Seres Therapeutics 2018 R&D Event

Focus on microbiome impact on immune biology:
Ulcerative Colitis and immuno-oncology

May 24, 2018
New York City

SERES THERAPEUTICS™

Leading the Microbiome Revolution

Forward looking statements

Some of the statements in this presentation constitute “forward looking statements” under the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements on the timing and results of our clinical trials, the sufficiency of our financial resources, and dysbiosis as an underlying cause of disease or failed response to therapy. Such statements are subject to important factors, risks and uncertainties (such as those discussed under the caption "Risk Factors" in the Company’s Report on Form 10-Q filed on May 8, 2018 and its other filings with the SEC) that may cause actual results to differ materially from those expressed or implied by such forward looking statements. Any forward looking statements included herein represent our views as of today only. We may update these statements, but we disclaim any obligation to do so.

Agenda

8:00-8:10 a.m.
Opening Remarks
Roger Pomerantz, M.D., Seres President, CEO and Chairman

8:10-8:20 a.m.
The microbiome as a new therapeutic modality
Will Dere, M.D., Seres Board Member

ULCERATIVE COLITIS
8:20-8:40 a.m.
Pathology and role of the microbiome
Alan Moss, M.D., Beth Israel Deaconess Medical Center

8:40-9:05 a.m.
SER-287 Phase 1b results and continued late stage development
Shelley Trucksis, Ph.D., M.D., Seres Executive Vice President and Chief Medical Officer and Matthew Henn, Ph.D., Seres Executive Vice President, Microbiome Research and Development

9:05-9:25 a.m.
Microbiome therapeutic development
Stephen Hanauer, M.D., Northwestern University

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Break

IMMUNO-ONCOLOGY
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Microbiome therapeutics and immuno-oncology – Charting a path forward
Jennifer Wargo, M.D., MD Anderson Cancer Center

10:00-10:30 a.m.
Q&A Session

Roger Pomerantz, M.D. is Seres President, CEO, and Chairman of the Board. Previously, he held a series of senior leadership positions at Merck & Co., Inc. Dr. Pomerantz is an internationally recognized expert in HIV molecular pathogenesis and latency and has developed ten approved infectious disease drugs in important diseases including HIV, HCV, tuberculosis, and *Clostridium difficile* infection.

David Cook, Ph.D. is Seres Executive VP of R&D and CSO. He has over 20 years experience as a scientist and entrepreneur and has held multiple senior operating and management positions in the biotech industry, leading teams in the development and commercialization of several products. He has been directly responsible for obtaining marketing authorization from the EU for four medical products and is a co-inventor on more than 25 patents.

Michele (Shelley) Trucksis, Ph.D. M.D. is Seres Executive VP and CMO. She has over 25 years of experience in medicine and infectious diseases. Previously, she served as Executive Director of Merck Research Laboratories with responsibility for clinical and global product development functions and development strategy in antibacterials, antifungals and anti-cytomegalovirus drug candidates.

Matthew Henn, Ph.D. is Seres Executive VP, Microbiome R&D. He was previously Director of Viral Genomics and Assistant Director of the Genome Sequencing Center for Infectious Diseases at the Broad Institute. He has published over 60 research papers and has served on various NIH and CDC working groups on antimicrobial resistance and microbiome research and as a scientific advisor for the Forsyth Institute and NIH's Viral Pathogen Bioinformatics Resource Center.

Willard Dere, M.D. is a Seres Board Member, Professor of Internal Medicine; B. Lue and Hope S. Bettilyon Presidential Endowed Chair in Internal Medicine for Diabetes Research, Executive Director of Personalized Health, and Co-Principal Investigator of the Center for Clinical and Translational Science at the University of Utah Health Sciences Center. Before re-joining academia in November 2014 he was in the biopharmaceutical industry for 25 years, including serving as head of global development, and both corporate and international chief medical officer at Amgen.

Jennifer Wargo, M.D. is Associate Professor of Genomic Medicine and Surgical Oncology at MD Anderson Cancer Center. Dr. Wargo's career commitment is to advance the understanding and treatment of disease through science. At MD Anderson she runs a translational research laboratory studying the genetics of melanoma and other cancers with the goal of understanding what allows them to grow, spread and evade the immune system.

Alan Moss, M.D. is Associate Professor of Medicine, Harvard Medical School; Gastroenterologist, Beth Israel Deaconess Medical Center (BIDMC); and Director of Translational Research, IBD Center, BIDMC. He is a Fellow of the of the American College of Gastroenterology, author of over 120 research papers, and an associate editor for the Journal of Crohn's & Colitis (ECCO), Frontline Gastroenterology (BMJ) and the World Journal of Gastroenterology.

Stephen Hanauer, M.D. is the Clifford Joseph Barborka Professor of Medicine, Gastroenterology and Hepatology, and Medical Director of the Digestive Health Center at Northwestern University Feinberg School of Medicine. An international leader in the treatment of IBD, he is chair of the International Organization for IBD and secretary-elect of the American College of Gastroenterology. He previously served as chair of the FDA Gastrointestinal Drugs Advisory Committee and authored the FDA's "Guidelines for Clinical Evaluation of Drugs for Patients with Inflammatory Bowel Disease."

Seres Mission: *Transform the lives of patients worldwide with revolutionary microbiome therapeutics*

- **First publicly traded company** focused on microbiome therapeutics
- **First clinical study starts**:
  - Biologically sourced microbiome therapy – SER-109 for multiply recurrent *C. diff*.
  - Fermented, rationally-designed, microbiome therapy – SER-262 for primary *C. diff*.
  - Microbiome therapy for chronic inflammatory condition – SER-287 for ulcerative colitis
- **Only company with microbiome human clinical data** (SER-109, SER-287, SER-262)
- **First Phase 3 clinical study** for microbiome therapy – SER-109
- **Leader** in microbiome research capabilities (e.g., computational biology, microbiology)
- **First GMP manufacturing capabilities**
- **First FDA release specs** for microbiome drug candidate
- **Foundational intellectual property**

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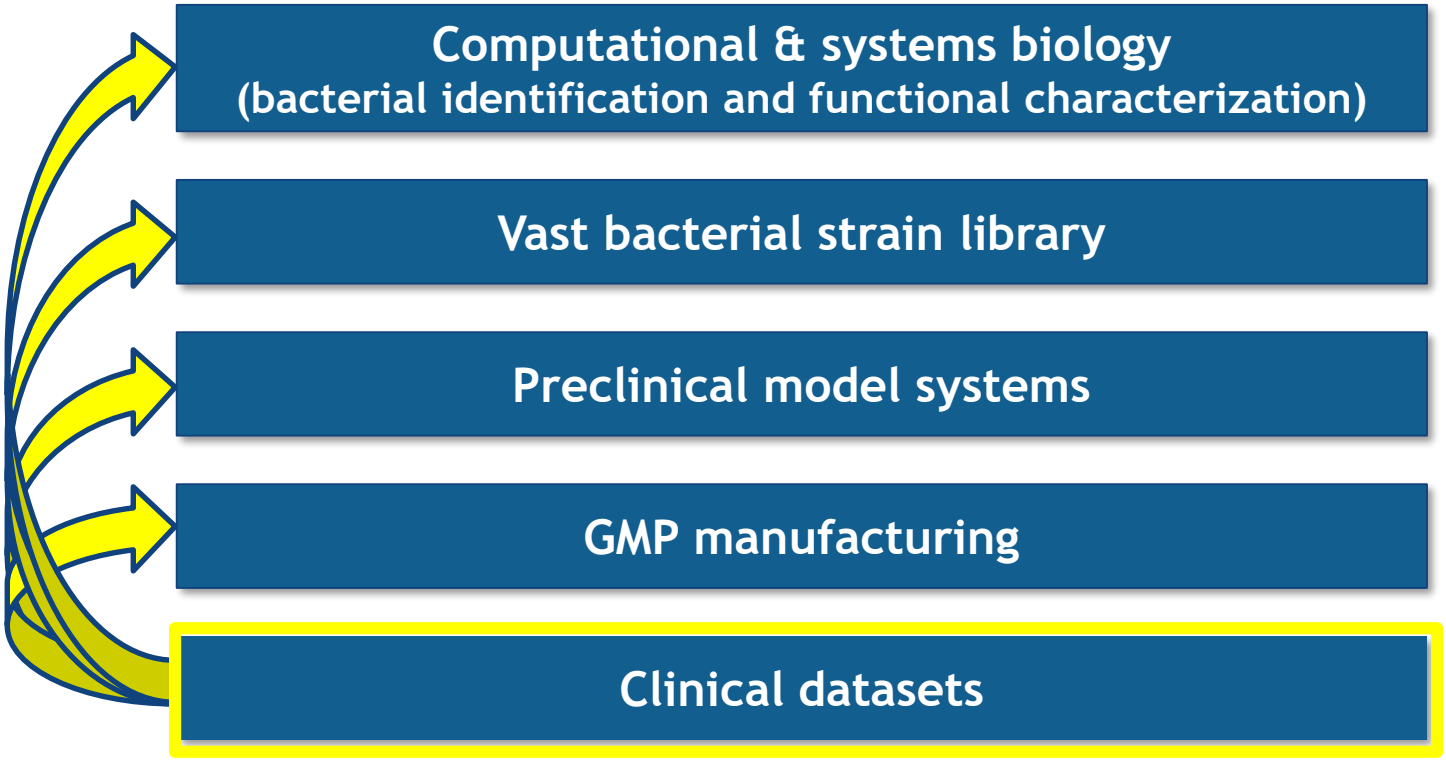
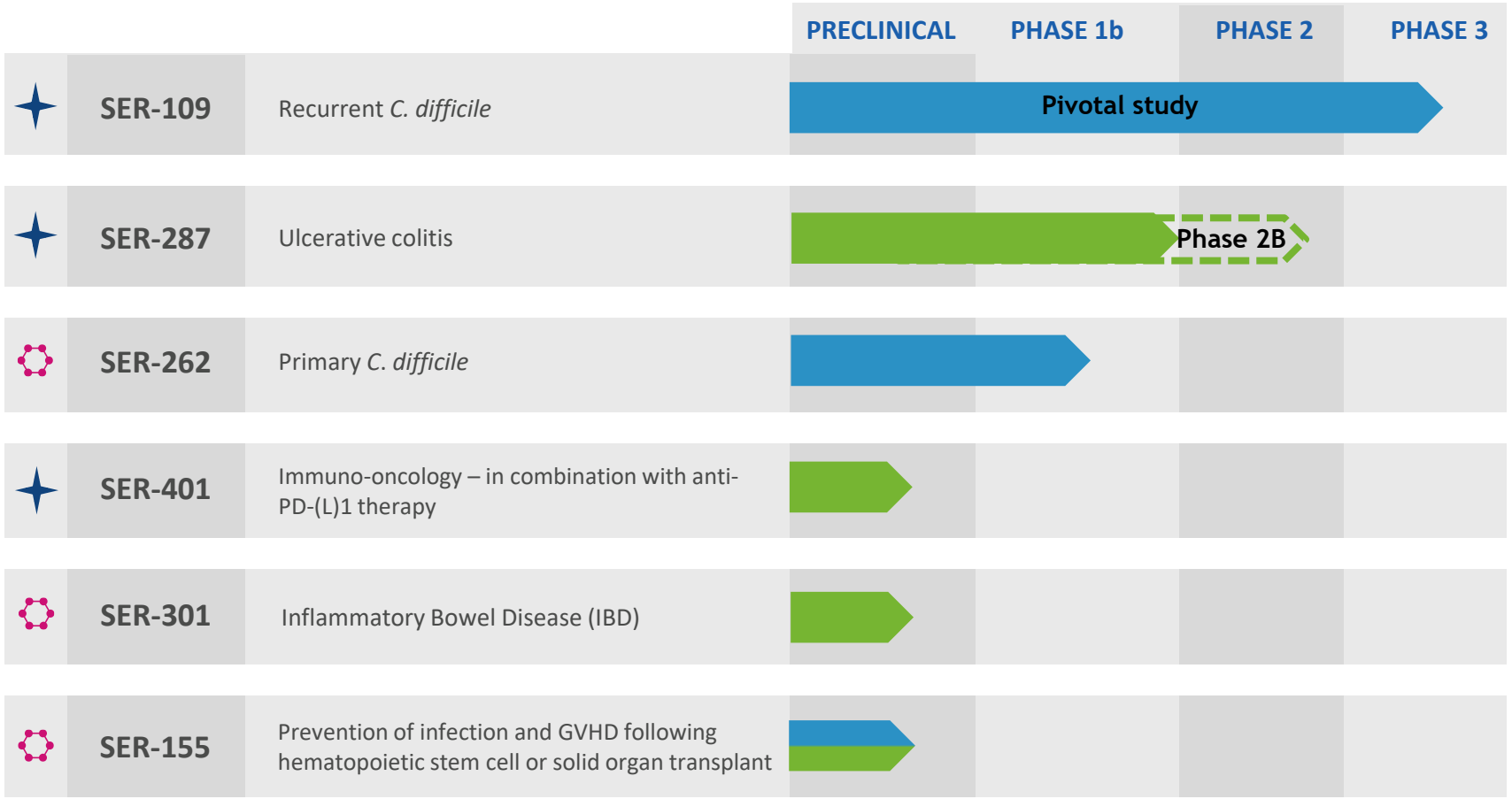
R&D capabilities drive drug development productivity



Seres is the only company with clinical efficacy/ safety data and microbiome datasets

Robust microbiome therapeutics pipeline



Research Collaborations

Memorial Sloan Kettering Cancer Center · Penn · MAYO CLINIC · MASSACHUSETTS GENERAL HOSPITAL · MD Anderson Cancer Center · PARKER INSTITUTE for CANCER IMMUNOTHERAPY

Collaboration with Nestlé Health Science regarding *C. difficile* and IBD programs for markets outside of North America

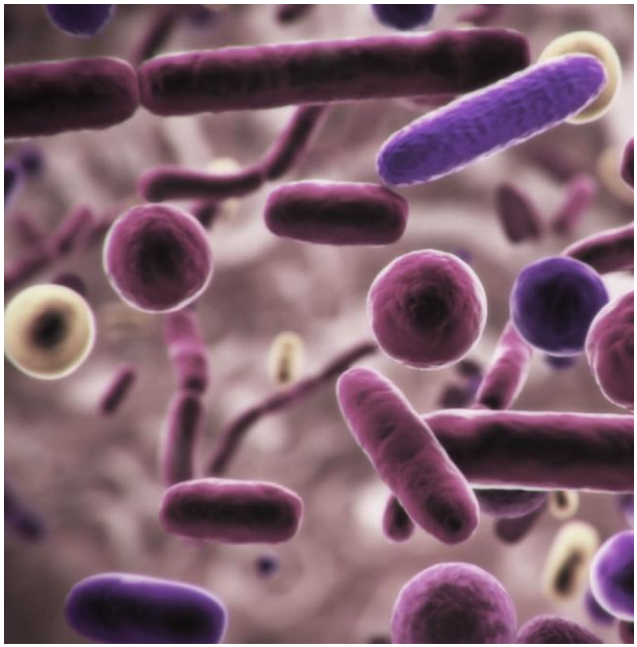
C. difficile infection

Clinically demonstrated link to GI microbiome dysbiosis

Infectious disease caused by toxin-producing anaerobic, spore-forming bacteria, resulting in diarrhea, abdominal pain, fever, and nausea

Leading U.S. cause of hospital-acquired infection

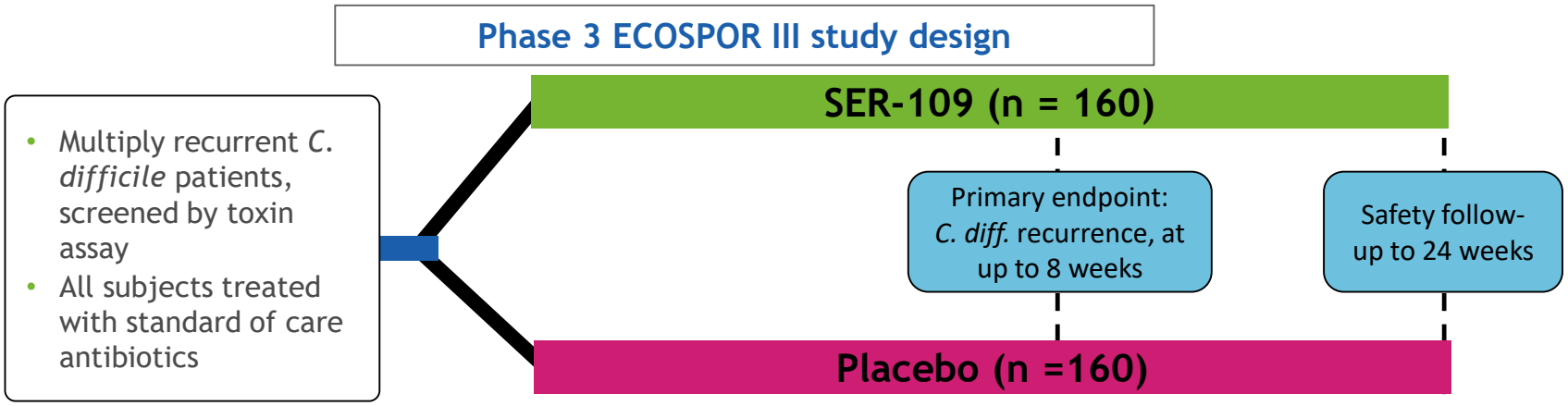
- Approximately 29,000 deaths/year
- ~25% of patients with primary *C. difficile* recur
- Risk of relapse increases with each recurrence
- Multiply recurrent *C. difficile* infection incidence increased 188% between 2001-2010



Sources: Leffler and Lamont, New England Journal of Medicine, 2015; Ma et al. Annals of Internal Medicine, 2017.

