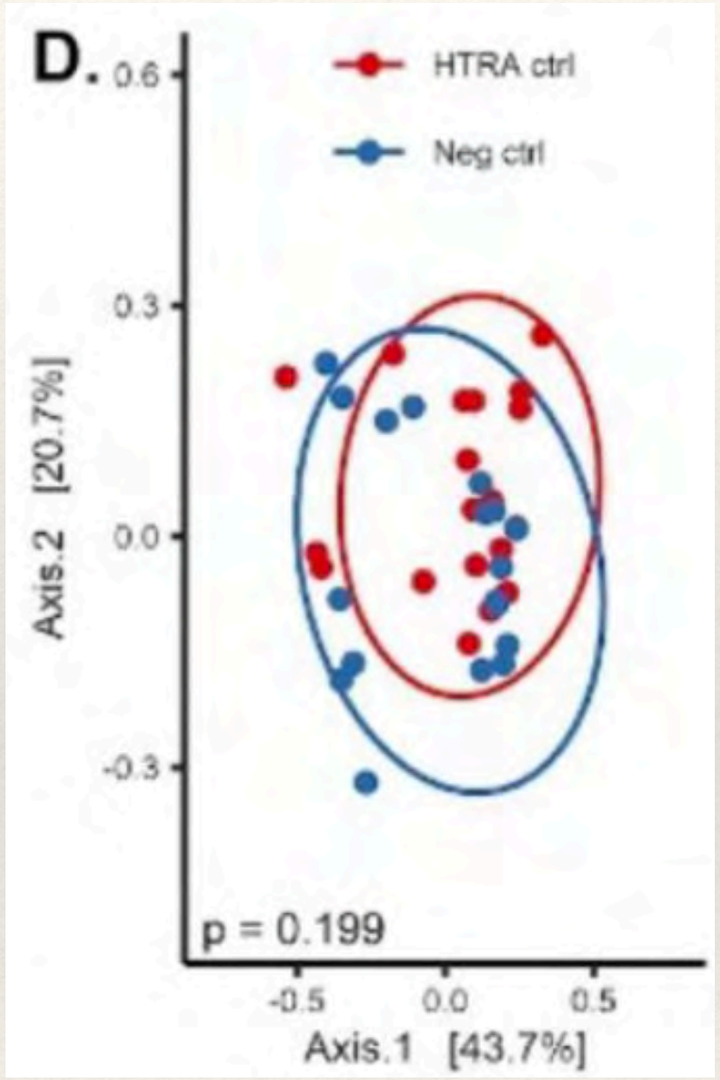


C.diff causes colonic shortening in mice and that was prevented when CD mice were given HtrA.



Stool from mice had no active *C.diff* toxins vs. mice that did not get HtrA.

HtrA does not alter the Gut Microbiome



HtrA does not change the gut microbiome.

This is SUPER important !!

Remember the gut microbiome change is what leads to C.diff in the first place!

Summary

- This provides early clues of how FMT's and/or microbiota restoration (DMC's) may be working.
- HtrA protects against CD mediated disease by neutralizing CD toxins and preventing disease and death in mice.
- Since HtrA works on the toxins and not the bacteria - there should not be an issue with resistance - the bacteria is unaffected !!.
- This is the first time that a bacterially derived protein has been identified as a potential therapy against a bacterial disease.

Next Steps

- Is HtrA safe?
- Is it pH stable at the acid levels found in the human GI tract?
- Does it work in humans?
- When/how would you give it? With antibiotics? without?

Funding Sources

The US National Institute of Health

The Canadian Institute of Health Research

The South Eastern Academic Medical Organization

THU
29

January 29 @ 1:30 pm EST

Carbapenem-Resistant Enterobacterales in Healthcare and Community Settings

Otter, Imperial College London

$40.00

February 2026

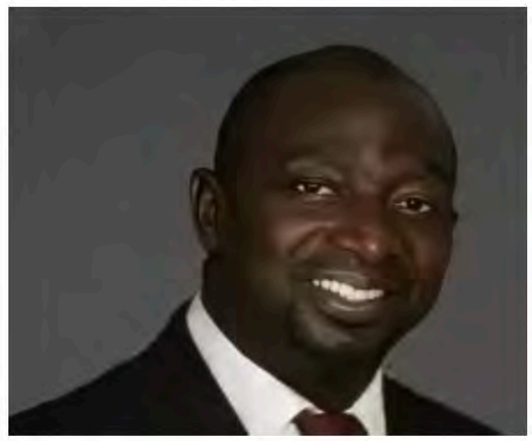
THU
5

February 5 @ 1:30 pm EST

Is LTC Prepared for the Next Pandemic?

Ayukekbong, Editor-in-Chief, Canadian Journal of Infection Control

$40.00

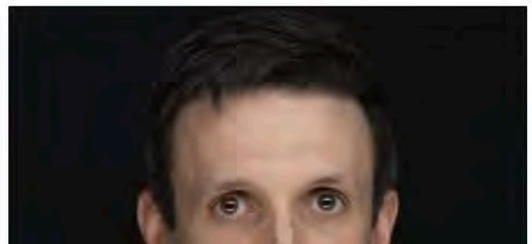


THU
12

February 12 @ 1:30 pm EST

Code Red: Measles On the Ward

Prof. Yves Longtin, McGill University



Thanks to Teleclass Education

PATRON SPONSORS

Diversey
A SOLENIS COMPANY

diversey.com

VIROX
TECHNOLOGIES INC.

virox.com

gama healthcare

gamahealthcare.com