Phase 3 SER-109 ECOSPOR III study – enrollment progress ongoing

- FDA Breakthrough and Orphan Drug designation
- Based on FDA feedback, ECOSPOR III designated as a Phase 3 study
- Phase 3 study incorporates key learnings from prior clinical studies:
  - SER-109 dose is approximately 10-fold higher than dose used in Phase 2 study
  - *C. difficile* toxin assay to be used at study entry and for primary endpoint



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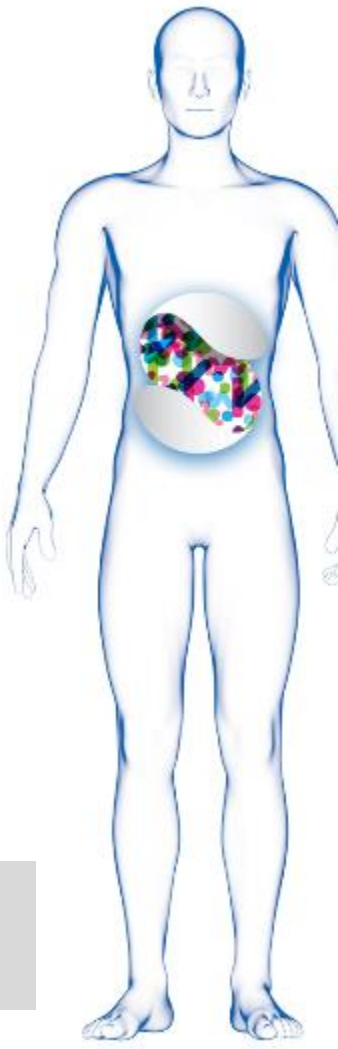
The microbiome is essential to human health

- Human gastrointestinal microbiome is a vast interacting network of organisms
- Microbial ecology provides essential functions for the host:
  - Modulation of immune system
  - Colonization resistance against potential pathogens
  - Regulation of host metabolism
  - Synthesis of certain vitamins
  - Breakdown of carbohydrates



Significant opportunity for microbiome therapeutics to impact disease outcomes

Microbiome PK and PD may be measured, and are increasingly well understood

Pharmacokinetics (PK)

- *Kinetics of product engraftment: the presence of bacteria in the drug in subjects over time*

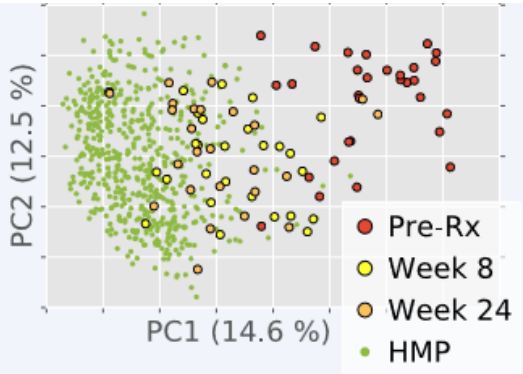
Pharmacodynamics (PD)

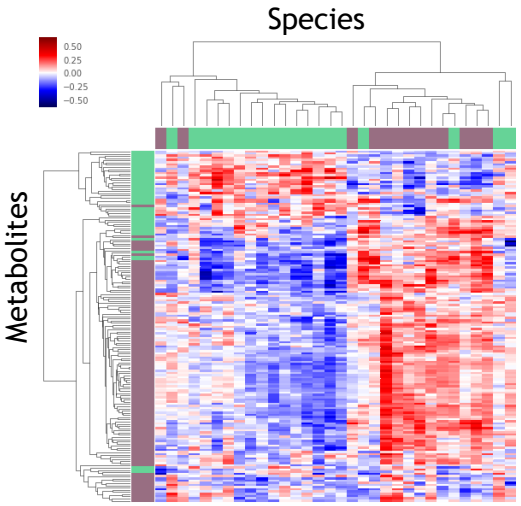
- *Overall changes in the composition of the microbiome and corresponding alterations in microbial metabolites and host biomarkers*

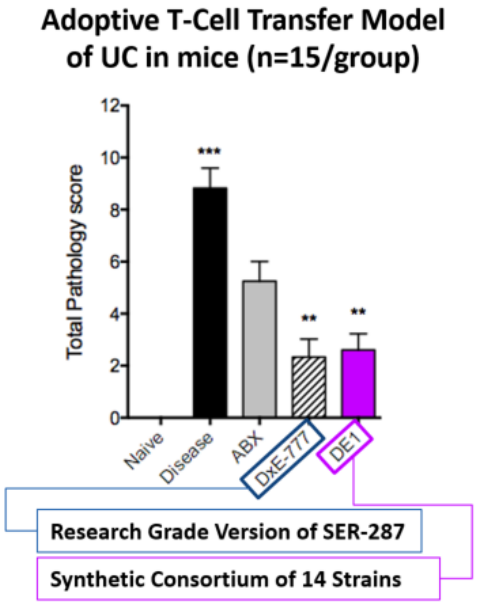
Modification of the microbiome results in downstream changes in biology

Illustrative data from various Seres programs

Microbiome change (Pharmacokinetics) → Active metabolites (Pharmacodynamics) → Impact on downstream biology







Multiple factors are now accelerating microbiome drug development

Company

- Accumulating clinical data (efficacy, safety, PK/PD)
- Powerful new research tools
- Advanced manufacturing capabilities
- Accumulating regulatory expertise

External Environment

- NIH & government agency funding accelerating basic microbiome research
- Increasing large pharma and biotech focus on the microbiome

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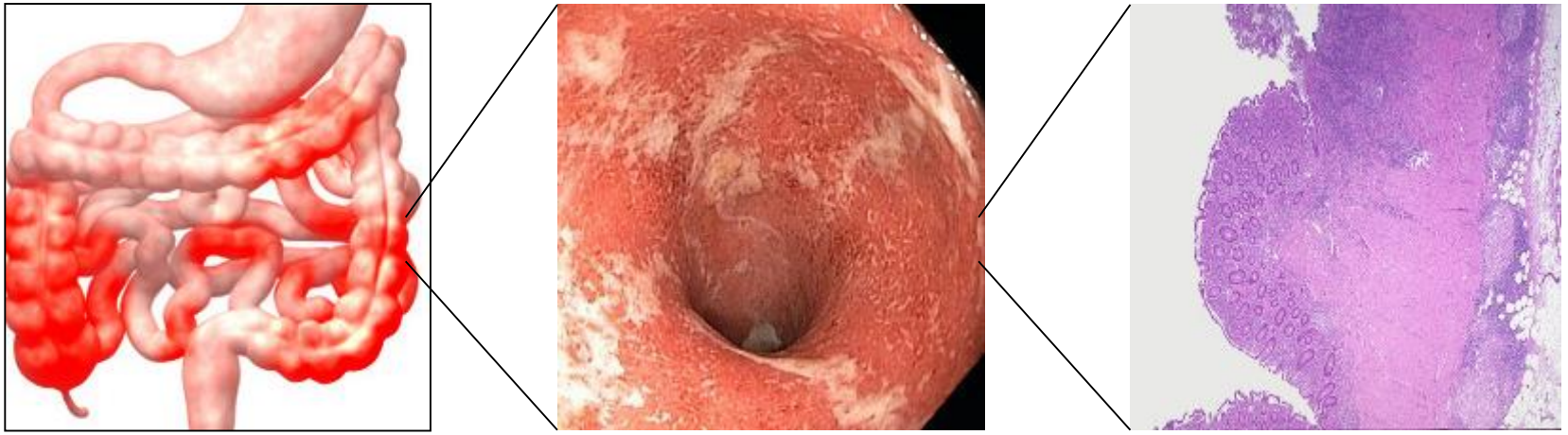
Ulcerative Colitis (UC)



Symptoms
- Abdominal pain
- Diarrhea
- Urgency

Appearance
- Inflammation
- Ulcers

Complications
- Strictures
- Cancer
- Megacolon

- *80% with at least one relapse within 10 years of diagnosis*
- *20% require colectomy for acute complications or refractory disease*

Solberg I *et al. Scand J Gastro* 2009; 44:431-440.
Bernstein CN *et al. Inflamm Bowel Dis* 2010: 16: 112-124.

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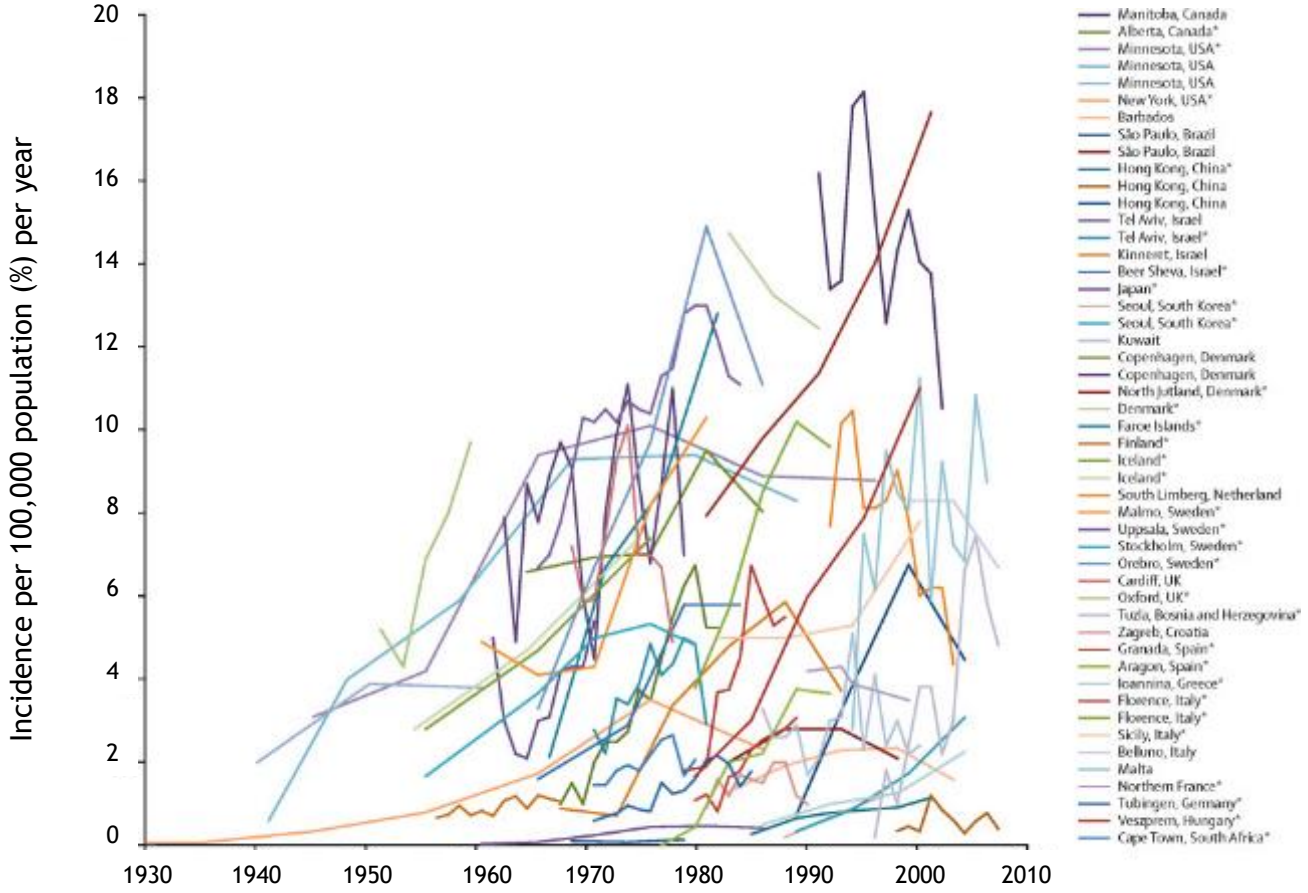
Rising incidence of Ulcerative Colitis



Ungaro et al. *Lancet*. 2016

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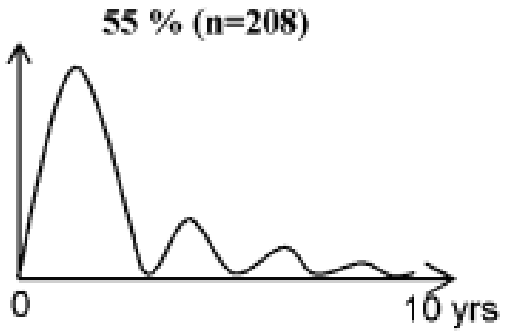
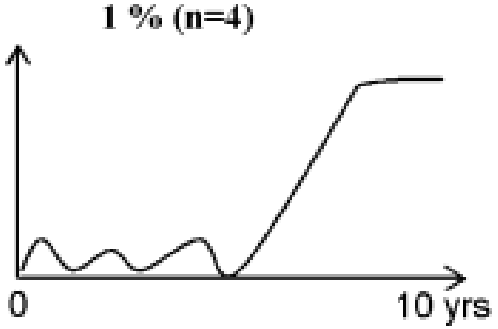
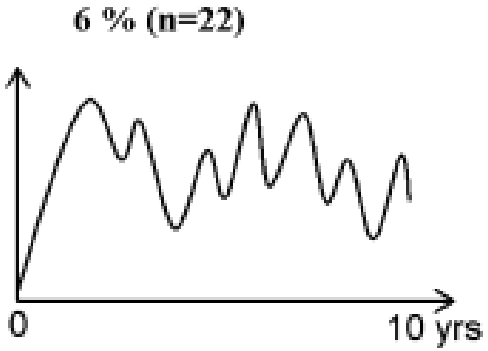
Natural history of Ulcerative Colitis



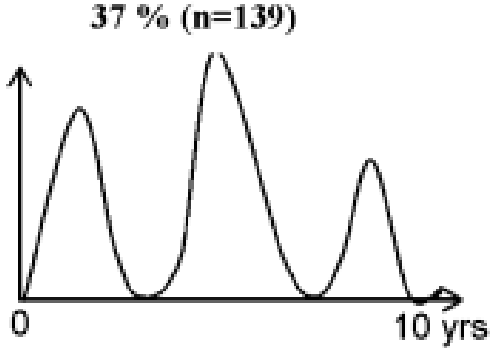
Curve1: Remission or mild severity of intestinal symptoms after initial high activity



Curve 2: Increase in the severity of intestinal symptoms after initial low activity



Curve 3: Chronic continuous symptoms



Curve 4: Chronic intermittent symptoms

Solberg I *et al. Scand J Gastro* 2009; 44:431-440.

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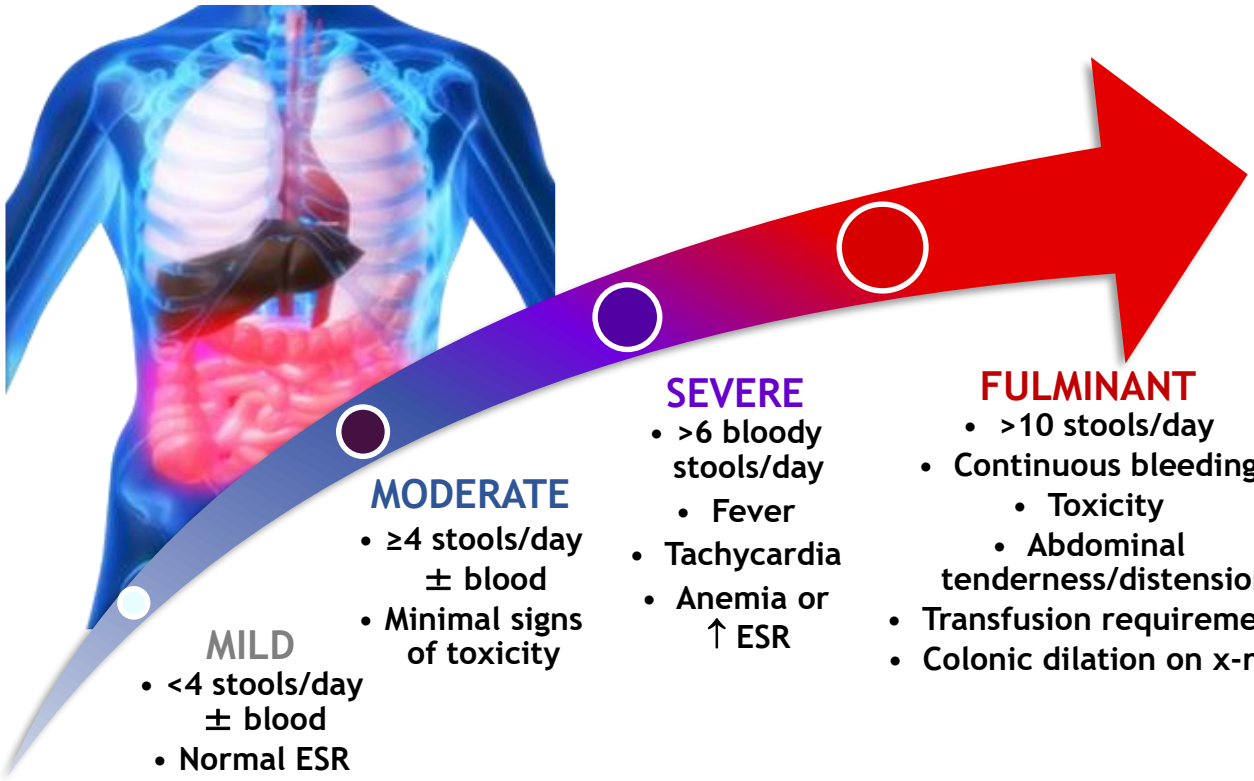
Classification of Ulcerative Colitis severity



Truelove SC, Witts LJ. *Br Med J*. 1955;2(4947):1041-8;
Kornbluth A, Sachar DB. *Am J Gastroenterol*. 2010;105(3):501-23

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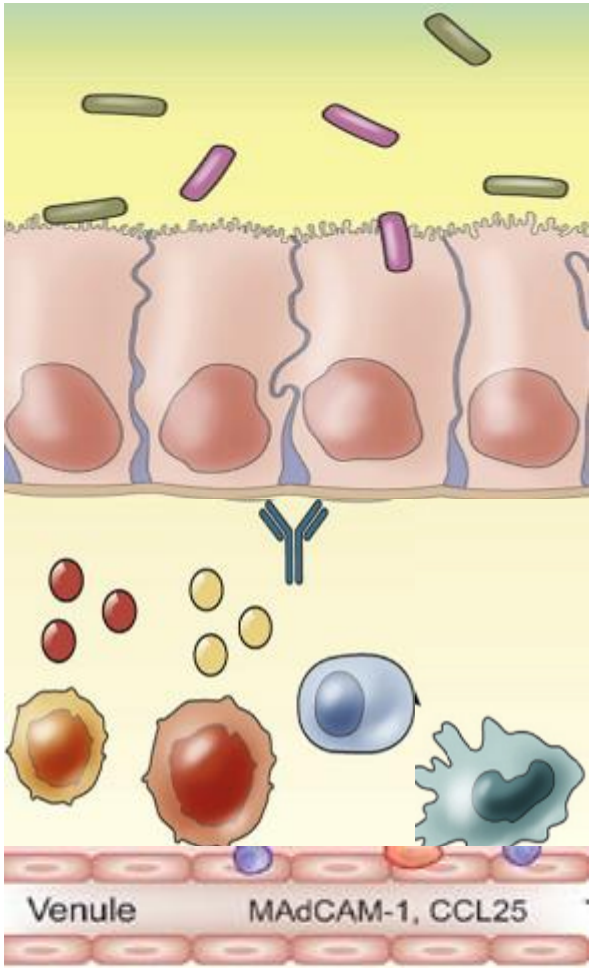
Pathogenesis

Gut Lumen

Gut Epithelium

Lamina Propria

Blood Vessel



Microbial communities
Environmental Triggers

Genetic susceptibility
Immune Dysfunction

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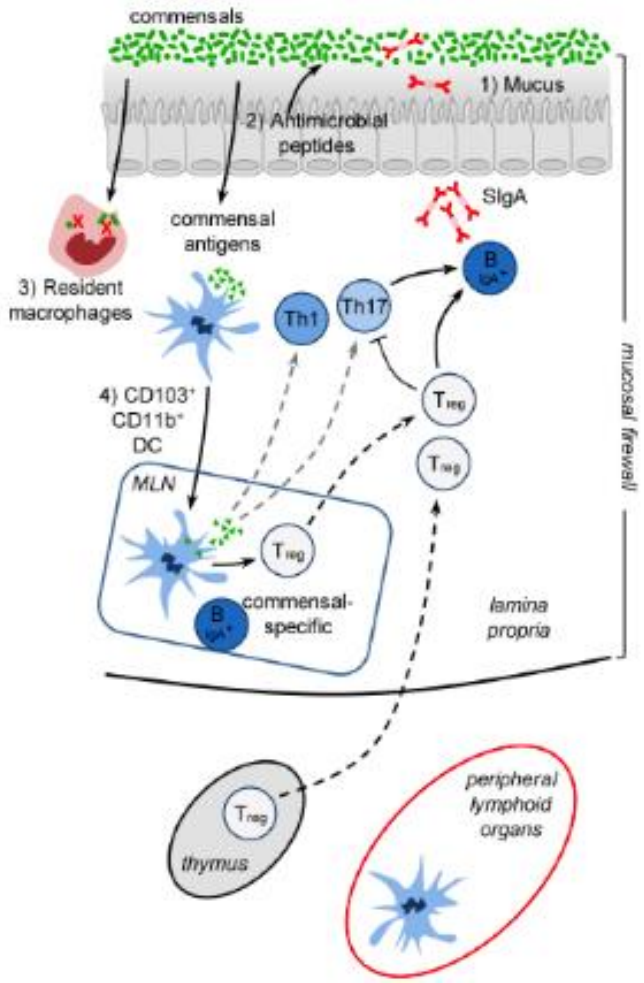
Microbiome is critical to epithelial integrity

Microbiota metabolize dietary fiber into short chain fatty acids (SCFAs), critical to gut integrity



Belkaid Cell 2014

Sartor Gastro 2008; Sokol IBD 2009; Lopetuso Gut pathogens 2013; Morgan Genome Biol 2012; Backhed 2012; Cell Host Microbe Fig 1A and Fig 1B; Segain JP Gut 2000; Saleh Immunity 2011; Shawki Cellular and Molecular Gastro Hep 2016; Saleh Immunity 2011; Noah N Cell 2014; Lopetuso Gut Pathogens 2013; Sansonetti Nature 2011; Johansson PNAS 2011; Fava WJG 2011; Cash HL Science 2006; MacPherson AJ Nat Rev Imm 2004; Bouskra D Nature 2008

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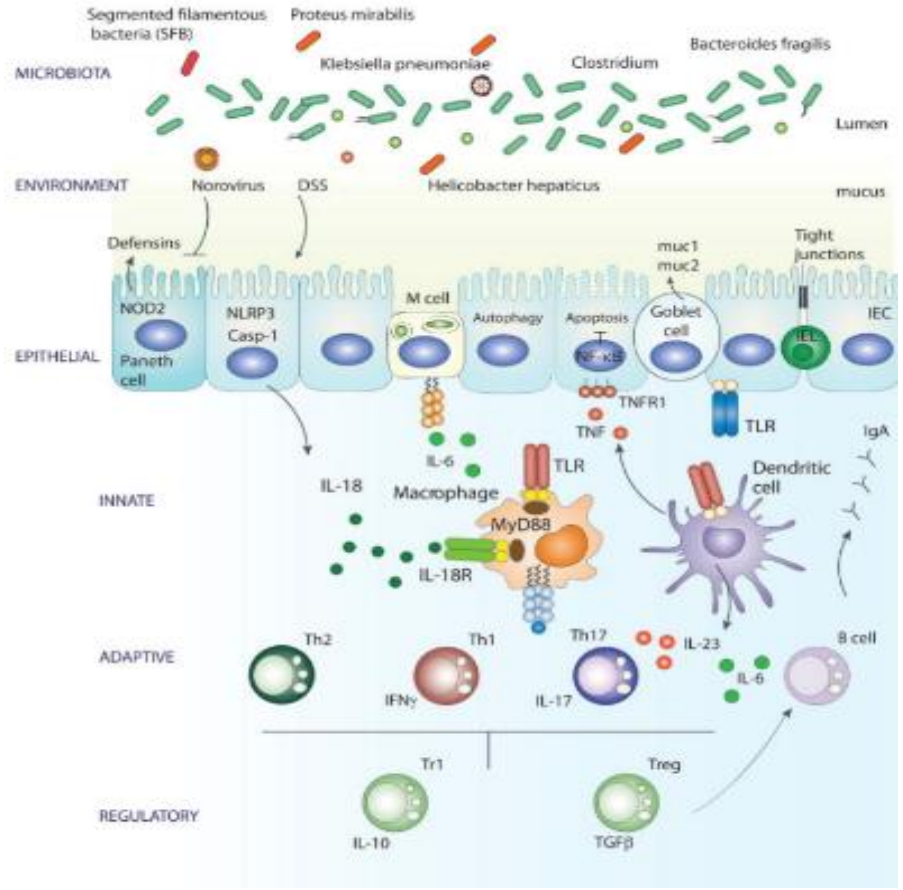
Microbiota support mucosal immunity

Gut homeostasis is maintained through a dialogue between the microbiota and the innate, adaptive, and regulatory immune systems



Saleh Immunity 2011, Backhead Cell Host Microbe 2012

Johansson PNAS 2011; Buela KA, Omenetti 2015 DOI: 26398682; Planer JD Peng Science 2016 DOI: 27279225; Abt Curr Opin Imm 2014; Saleh 2011; Sokol IBD 2009; Sartor Gastro 2008; Atarashi Nature 2013; Kostic Gastro 2014; Lathrop Nature 2012 Lopetuso Gut Pathogens 2013; Hill DA 2010; Brown EM 2013; Belkaid Y 2014; Neurath 2014; Buffie Nat Rev Immunol 2013; Duan J Kasper Cell Host Microbe 2010; Hooper LV Science 2012; Lathrop SK Nature 2012; Duan Kasper Cell Host Microbe 2010; Rakoff-Nahoum 2004

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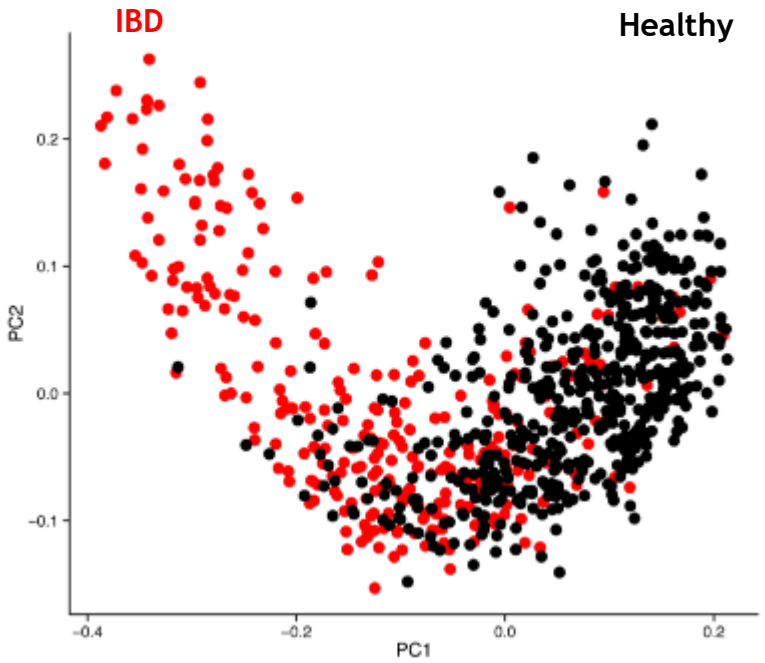
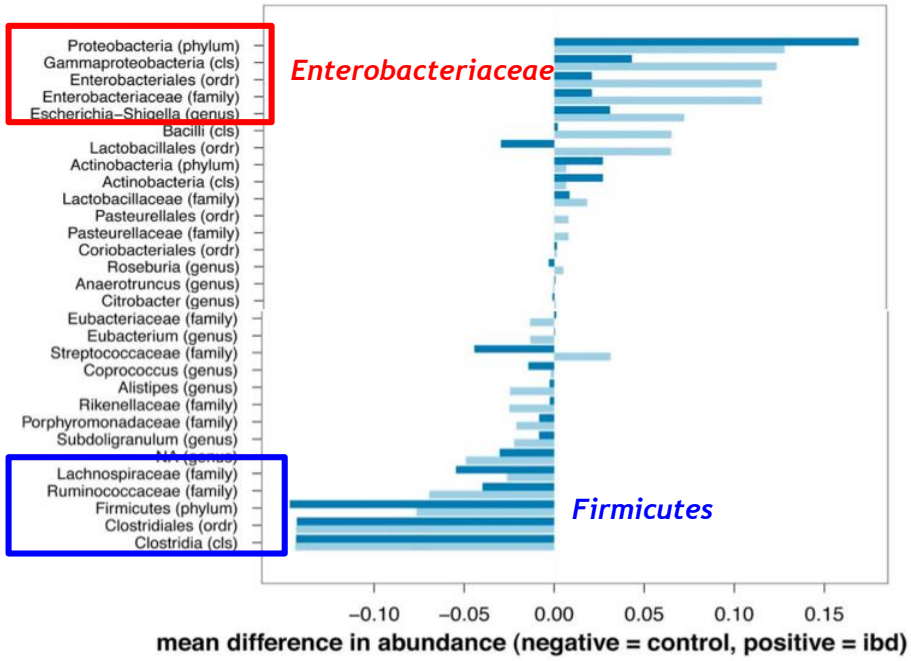
IBD patients have microbiome dysbiosis

Imhann et al., Gut *2017 (n=895)*



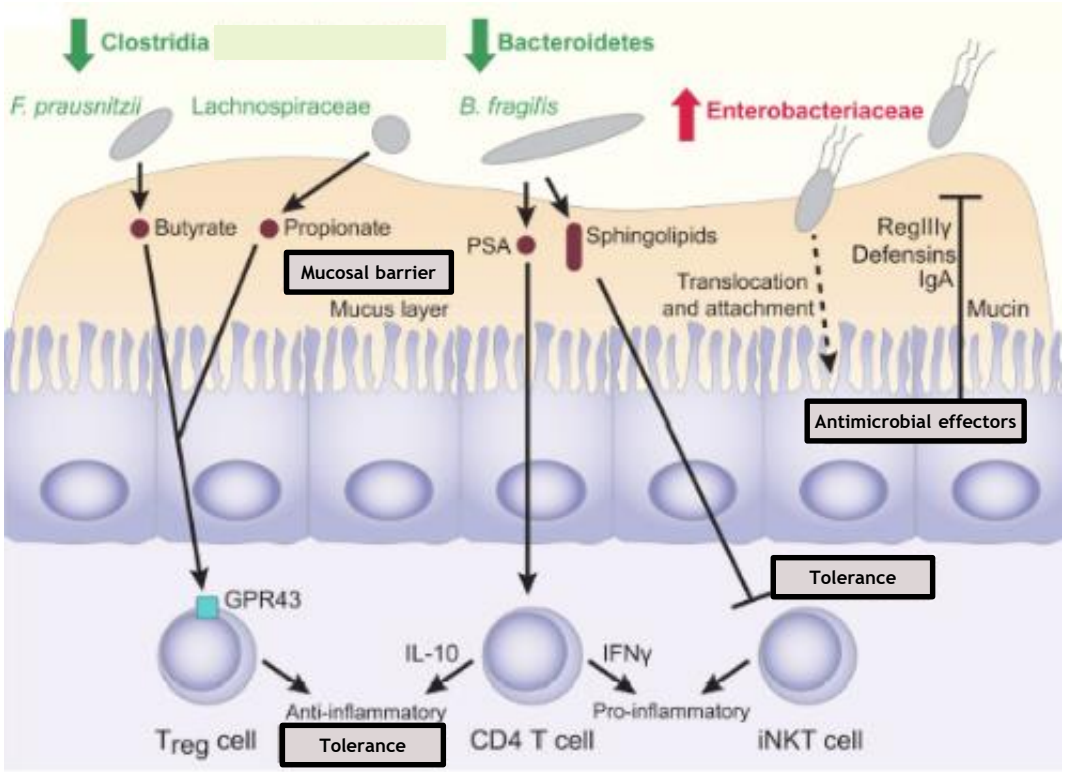
Papa et al *PLOS One* 2012 (n=91)



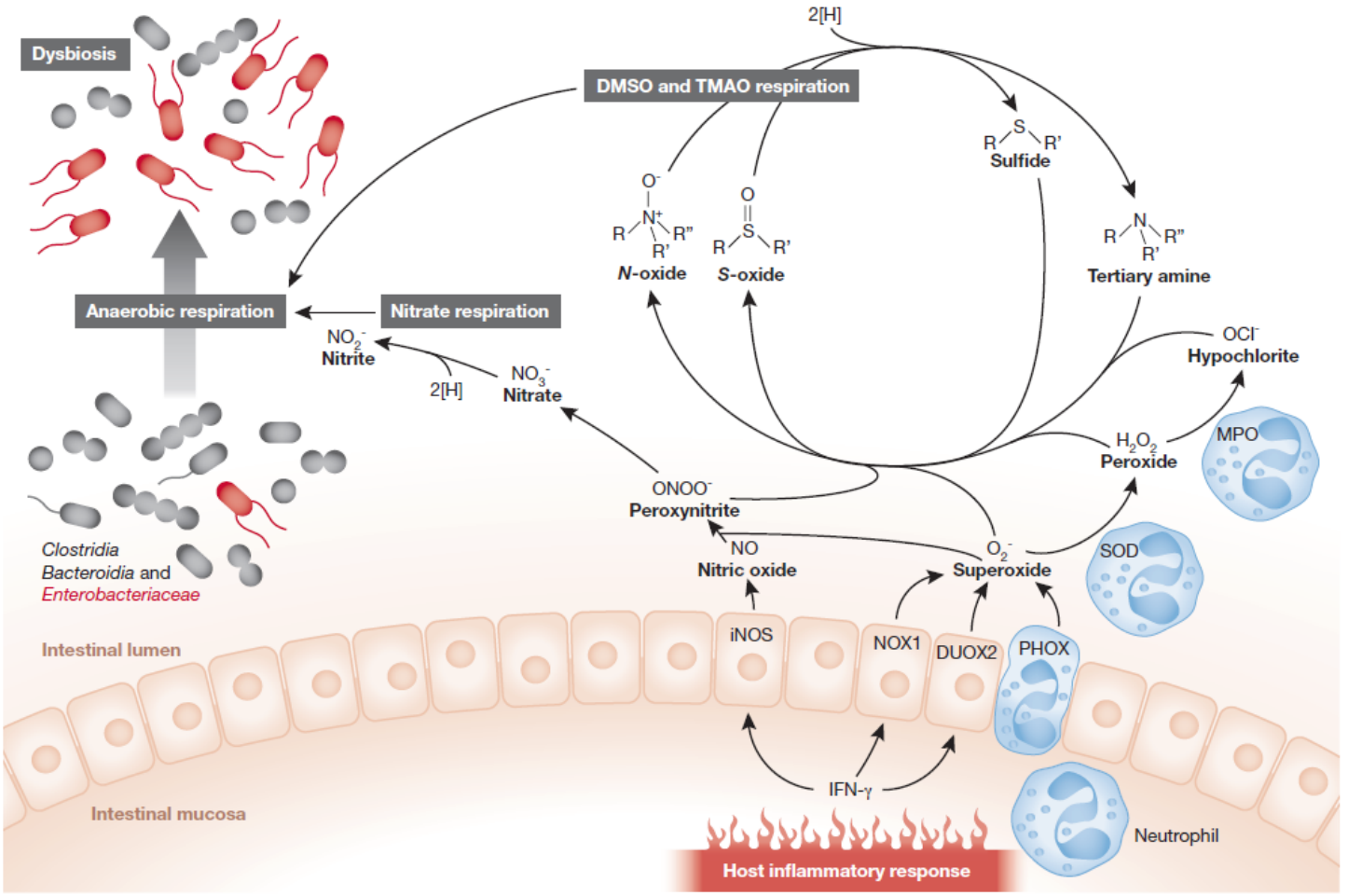
- Decreased abundance of short chain fatty acid (SCFA) producing organisms

Microbial stimuli can trigger inflammatory cytokine cascade

Microbial products or antigens stimulate mucosal immune cells and activate TLRs to produce pro-inflammatory cytokines



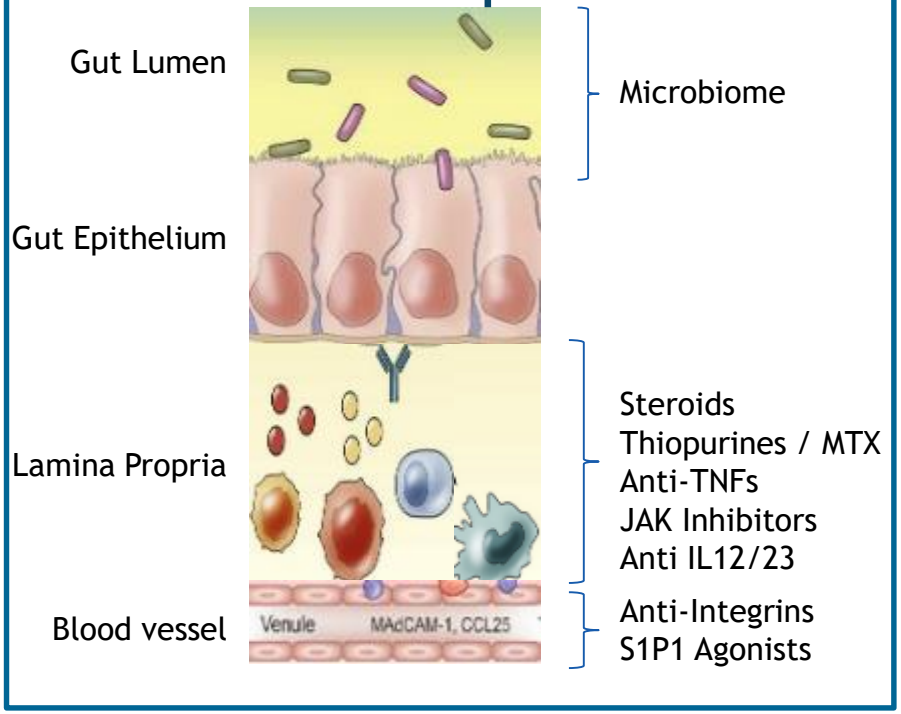
Enterobacteriaceae promotes, and *Clostridiales* suppresses, inflammation



Winters *et al. EMBO Reports* 2013

Microbiome acts through multiple pathways at physiologically relevant concentrations to alter immunological tone

Existing Agents All Act on Same Side of Gut Epithelium



- **Specific consortia of microbes affect T cell activation, cytokine networks and immune cell trafficking**
- **Demonstrated molecular mechanisms:**
  - **SCFAs:** increase Tregs; inhibit HDACs; act on PPAR-γ to downregulate iNOS; enhance tight junctions; reduce epithelial IL-8
  - **Trp metabolites:** modulate Ahr-dependent gene expression to enhance barrier integrity and modify Th17 and Treg function
  - **Bile acid metabolites:** alter pro-inflammatory signaling and barrier integrity through FXR and TGR5 pathways
  - **TLR agonists:** change signaling through inflammasome, modulate cytokines from Th17 cells and APCs

Microbiome therapeutics represent a novel modality to treat intestinal inflammation

Potential of Microbiome Therapeutics:

1. *Address key components of IBD pathogenesis*
2. *Offer safety advantages over current agents*
3. *Ideal for combination therapy*

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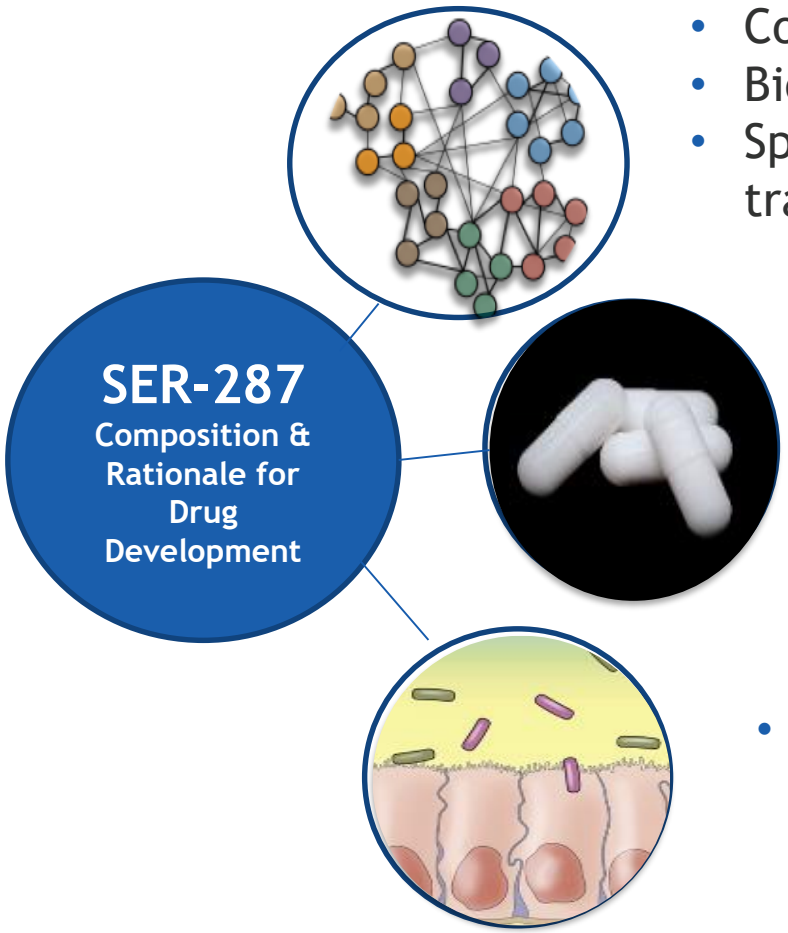
SER-287 overview



- Consortium of Firmicute bacterial spores
- Biologically sourced from healthy screened donors
- Spore purification process mitigates risk of transmission of infectious agents

- Spores are resistant to gastric acid allowing formulation into capsules
- Dormant bacterial spores germinate and engraft in the gastrointestinal tract

- Leverages compositional and functional changes in the gut microbiome to suppress colonic inflammation

Fecal microbiota transplantation has established proof of concept for the role of the microbiome in Ulcerative Colitis

- McMaster University, Toronto[1]
  - 70 patients with active UC; 6x FMT q1 week
  - 24% remission in FMT vs. 5% in POB at 7 weeks
  - Responders increased microbiota diversity
  - 7 responders received FMT from a single donor who had high Firmicute diversity & abundance
- Academic Medical Center, Amsterdam[2]
  - FMT recipients trended toward higher response rate (41.2%) vs. controls (25%) at 12 weeks
- University of Graz, Austria[3]
  - 17 patients with Mayo Score ≥ 5 and ≤ 11; 10 days of antibiotics followed by 5x FMT q 2 weeks
  - 23% endoscopic remission (Mayo ≤ 2); 58% response (reduction in Mayo ≥ 3)
- University of New South Wales, Australia
  - 81 patients with active UC (Mayo 4-10) given fecal enemas 5d/wk for 8 wks
  - Steroid-free remission and endoscopic improvement in 27% FMT vs. 8 % Pbo

THE LANCET

Multidonor intensive faecal microbiota transplantation for active ulcerative colitis: a randomised placebo-controlled trial

Sudarshan Paramsothy, Michael A Kamm, Nadeem O Kaakoush, Alissa J Walsh, Johan van den Bogaerde, Douglas Samuel, Rupert W L Leong, Susan Connor, Watson Ng, Ramesh Paramsothy, Wei Xuan, Enmoore Lin, Hazel M Mitchell, Thomas J Borody

	Faecal microbiota transplantation (n=41)	Placebo (n=40)	Risk ratio (95% CI)	p value
Primary outcome				
Steroid-free clinical remission and endoscopic remission or response*	11 (27%)	3 (8%)	3·6 (1·1–11·9)	0·021
Secondary outcomes				
Steroid-free clinical remission†	18 (44%)	8 (20%)	2·2 (1·1–4·5)	0·021
Steroid-free clinical response‡	22 (54%)	9 (23%)	2·4 (1·3–4·5)	0·004
Steroid-free endoscopic remission§	5 (12%)	3 (8%)	1·6 (0·4–6·4)	0·48
Steroid-free endoscopic response¶	13 (32%)	4 (10%)	3·2 (1·1–8·9)	0·016

*Total Mayo score ≤2, with all subscores ≤1, and ≥1 point reduction from baseline in endoscopy subscore. †Combined Mayo subscores of ≤1 for rectal bleeding plus stool frequency. ‡Decrease of ≥3 points or ≥50% reduction from baseline (or both) in combined Mayo subscores for rectal bleeding plus stool frequency. §Mayo endoscopy subscore 0. ¶Mayo endoscopy subscore ≤1, with ≥1 point reduction from baseline.

Table 2: **Primary and secondary outcomes at week 8**

[1]Moayyedi P, et al. Gastroenterology, 2015,
[2]Rossen NG, et al. Gastroenterology, 2015
[3]Gorkiewicz et al, confidential communication
[4]Paramosthy et al. Lancet, 2017

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SER-287 Phase 1b study objectives

Primary Objectives:

- Safety and tolerability
- Engraftment of SER-287 dose species into the recipient

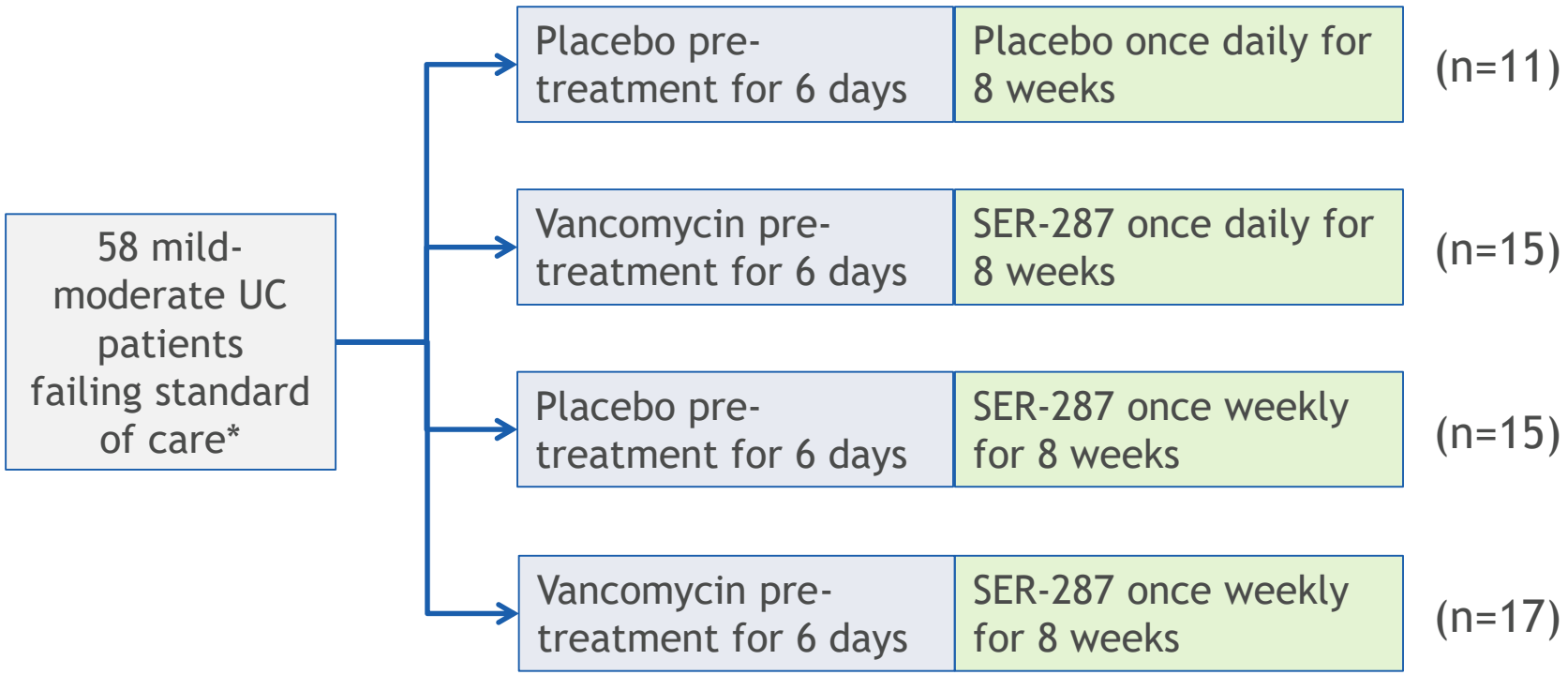
Select Secondary Objectives Evaluated at Week 8 of induction:

- Clinical remission defined as Total Modified Mayo Score (TMMS) ≤2 plus endoscopic subscore (ESS) of 0/1
- Endoscopic improvement defined as a decline in ESS of ≥ 1
- Clinical Response defined as ≥3 point decline from baseline TMMS *plus either* a) ≥1 point decline in rectal bleeding subscore; or b) absolute rectal bleeding subscore of 0 or 1

Post-hoc analysis:

- Histologic changes using the Robarts Histologic Scoring system

SER-287 Phase 1b Ulcerative Colitis study



* Study designed to enroll 55 patients, with 15 in SER-287 treatment arms and 10 in the placebo / placebo arm

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Why pretreat with antibiotics?

Creates an **“ecologic niche”** for better engraftment of SER-287 species

Why pretreat with antibiotics?

Creates an **"ecologic niche"** for better engraftment of SER-287 species

Why oral vancomycin?

Rationale:

- Favorable safety profile with minimal systemic exposure
- Low risk for inducing *Clostridium difficile* infection
- Has activity against Gram positive anaerobes which constitute a significant portion of the gut microbiome

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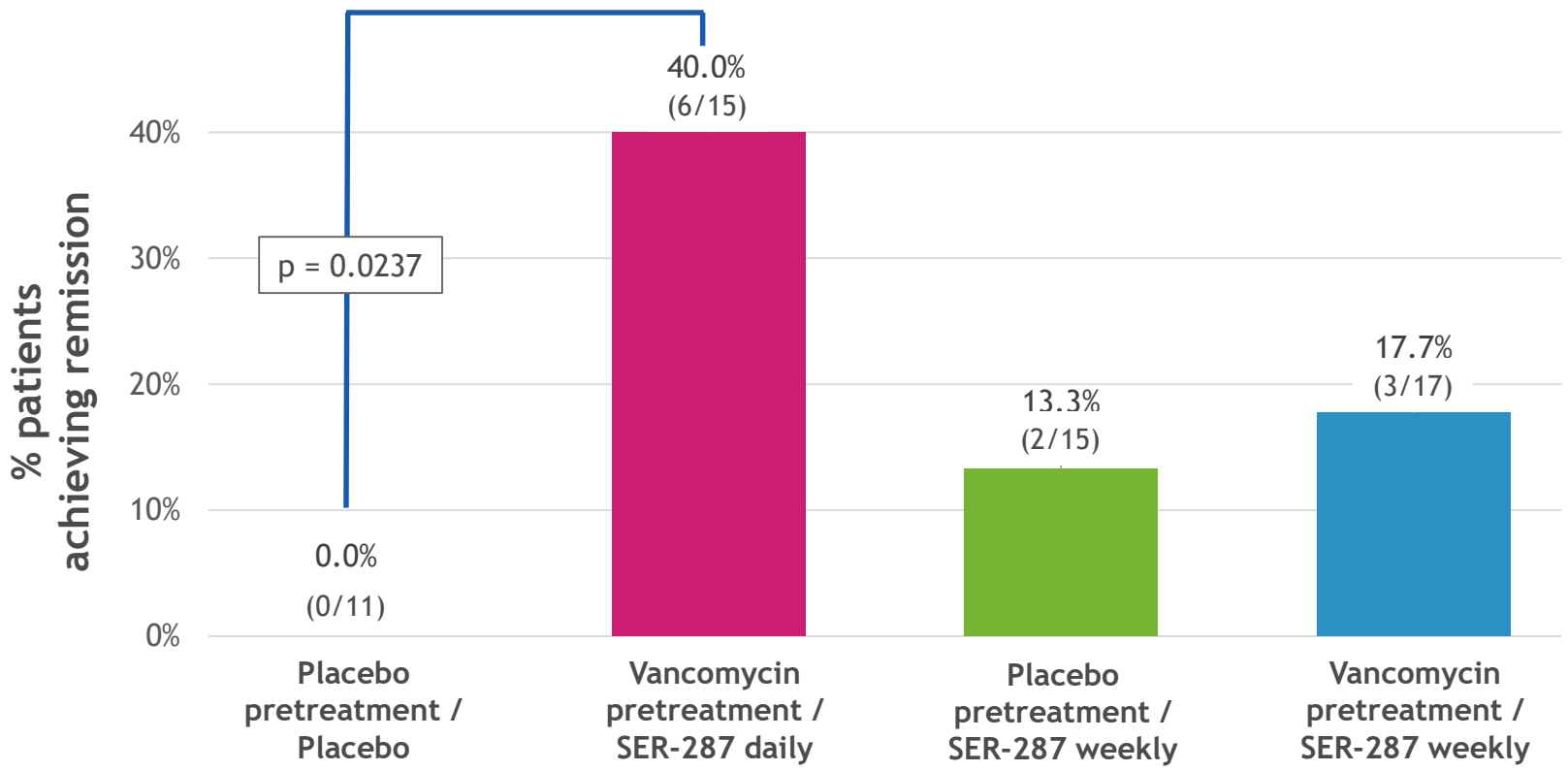
Significant and dose dependent impact on remission



Remission = Total Modified Mayo score ≤ 2 AND endoscopic subscore ≤ 1
Note: Missing data treated as failure

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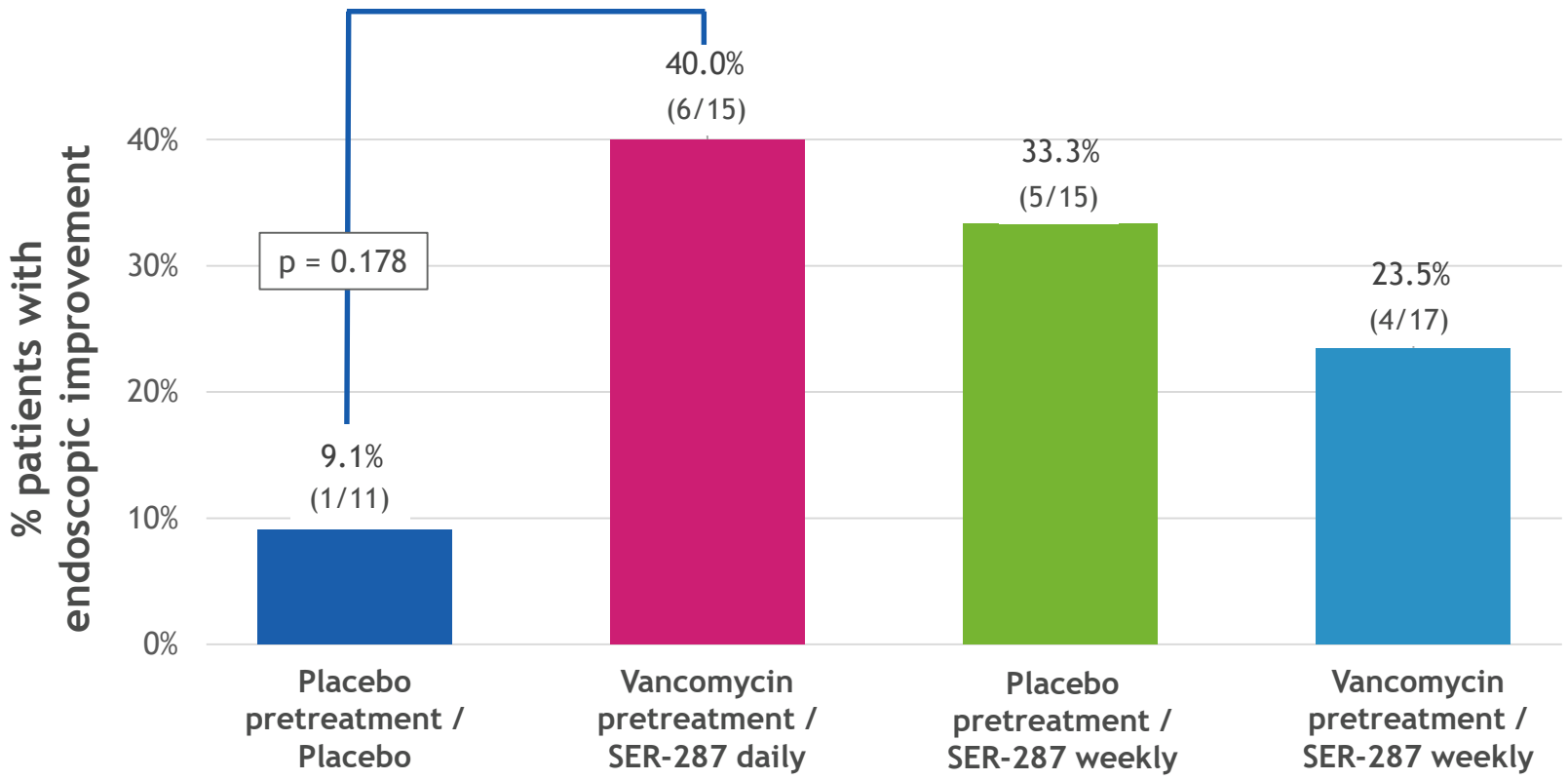
Dose dependent impact on endoscopic improvement



Endoscopic Improvement: Decrease in endoscopic subscore ≥ 1
Note: Endoscopy readings were centrally read by blinded readers, missing data treated as failure

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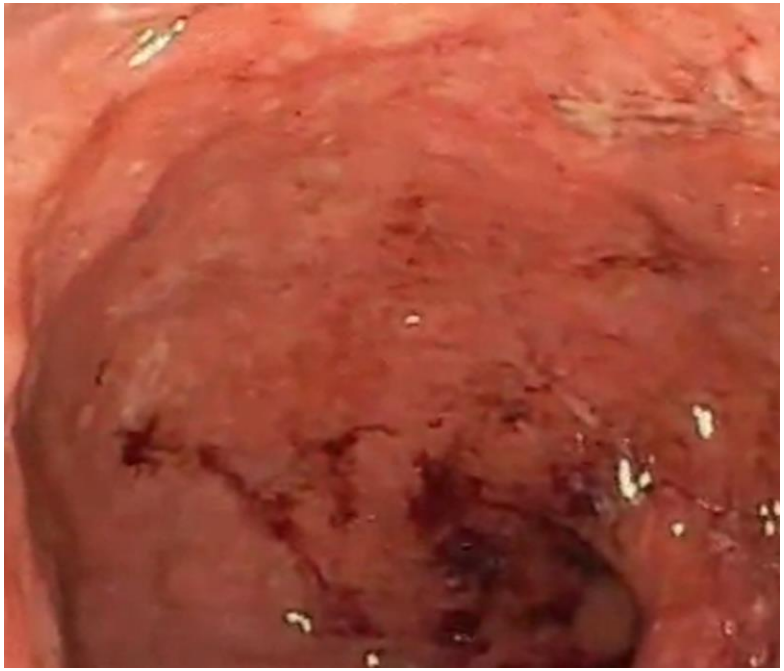
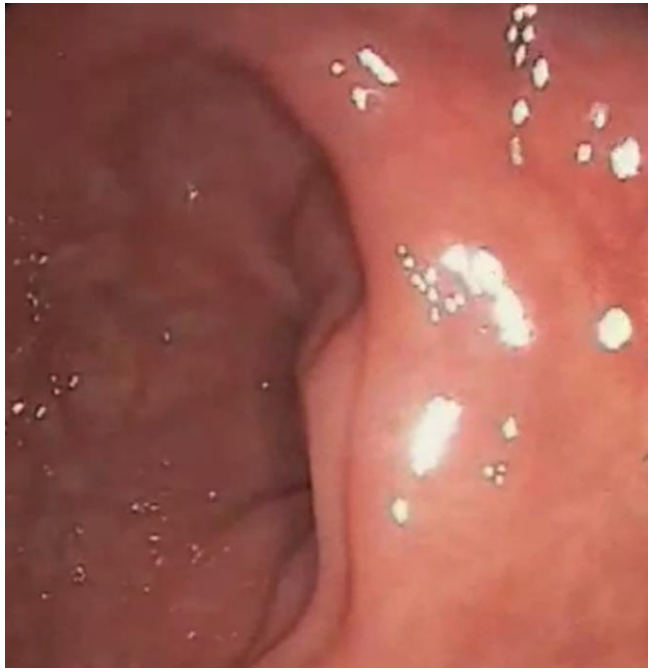
Illustrative endoscopy improvement — SER-287 daily treatment

Pre-treatment endoscopy showing the sigmoid colon with spontaneous bleeding and ulceration



Post-treatment day 64 endoscopy



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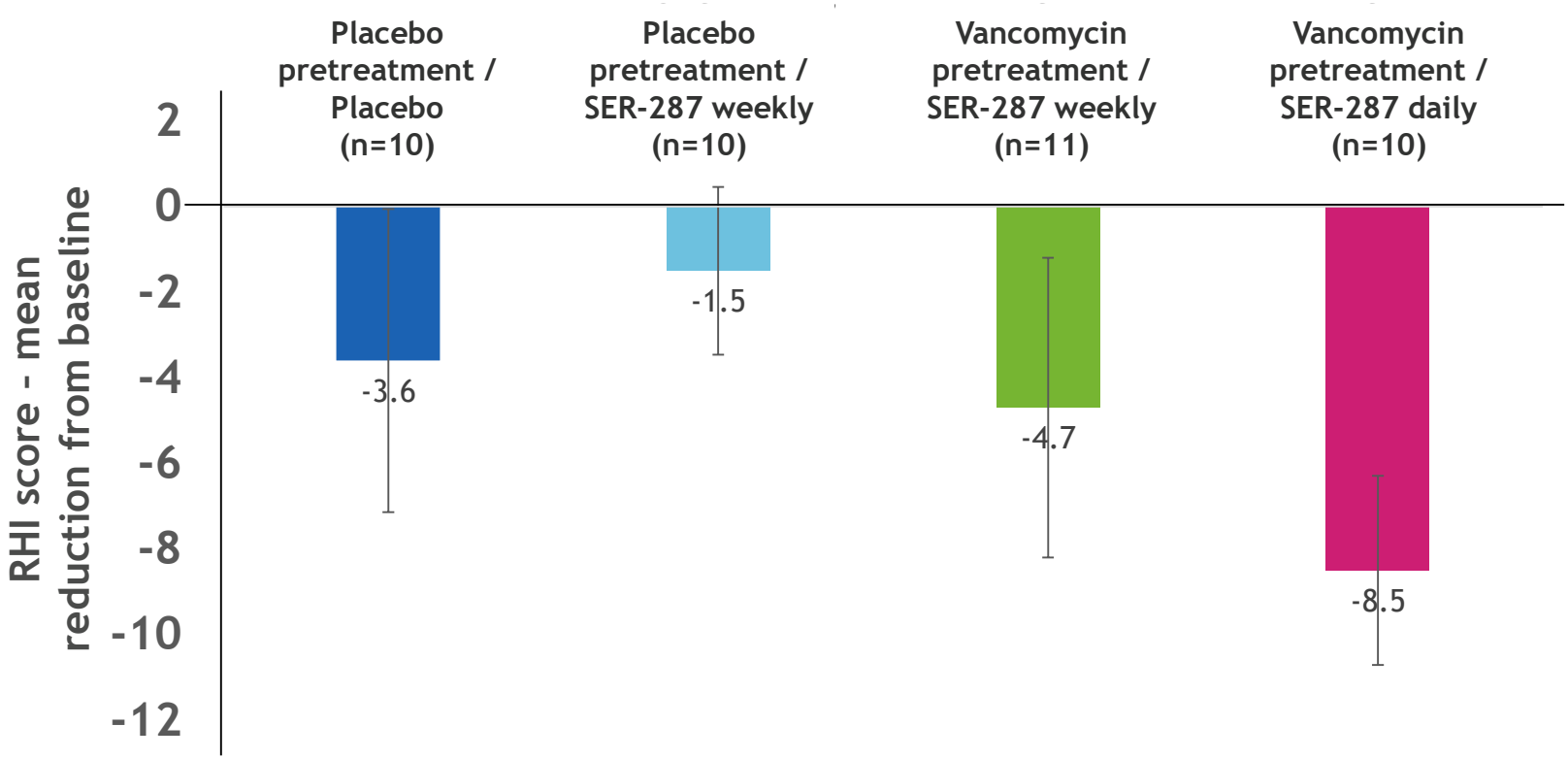
Histological healing RHI score change 8 weeks post SER-287 administration



Subjects with normal histology at baseline were excluded

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Analysis of patients previously treated with biologics

- 6 patients in the study were previously treated with biologics for ulcerative colitis:
  - 4 patients in vanco pre-treat, SER-287 daily arm
  - One in vanco pre-treat, SER-287 weekly arm
  - One in placebo arm
- Of the 4 patients in the vanco pre-treat, SER-287 daily arm:
  - 2 (50%) achieved clinical remission
  - 3 (75%) achieved endoscopic improvement

Favorable SER-287 Phase 1b safety profile

- SER-287 administration arms demonstrated a similar safety profile to placebo
- No serious drug-related adverse events
- No subject discontinuations in the SER-287 daily treatment arm
- Reduced gastrointestinal adverse events provide an independent assessment of efficacy with decreased disease activity
  - SER-287 daily arm GI AEs: 2/15 (13.3%) vs. placebo arm: 5/11 (45.5%)

SER-287 Engraftment & Mechanism of Action

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Leading the Microbiome Revolution

SER-287 Phase 1b PK and PD results provide support for the mechanism of action

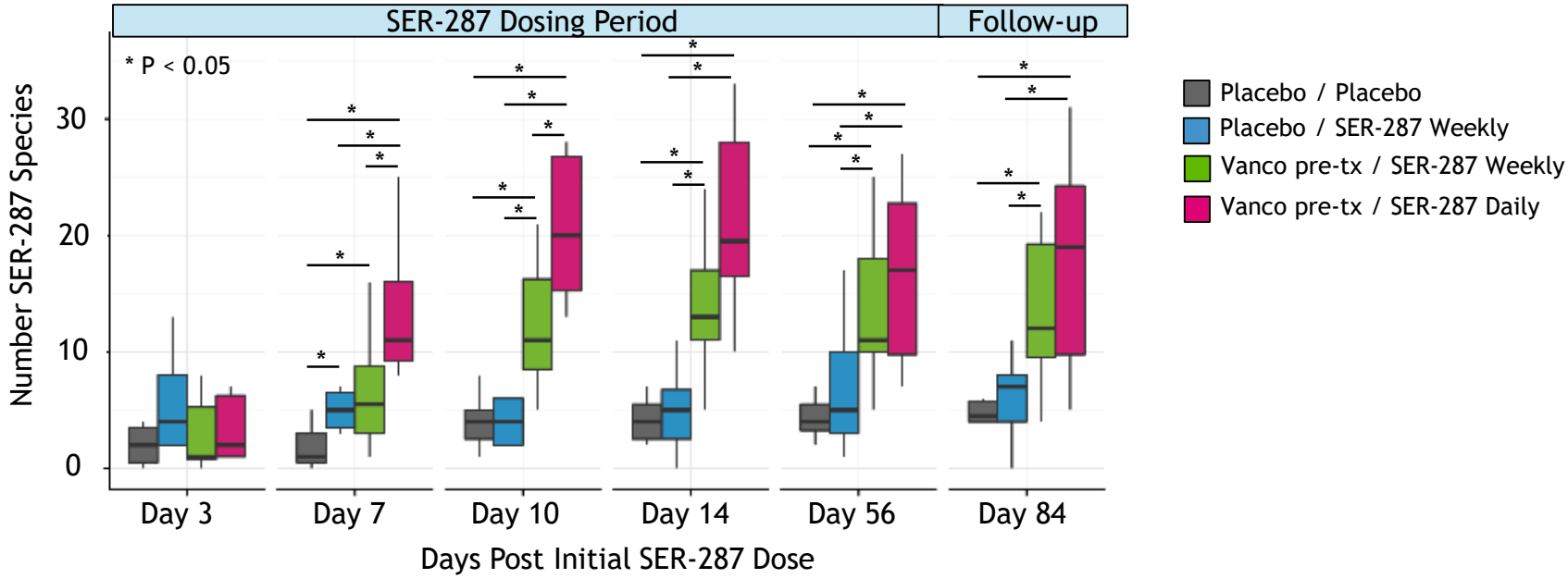
Pharmacokinetics (PK)

- *Kinetics of product engraftment: the presence of bacteria in the drug in subjects over time*

Pharmacodynamics (PD)

- *Overall changes in the composition of the microbiome and corresponding alterations in microbial metabolites and host biomarkers*

Pharmacokinetics: Significant engraftment of SER-287 species starting 7 days post treatment



- **Engraftment is greatest in daily dosing arm – arm with largest number of clinical remissions**
- **Engraftment in vancomycin arms is dose-dependent; significantly greater in daily dose**
- **In the weekly dosing arms, engraftment is significantly greater in arm with vancomycin pre-tx**
- **Engraftment is durable through last sampling timepoint; 4 weeks post-dosing with SER-287**
- **SER-287 engraftment leads to broader changes in the composition of subjects' intestinal microbiome that can differentiate clinical remission from non-remission subjects**

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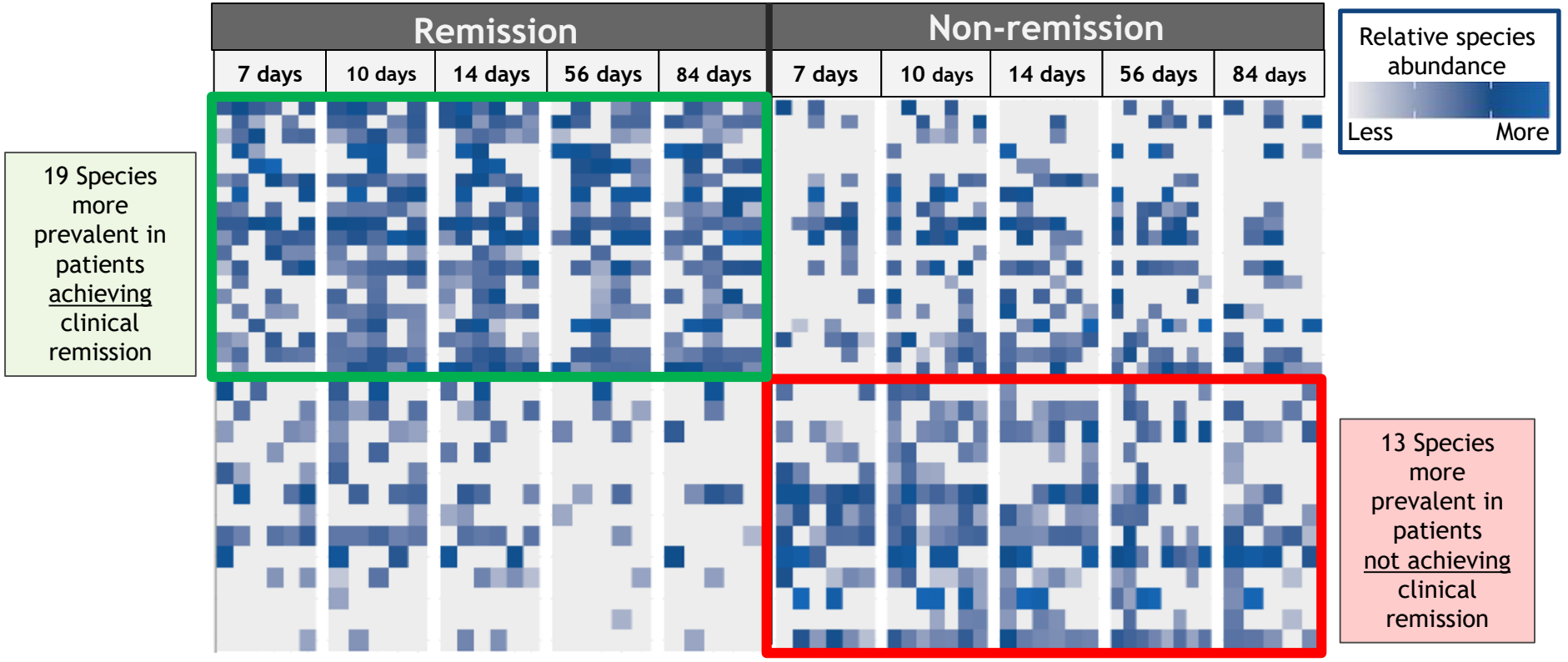
Identified bacterial species signature that associates with clinical remission vs non-remission



- Predictive species include both SER-287 bacteria and others augmented by treatment
- Functional characterization of signature species is informing drug mechanism of action

Relative abundance heatmap depiction of bacterial species prevalence from vanco/SER-287 daily study arm patients.
Each row represents a single bacterial species and each column represents a single patient at a given timepoint.
Shading of each square illustrates the relative abundance of each species.

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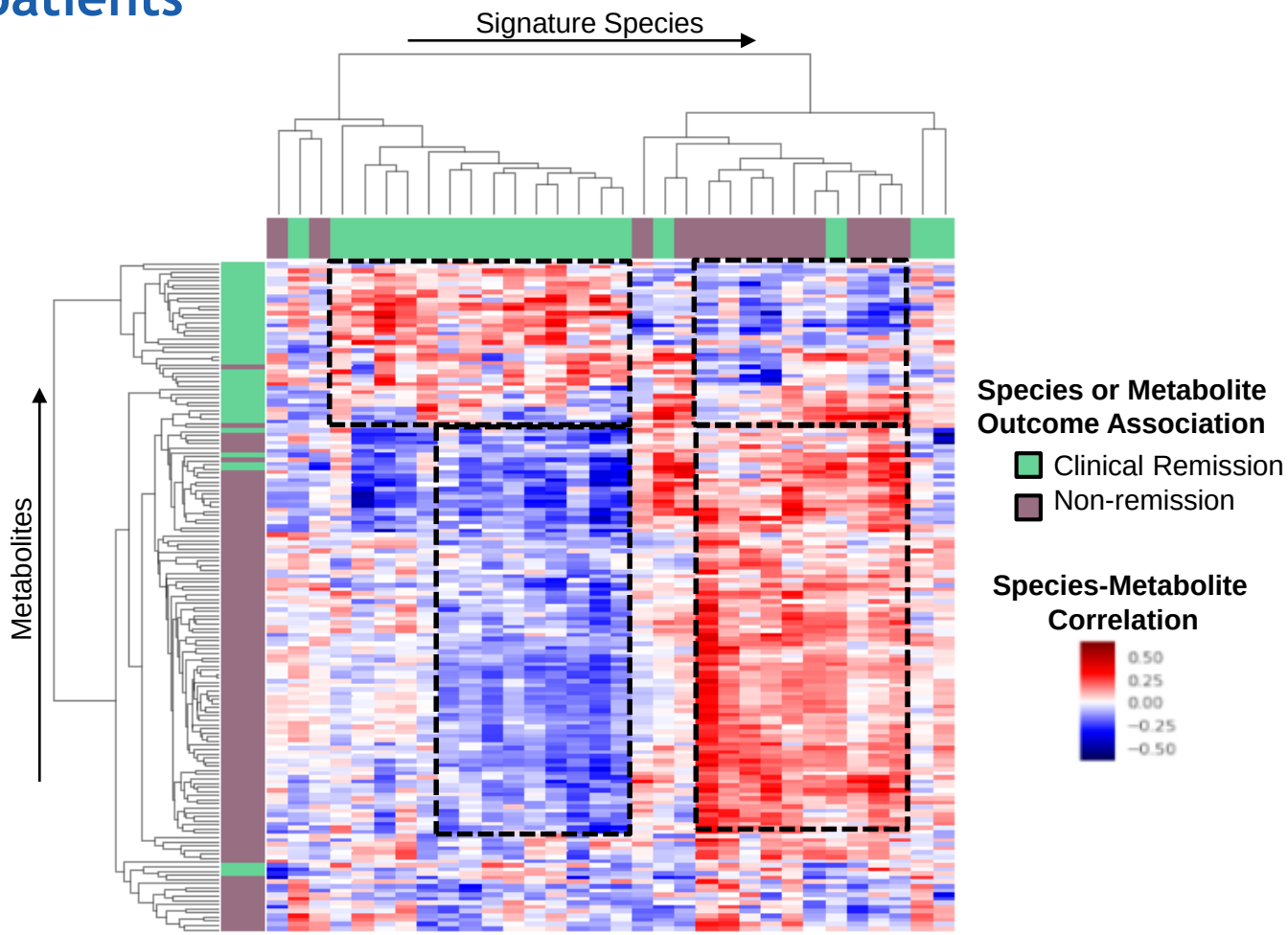
Pharmacodynamics: Signature species associated with clinical remission are strongly correlated with metabolite shifts within SER-287 treated patients

- Strong correlation between species and metabolites that predict clinical remission
- Metabolomic signature of clinical remission represents diverse functional pathways; many pathways identified are implicated in IBD and immune dysregulation



Heatmap depicts correlation between relative abundances of signature bacterial species and metabolites. Species and metabolites associated with clinical remission using independent methods are also shown.

Metabolic pathways modulated by SER-287 and associated with clinical remission impact inflammatory and immune state

- **Short Chain Fatty Acids (SCFAs):**
  - Promote anti-inflammatory responses: enhance epithelial tight junctions, increase in regulatory T cells (Treg), inhibit histone deacetylases, reduce epithelial interleukin 8 (IL-8), act on PPAR-γ to downregulate inducible nitric oxide synthase (iNOS)
- **Tryptophan (Trp) metabolites:**
  - Promote anti-inflammatory responses: induce AhR-dependent gene expression that is associated with down-regulation of interferon gamma (INFγ) and tumor necrosis factor alpha (TNFα) and upregulation of interleukin 22 (IL-22); enhance epithelial integrity and mucus secretion
- **Bile acid metabolites:**
  - Alter pro-inflammatory signaling and epithelial barrier integrity through FXR and TGR5 pathways

Bile acid metabolism can impact IBD and immune regulation

Liver → BSH* → **Primary Bile Acids (1° BA)** → 7αDH* → **Secondary Bile Acids (2° BA)**

Glycine/Taurine Conjugates

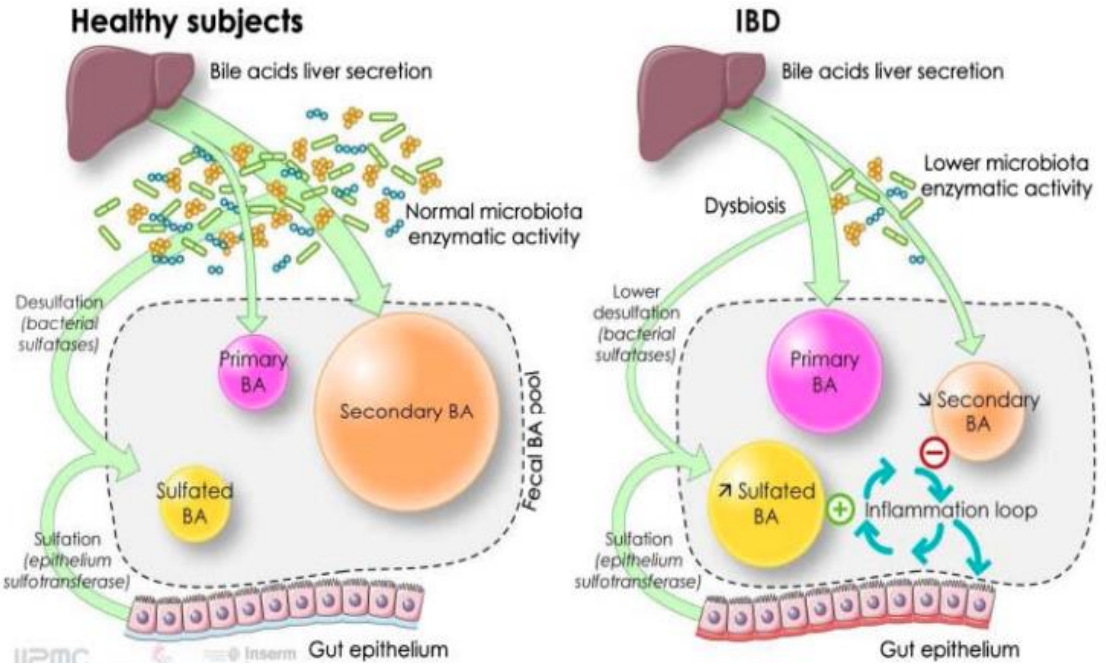
Cholic acid (CA)
Chenodeoxycholic acid (CDCA)

Deoxycholic acid (DCA)
Lithocholic acid (LCA)

Additional 2°
Bile Acid derivatives

*microbial mediated metabolism

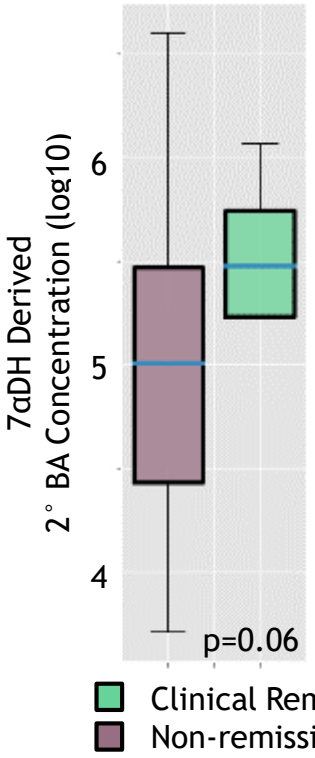
- **2° BA are generally reduced in IBD with lowest levels in subjects with active disease**
- **2° BA signal via FXR and TGR5; modulate anti-inflammatory pathways**
  - **FXR** - modulates NFkB to regulate cytokine production
  - **TGR5** - modulates cAMP mediated pathways to suppress inflammatory responses



Duboc H, et al. 2013. Gut. 62:531-539

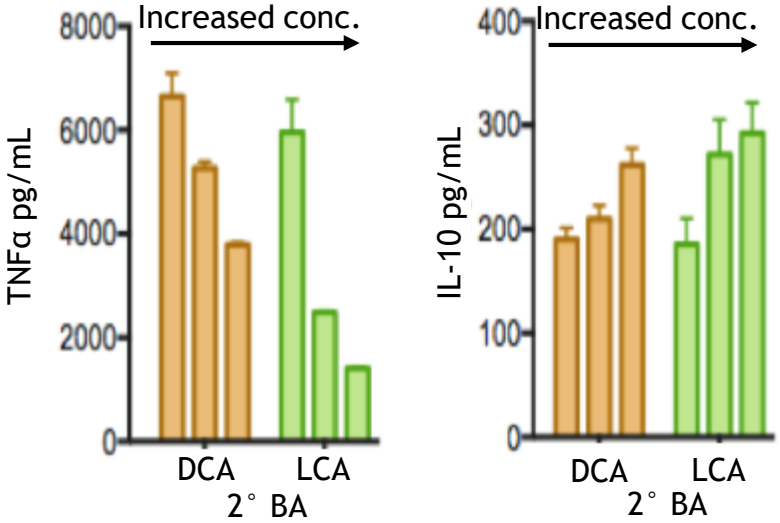
Secondary bile acids metabolism is increased in subjects with clinical remission

Secondary bile acids (2° BA) derived from microbial mediated metabolism are positively associated with clinical remission



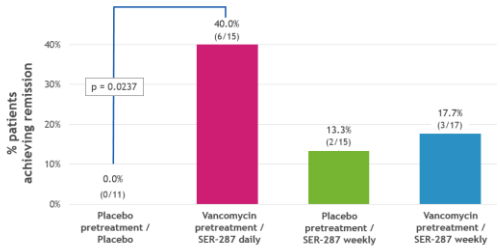
- Across all SER-287 treatment arms, subjects with clinical remission had greater levels of 2° BA by 8 weeks post treatment
- Identified specific SER-287 engrafting species that associate with variation in 7α-dihydroxylation (7αDH) 2° BA levels in treated subjects

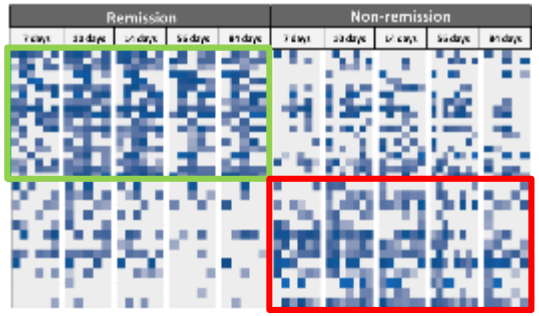
Secondary bile acids (2° BA) have confirmed dose dependent anti-inflammatory effects in peripheral blood mononuclear cells in vitro

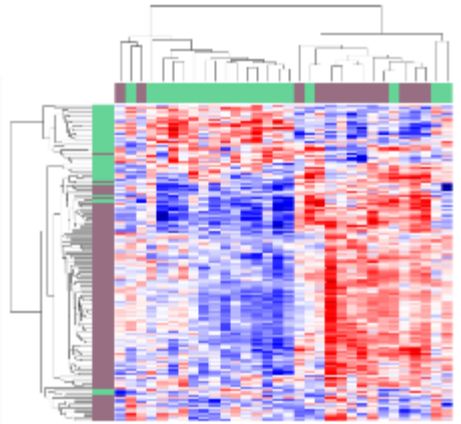


- Increased concentrations of 2° BA lead to decrease in pro-inflammatory TNFα and increase in anti-inflammatory IL-10
- Observed in PBMCs and isolated monocytes

SER-287 Phase 1b data demonstrate clinical effect and provide supportive molecular mechanistic data







CLINCAL OUTCOME

Dose dependent clinical remission

SPECIES SIGNATURES

Engraftment (PK) associated with clinical remission

METABOLITES & PATHWAYS

Metabolites and functional pathways (PD) associated with remission and microbiome change

SER-287 Presentations at Digestive Disease Week 2018

***Oral Presentation*: SER-287 Phase 1b clinical trial results in mild-to-moderate ulcerative colitis during "Distinguished Abstract Plenary"**

- Date: June 2nd 10:30-10:45 am
- Speaker: Bharat Misra, M.D. (Borland Groover Clinic)

***Late Breaker Poster*: Data on engraftment of SER-287 dose species**

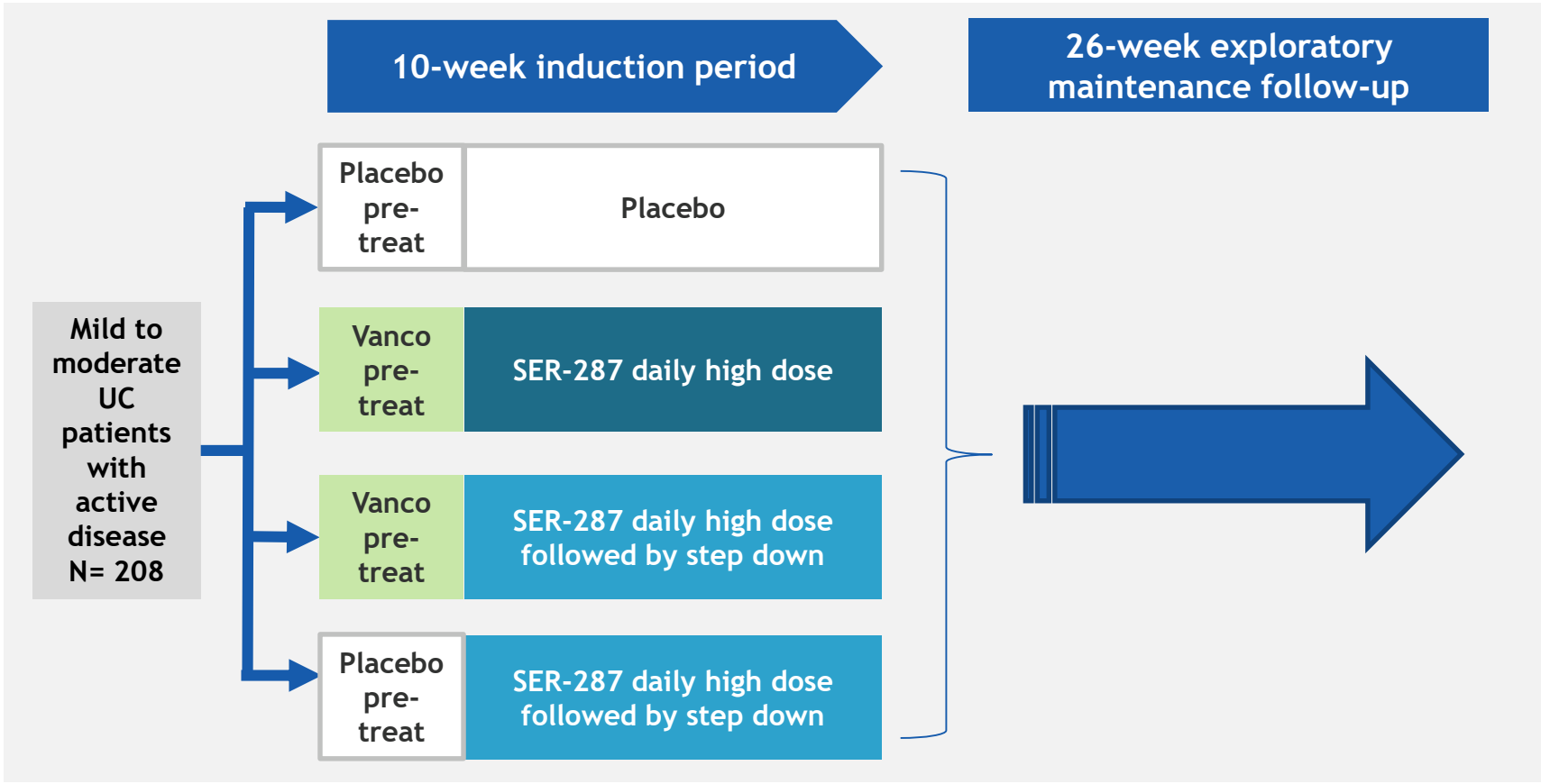
- Date: Tuesday June 5th 12:00-2:00 pm
- Presenter: Sheri Simmons (Seres Therapeutics)

***Scientific Symposium*: "Transforming the Therapeutic Landscape for Ulcerative Colitis: Putting a Spotlight on Microbiome Therapeutics"**

- Symposium Monday June 4th from 7:00-8:30 pm at Grand Hyatt Washington
- Speakers:
  - Maria Abreu, M.D. (U. Miami)
  - Jean-Frederic Colombel, M.D. (Mt. Sinai)
  - William Sandborn, M.D. (UCSD)

Planned SER-287 Phase 2B study design

- Study to further evaluate induction dosing and longer term maintenance efficacy
- Design expected to support potential FDA registrational data package and with compelling data may be considered a pivotal trial
- Expect to initiate study in the coming months



Six day pretreatment period with either placebo or oral vancomycin
Step down = two weeks of SER-287 daily high dose, followed by lower dose

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Agenda

8:00-8:10 a.m.
Opening remarks
Roger Pomerantz, M.D., Seres President, CEO and Chairman

8:10-8:20 a.m.
The microbiome as a new therapeutic modality
Will Dere, M.D., Seres Board Member

ULCERATIVE COLITIS
8:20-8:40 a.m.
Pathology and role of the microbiome
Alan Moss, M.D., Beth Israel Deaconess Medical Center

8:40-9:05 a.m.
SER-287 Phase 1b results and continued late stage development
Shelley Trucksis, Ph.D., M.D., Seres Executive Vice President and Chief Medical Officer and Matthew Henn, Ph.D., Seres Executive Vice President, Microbiome Research and Development

9:05-9:25 a.m.
Microbiome therapeutic development
Stephen Hanauer, M.D., Northwestern University

9:25-9:30 a.m.
Break

IMMUNO-ONCOLOGY
9:30-9:40 a.m.
Rationale for microbiome drug development in cancer
David Cook, Ph.D., Seres Executive Vice President of R&D and Chief Scientific Officer

9:40-10:00 a.m.
Microbiome therapeutics and immuno-oncology – Charting a path forward
Jennifer Wargo, M.D., MD Anderson Cancer Center

10:00-10:30 a.m.
Q&A Session

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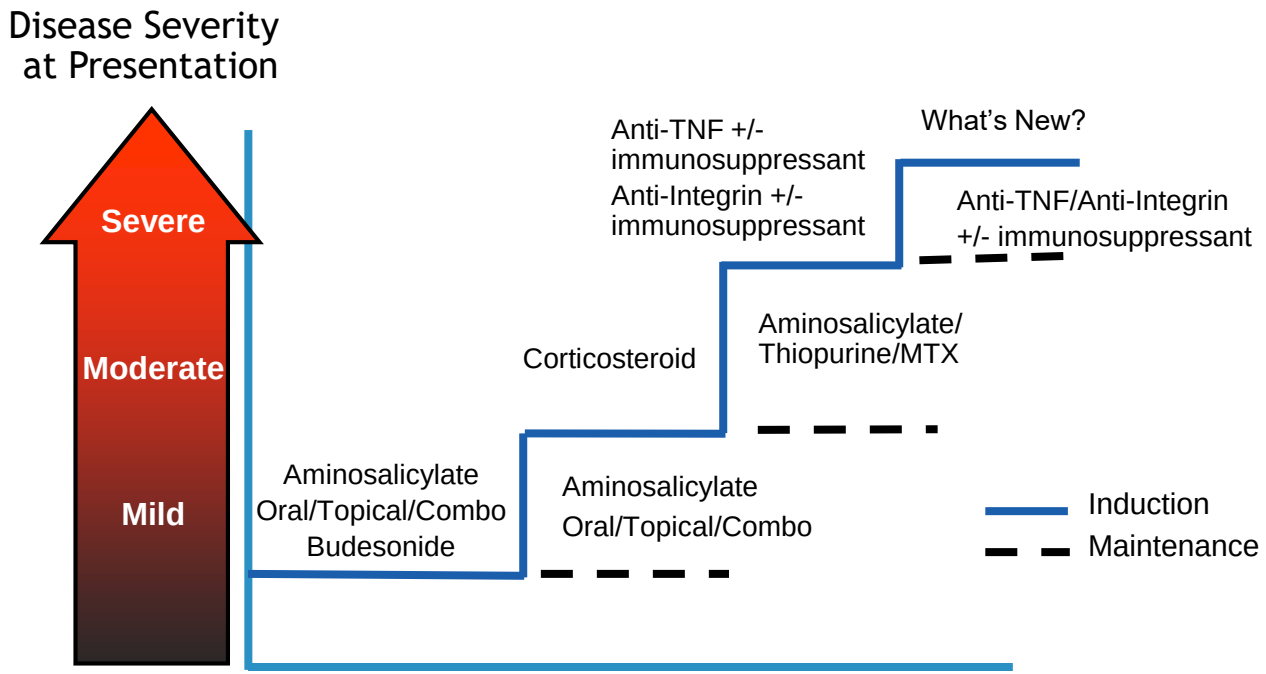
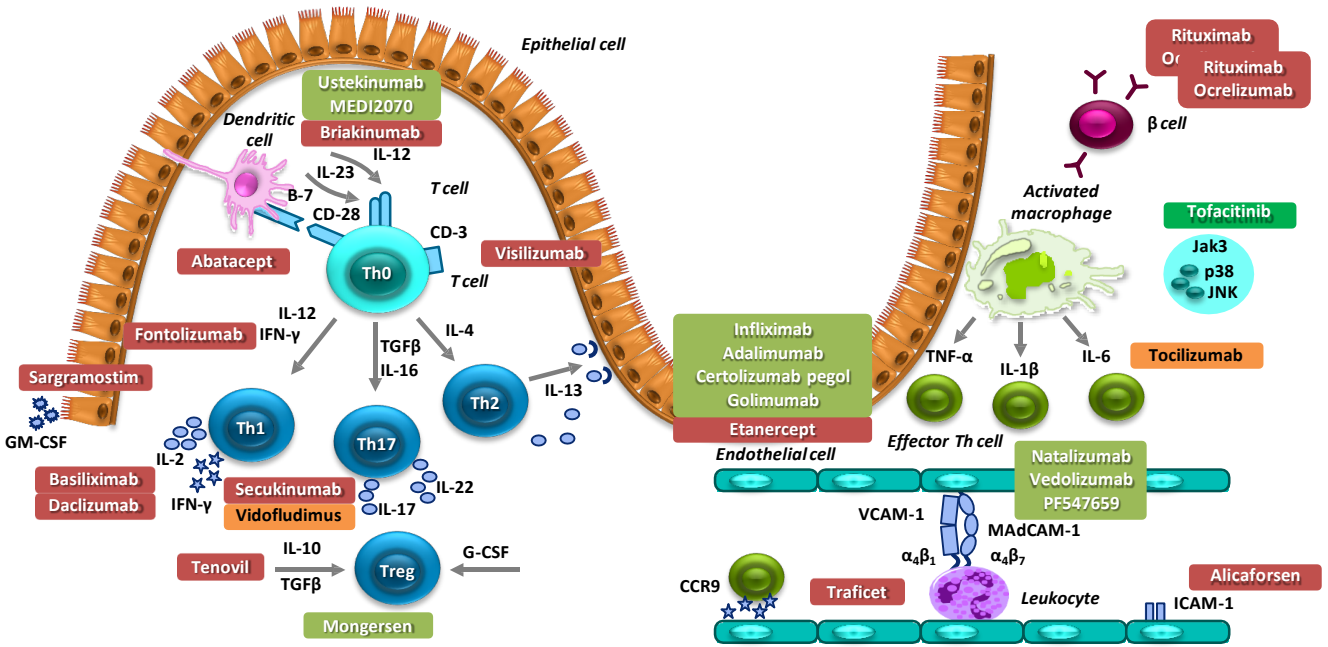
Sequential Therapies for Ulcerative Colitis

Therapy according to severity & prognosis at presentation or failure at prior step

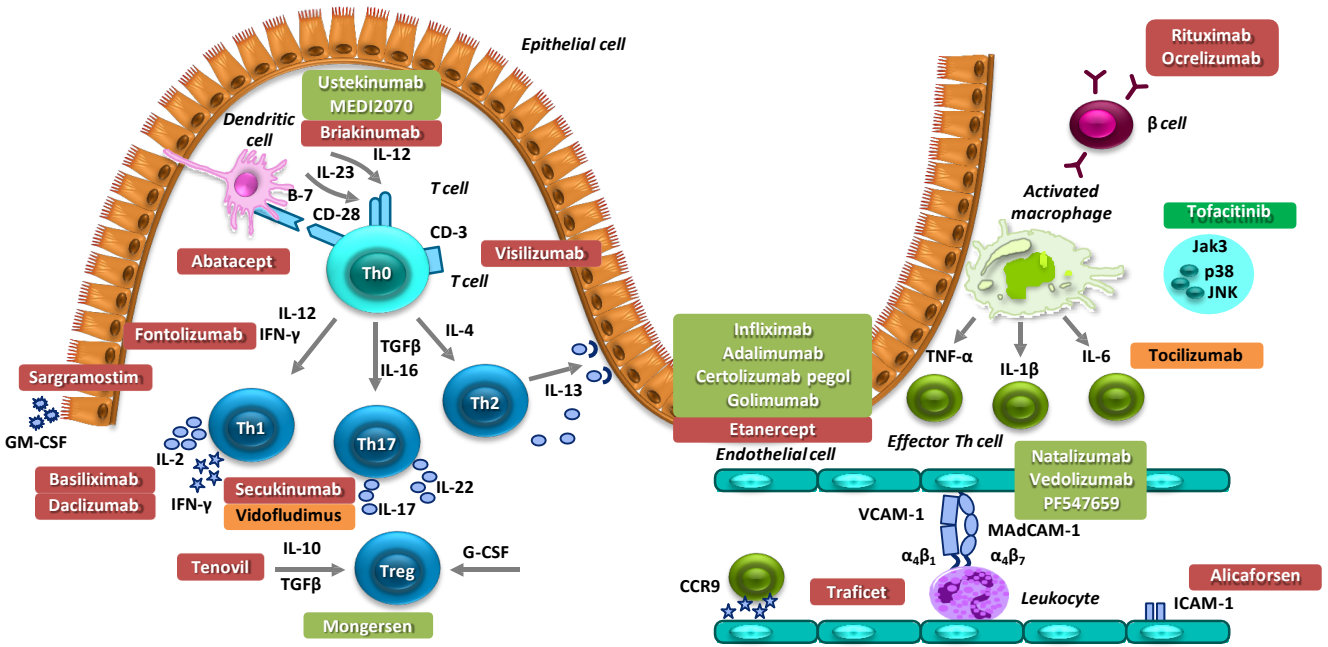


Success and failure in IBD drug development



Adapted from Danese S, et al. Gut 2012;61:918-932

Less than 30% remission rates in recent clinical studies



Success

Failure

Adapted from Danese S, et al. Gut 2012;61:918-932

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Drug development has followed a standard path so far…

Current indications & consequences for biologics

Indications

- **Moderate-Severe Disease**
- **Not Responding to Conventional Agents (or Anti-TNF agents)**

Consequences

- **Steroid-Refractory/Steroid-Dependent**
- No benefit & all risks
- **Long-disease duration**
- Least likely to respond
  - Refractory disease
  - Transmural complications
- **<50% Remission rates for "next generation agents"**

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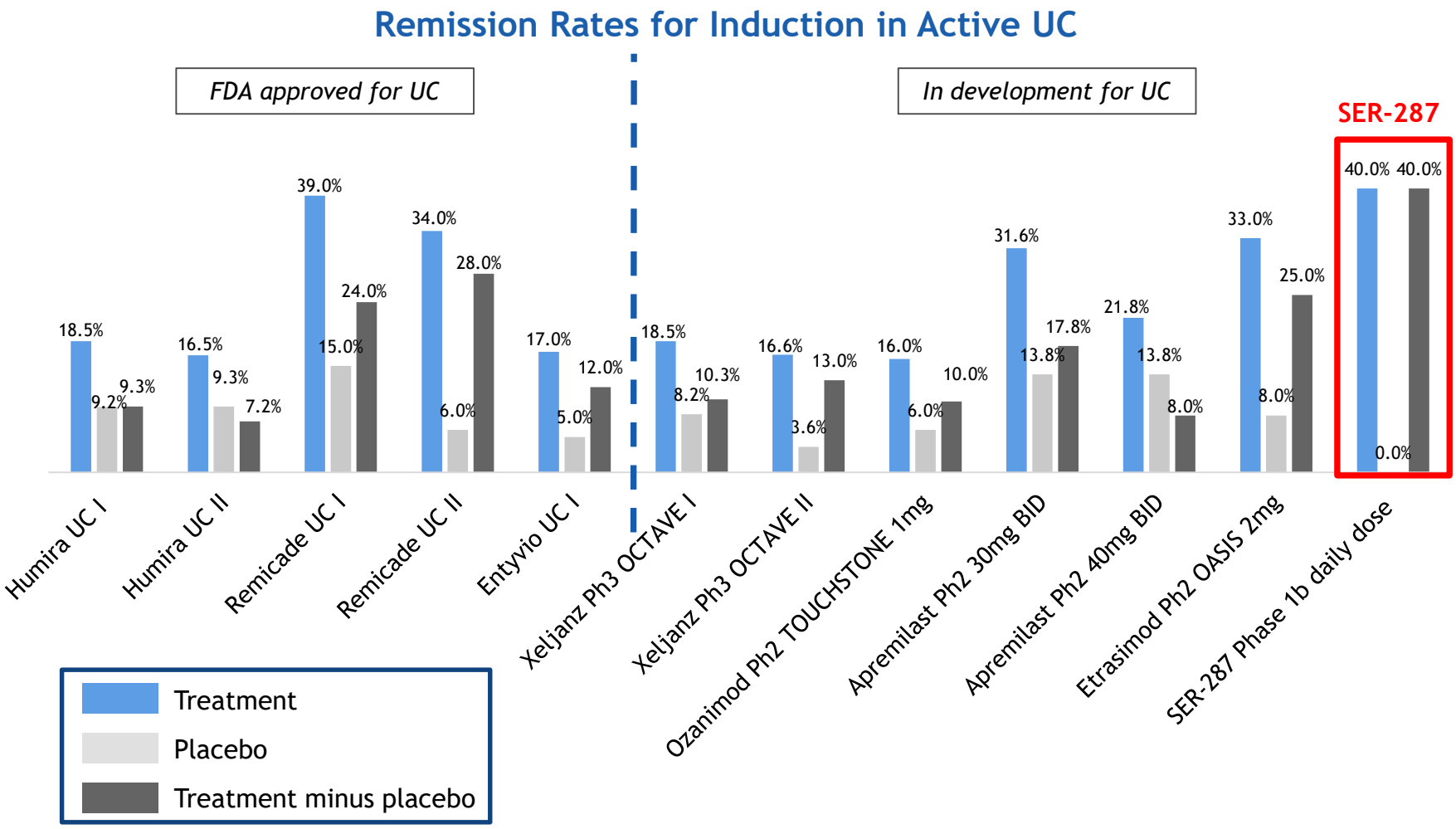
Favorable SER-287 efficacy relative to selected approved and development stage UC drugs



Adapted from Leerink Nov. 27 2017 report: Future of IBD: Category should double by 2023 despite GED-0301 disappointment; Note that study-to-study differences limit the ability to directly compare results.

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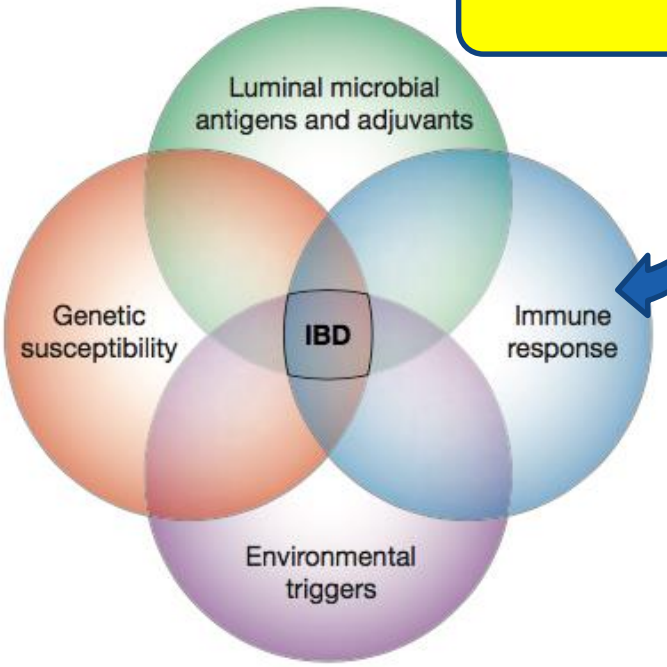
Current management of UC is directed towards host immunosuppression



Focus of drug discovery for past two decades

Rationale for targeting immune response:

- UC pathogenesis is thought to arise from disruption of immune tolerance to the gut microbiota in a genetically susceptible host
- R&D efforts have led to many drug approvals
  - However, off-target effects are observed (eg, infections, malignancies, lymphoma)
  - Modest clinical and endoscopic remission rates
  - Often require parenteral administration

Sartor Gastro 2017; Sartor Gastro 2008

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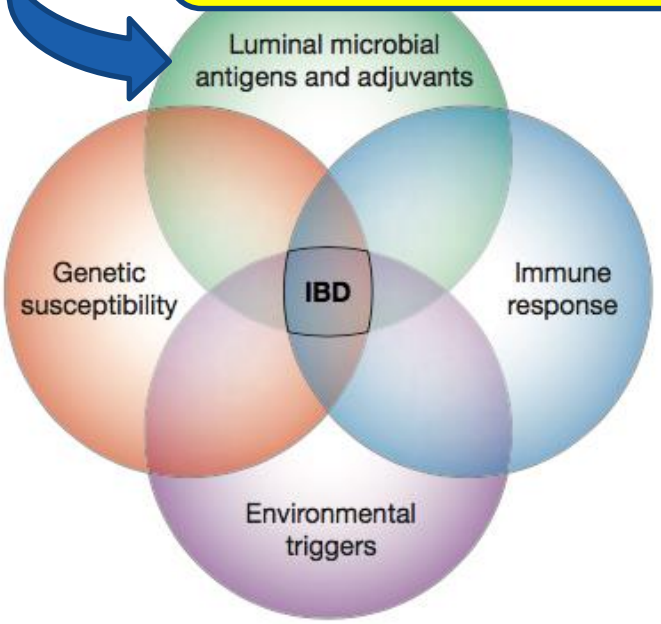
Current management of UC is directed towards host immunosuppression

To date, there are no approved UC drugs targeting the triggers of inflammation rather than inflammation itself



Unmet need for an oral nonimmunosuppressive therapeutic agent for UC treatment

Sartor Gastro 2017; Sartor Gastro 2008

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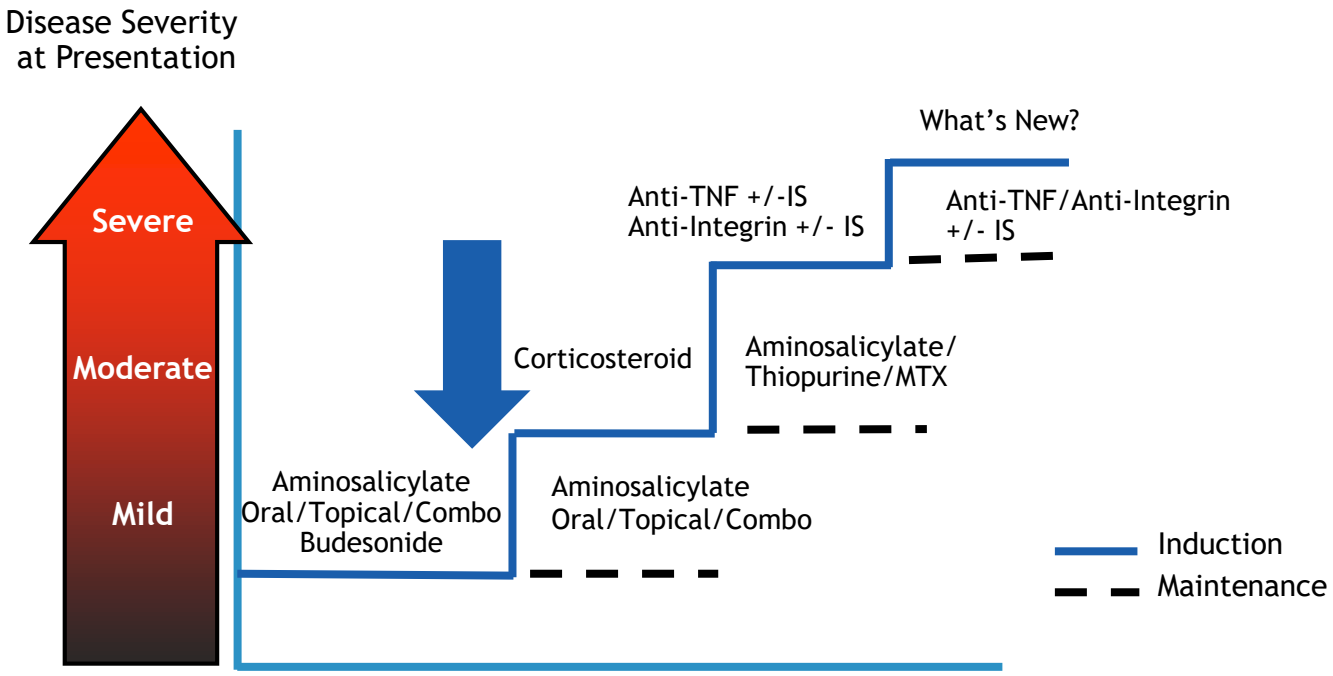
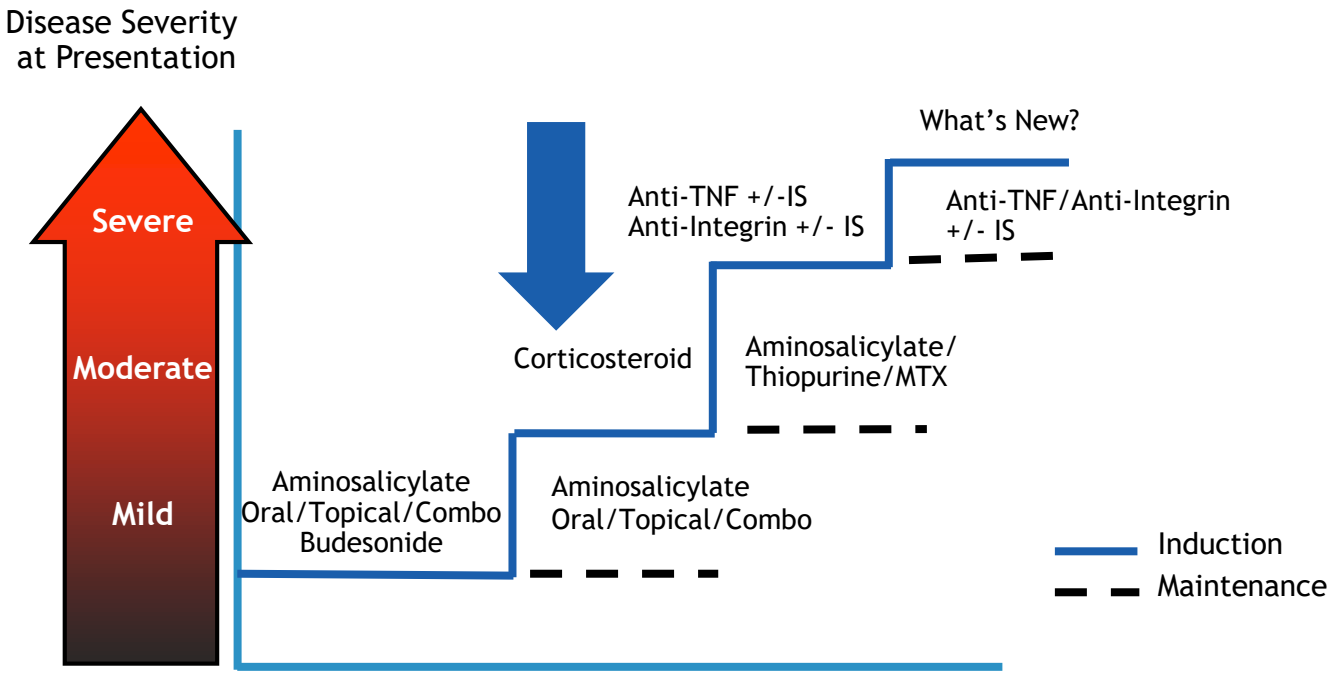
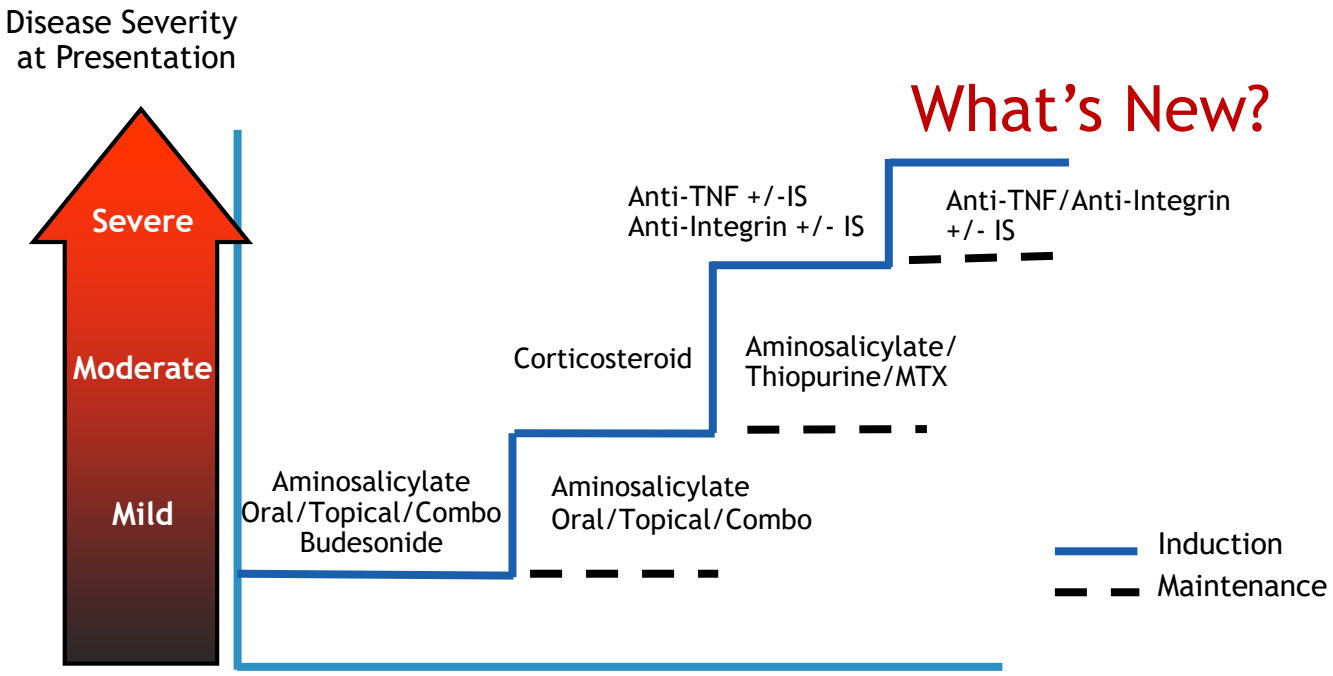
Improved 1st Line Therapies



Replacement of Steroids



What Are We Getting?



Potential SER-287 positioning

- Potential across broad spectrum of IBD:
  - ✓ Prior to biologics, other therapies with significant safety concerns
  - ✓ Pediatric patients
  - ✓ Following biologics (non-responder patients)
  - ✓ Combination therapy
  - ✓ Other forms of IBD (e.g., Crohn's disease)

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Microbiome therapeutics and immuno-oncology – Charting a path forward
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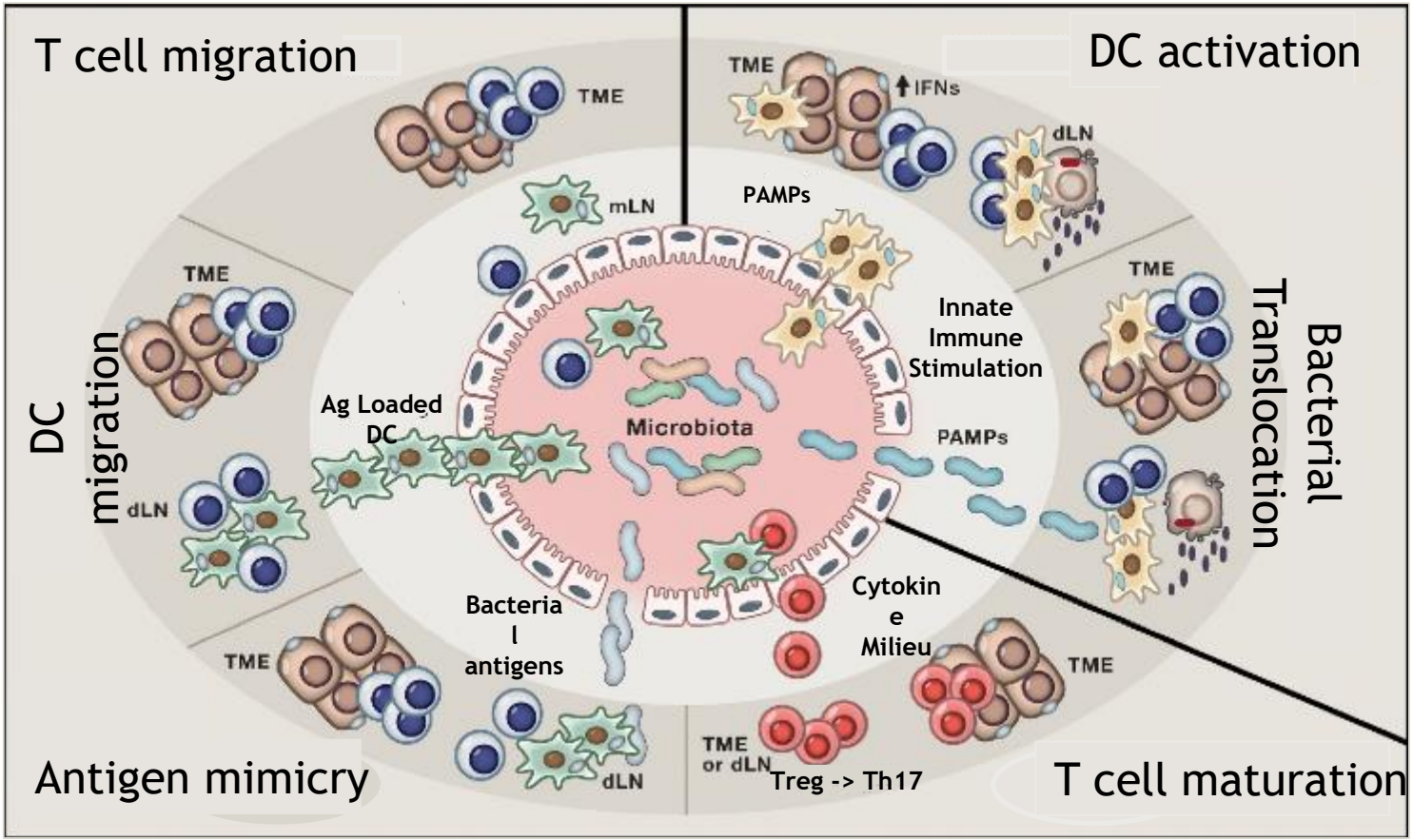
Robust evidence that microbes play mechanistic role in checkpoint inhibitor response



Gopalakrishnan *Science* 2017; Routy *Science* 2017; Matson *Science* 2018; Zitvogel *Cell* 2016; Chen and Mellman *Nature* 2017; Sivan *Science* 2015; Viaud *Science* 2015; Durbin *Nature* 2016; Chaput *Annals Oncol* 2017; Urribe-Hernanz *JCI Insight* 2018

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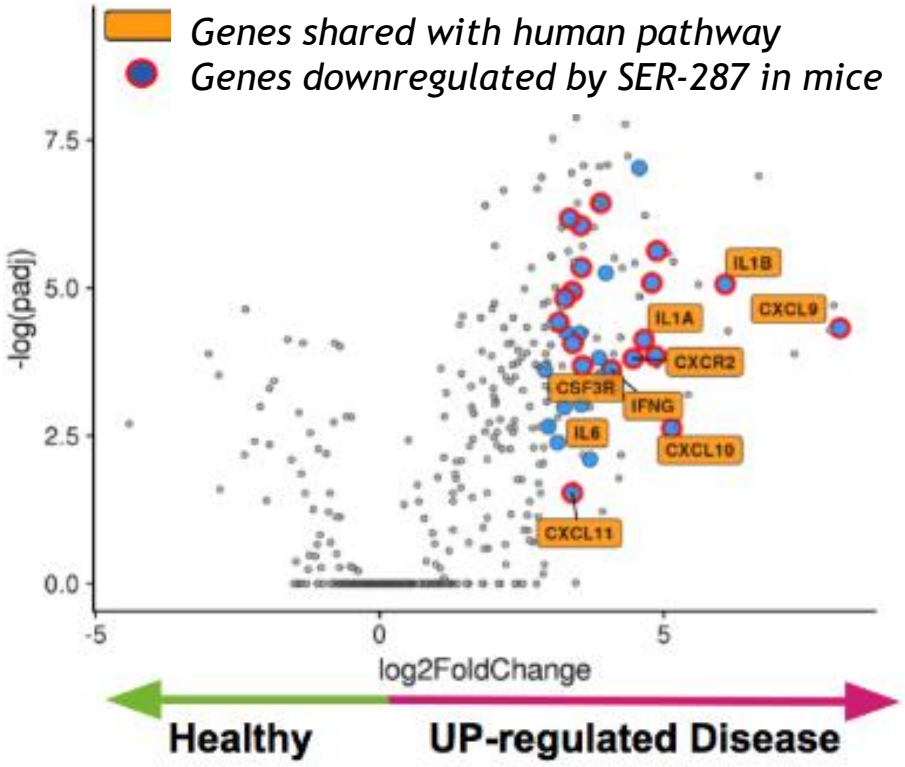
Modulation of inflammation in UC provides compelling rationale for modulating cancer immune set point

Adoptive T cell Transfer Model
Example: Cytokine-Cytokine Receptor

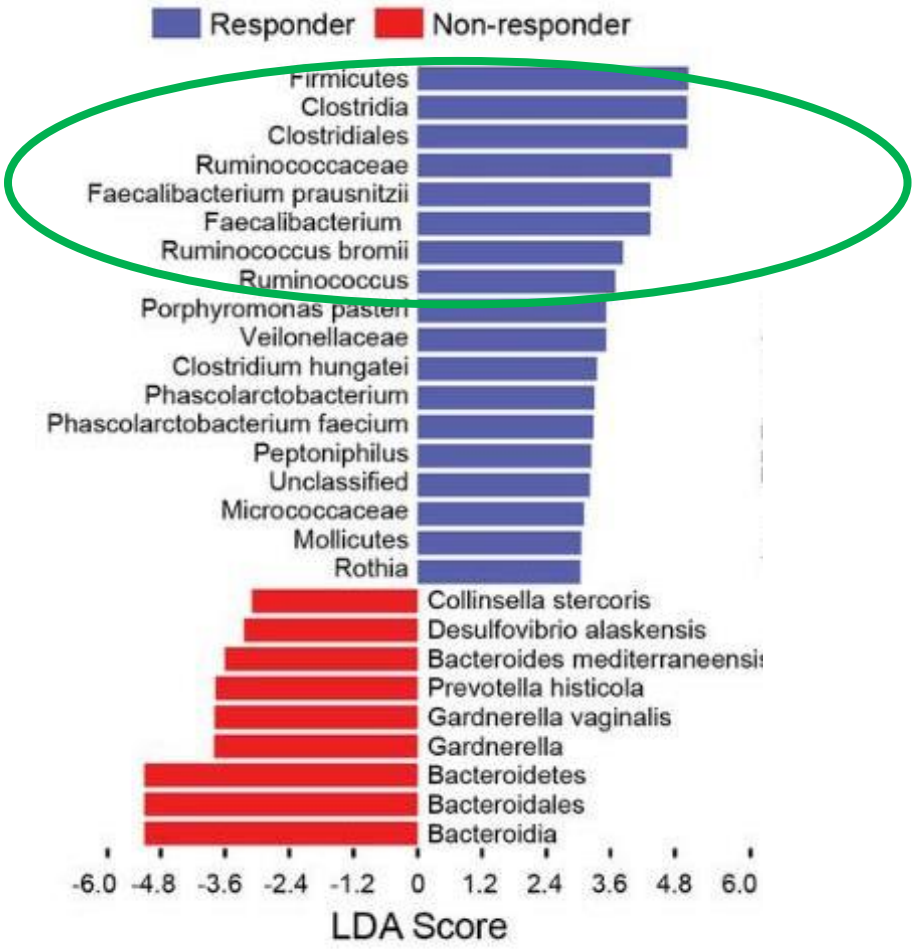


Key pathways characteristic of human UC are modulated by SER-287 in colitis model

- Jak-STAT pathway
- Chemokine signaling pathway
- Cytokine-cytokine receptor pathway
- NF-kappa B signaling
- TNF signaling
- Toll-like receptor signaling
- Cell adhesion molecules
- NOD-like receptor signaling

MDACC identified microbiome signature in melanoma patients who respond to anti-PD-1

- Signature driven by bacteria in the class Clostridia, family *Ruminococcaceae*, including *Ruminoccocus* and *Faecalibacterium*
- All spore formers that leverage deep Seres expertise in the biology and manufacturing of these organisms



Gopalakrishnan et al, Science 2017

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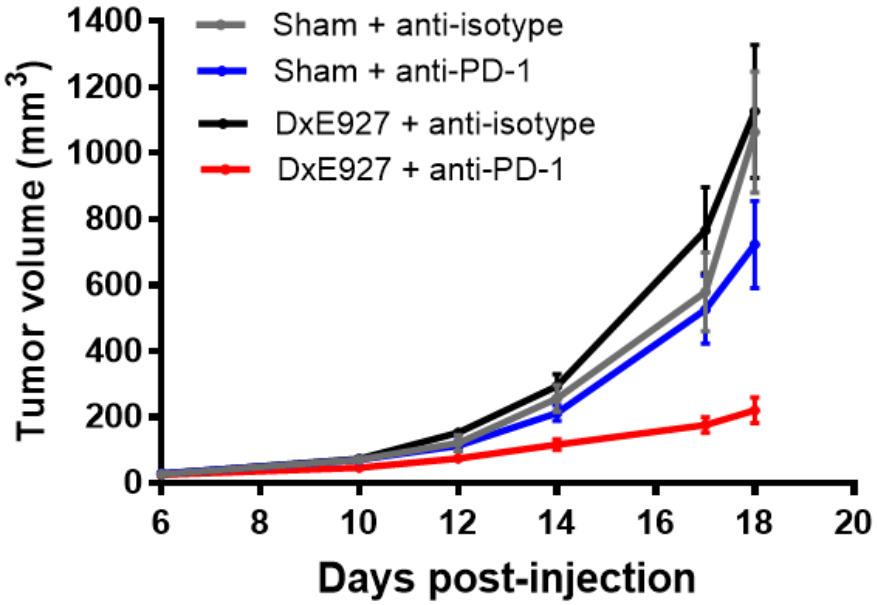
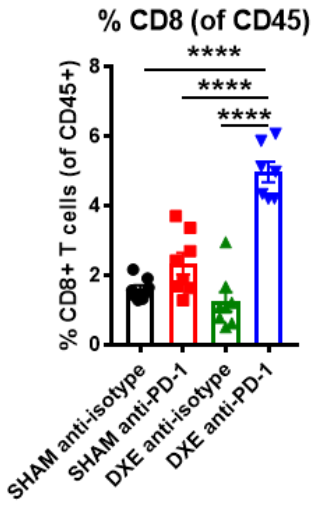
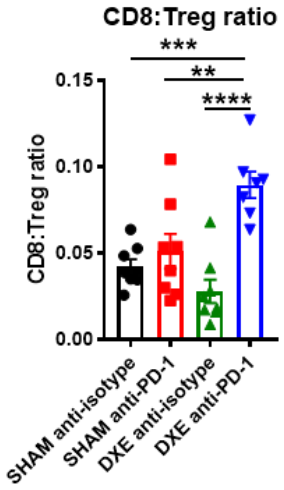
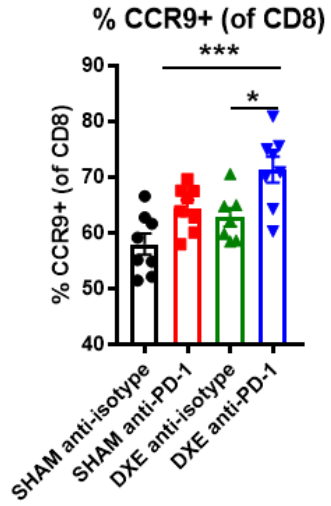
Treatment of mice with the microbiome signature composition restores anti-PD-1 efficacy after antibiotics









Note: Not all donor-derived bacterial spore compositions result in restoration of anti-PD-1 efficacy

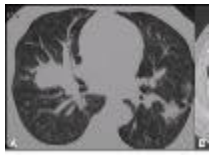
Collaborations with leading cancer centers to develop microbiome therapeutics

Patients treated with PD-1 axis therapies

Memorial Sloan Kettering Cancer Center

Services: Lung, melanoma, renal, bladder, Hodgkins

- Microbiome samples pre-tx, and at multiple time points
- Independently graded scans with RECIST scoring
- Sequencing and metabolomics



MD Anderson Cancer Center

PARKER INSTITUTE for CANCER IMMUNOTHERAPY

Seres Therapeutics, MD Anderson Cancer Center, and the Parker Institute for Cancer Immunotherapy Announce a Collaboration to Support the Investigation of Microbiome Therapeutics for Immuno-Oncology

- Seres option to license foundational intellectual property from MD Anderson related to the use of bacteria in combination with checkpoint inhibitors
- SER-401 targets favorable microbiome signature
- Collaborating on SER-401 clinical study in combination with PD-1 in melanoma

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Agenda

8:00-8:10 a.m.
Opening remarks
Roger Pomerantz, M.D., Seres President, CEO and Chairman

8:10-8:20 a.m.
The microbiome as a new therapeutic modality
Will Dere, M.D., Seres Board Member

ULCERATIVE COLITIS
8:20-8:40 a.m.
Pathology and role of the microbiome
Alan Moss, M.D., Beth Israel Deaconess Medical Center

8:40-9:05 a.m.
SER-287 Phase 1b results and continued late stage development
Shelley Trucksis, Ph.D., M.D., Seres Executive Vice President and Chief Medical Officer and Matthew Henn, Ph.D., Seres Executive Vice President, Microbiome Research and Development

9:05-9:25 a.m.
Microbiome therapeutic development
Stephen Hanauer, M.D., Northwestern University

9:25-9:30 a.m.
Break

IMMUNO-ONCOLOGY
9:30-9:40 a.m.
Rationale for microbiome drug development in cancer
David Cook, Ph.D., Seres Executive Vice President of R&D and Chief Scientific Officer

9:40-10:00 a.m.
Microbiome therapeutics and immuno-oncology – Charting a path forward
Jennifer Wargo, M.D., MD Anderson Cancer Center

10:00-10:30 a.m.
Q&A Session

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Disclosure information
Seres Research and Development Day

The gut microbiome and response to cancer therapy

Jennifer A. Wargo MD MMSc

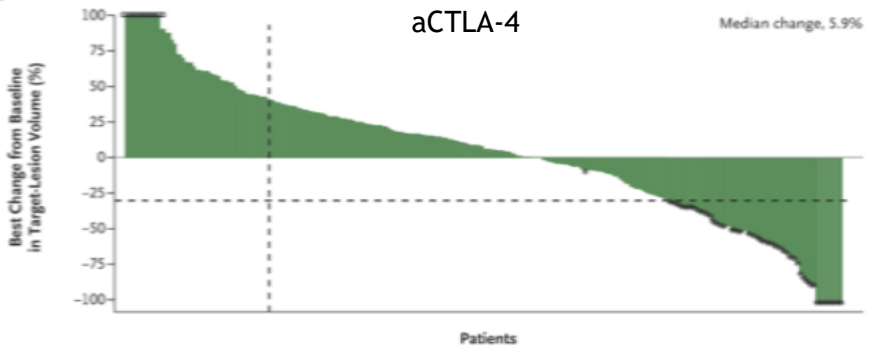
- I have the following financial relationships to disclose:

- Speaker's bureau: Imedex, Dava, Omniprex, Illumina, BMS
- Advisory board member: Roche - Genentech, GSK, Novartis, Astra-Zeneca
- Clinical trial support: Roche - Genentech, GSK, BMS, Novartis

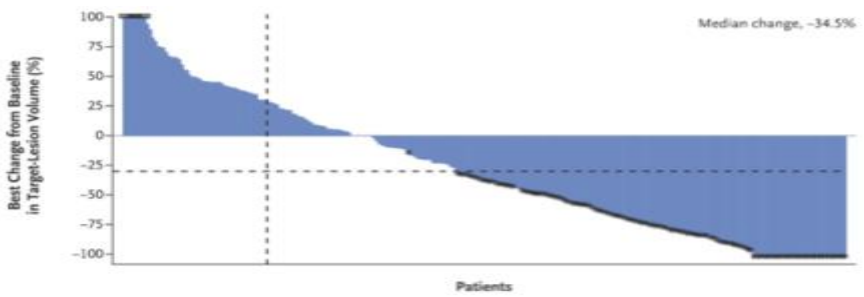
- I am a consultant and scientific advisor to Microbiome DX
- *I am co –Inventor on patent submitted by The University of Texas MD Anderson Cancer Center to the US Patent and Trademark Office based on this work (Patent # PCT/US1/53717)*

Major advances in the treatment of cancer through the use of immunotherapy (immune checkpoint blockade)

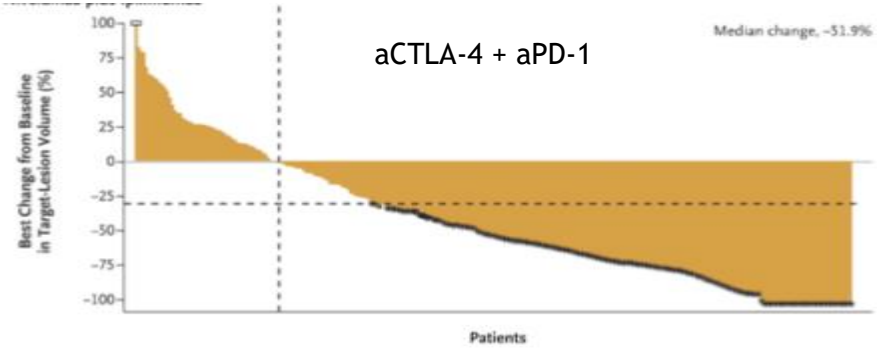
aCTLA-4

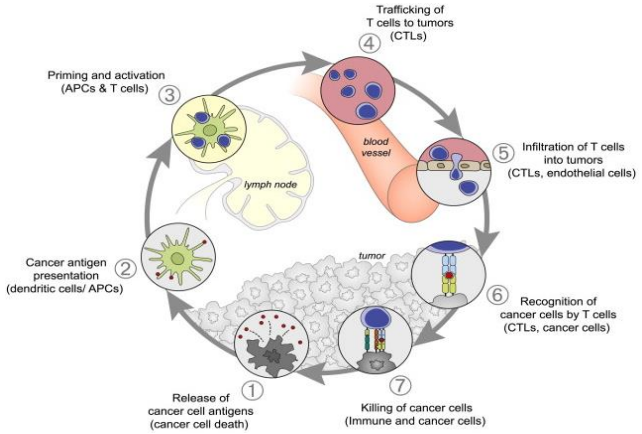


aPD-1



aCTLA-4 + aPD-1





However responses are not universal and not always durable, and there is a critical need to identify biomarkers of response, as well as strategies to improve responses

Chen & Mellman, Immunity 2013

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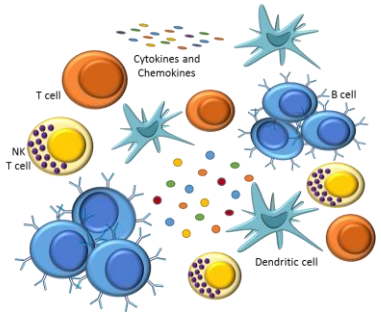
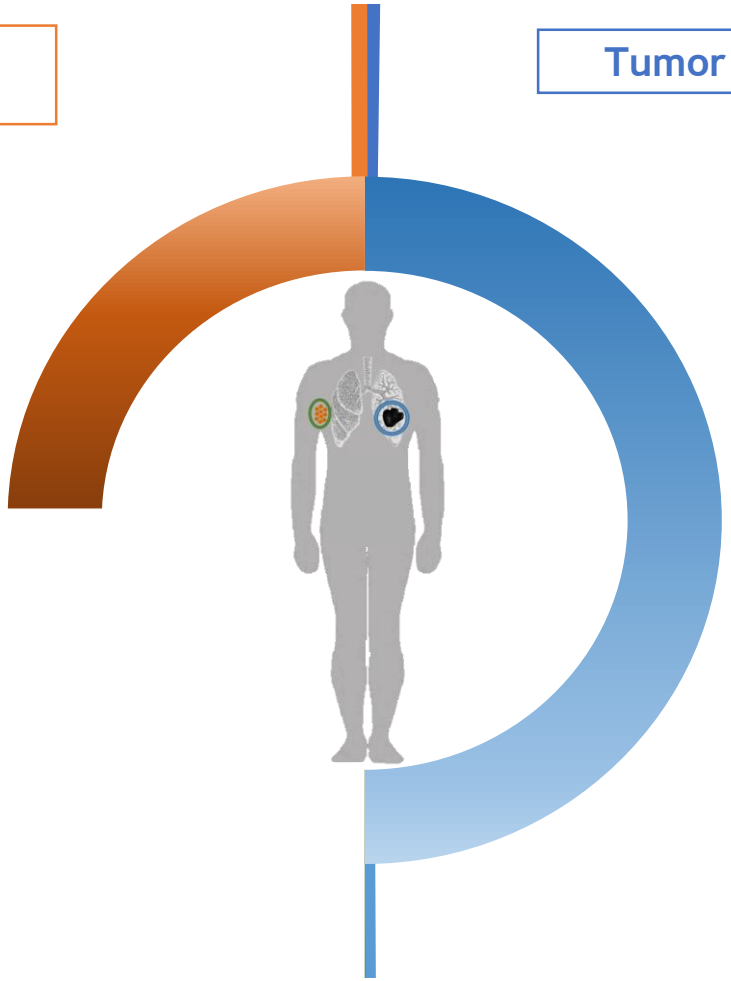
How can we better understand responses to therapy and optimize treatment regimens?

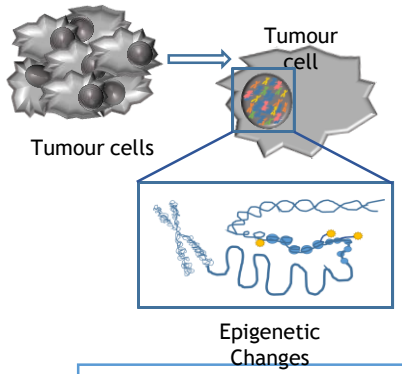
Responses are dependent on factors shaping tumor growth and immunity

Systemic Immunity
Innate and Adaptive

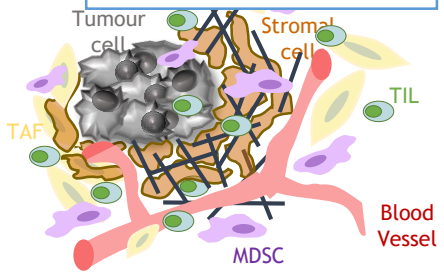




Tumor Genome and Epigenome



Tumor Microenvironment



Cogdill, Andrews, Wargo - British Journal of Cancer May 2017

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The human microbiome

100 trillion microbes

3% human body mass

1-10X microbes : human cells

10-100X microbial : human genes

largest # microbes – GI tract

There is a growing appreciation of the role of the microbiome in health and disease, & evidence that the microbiome can contribute to carcinogenesis and therapy response

Slide credit: Ami Bhatt and Robert Jenq

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There is a growing appreciation of the role of the microbiome in cancer

DOI: 10.1093/jnci/djs003
Advance Access publication on January 23, 2012.

Published by Oxford University Press 2012.

BRIEF COMMUNICATION

Fifteen-Year Effects of *Helicobacter pylori*, Garlic, and Vitamin Treatments on Gastric Cancer Incidence and Mortality

Jun-Ling Ma, Lian Zhang, Linda M. Brown, Ji-You Li, Wei-Dong Liu, Yuanreng Hu, David Pee

New written informed consents were obtained for the extended follow-up phase from May 2, 2003, to August 1, 2010. Data from 3365 eligible

Proinflammatory CD4^{+}CD45RB^{hi} Lymphocytes Promo and Intestinal Carcinogenesis in *Apc*$^{Min/+}$ Mice

Varada
Bruce H
Zhongming Ge,[1] Prashant R. Namb

MyD88 inhibition amplifies de cell capacity to promote pancreatic carcinogenesis via Th2 cells

Atsuo Ochi,[1] Andrew H. Nguyen,[2] Andrea S. Bedrosian,[1] Harry M. Mushlin,[2] Saman Zarbakhsh,[1] Rocky Barilla,[1] Constantinos P. Zambirinis,[1] Nina C. Fallon,[1] Adeel Rehman,[1] Yuliya Pylayeva-Gupta,[3] Sana Badar,[1] Cristina H. Hajdu,[4] Alan B. Frey,[2] Dafna Bar-Sagi,[3] and George Miller[1,2]

Grace Y. Chen,[1,3] Michael H. Shaw,[2,3] Gloria Redondo,[2,3] and Gabriel Núñez[2,3]

Division of Hematology and Oncology

Intestinal Neoplasia in the *Apc*^{Min} Mouse: Independence from the Microbial and Natural Killer (*beige* Locus) Status[1]

William F. Dove,[2] Linda Clipson, Karen A. Gould,[3] Cindy Luongo,[4] David J. Marshall, Amy R. Moser,[5] Michael A. Newton, and Russell F. Jacoby

McArdle Laboratory for Cancer Research [L. C., A. R. M.] and Laboratory of Genetics [W. F. D., K. A. G., C. L.], University of Wisconsin, Madison, Wisconsin 53706; Department of Medicine, Division of Gastroenterology [D. J. M., R. F. J.] and Department of Biostatistics, Comprehensive Cancer Center [M. A. N.], University of Wisconsin, Madison, Wisconsin 53792

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Immunoproliferative Small Intestinal Disease Associated with *Campylobacter jejuni*

LETTER

Adenoma-linked barrier defects and microbial products drive IL-23/IL-17-mediated tumour growth

doi:10.1038/nature11465

Sergei I. Grivennikov[1]*, Kepeng Wang[1,2]*, Daniel Mucida[3,4], C. Andrew Stewart[5], Bernd Schnabl[6], Dominik Jauch[1], Koji Taniguchi[1,7], Guann-Yi Yu[1], Christoph H. Österreicher[6,8], Kenneth E. Hung[9], Christian Datz[10], Ying Feng[11], Eric R. Fearon[11], Mohamed Oukka[12], Lino Tessarollo[13], Vincenzo Coppola[14], Felix Yarovinsky[15], Hilde Cheroutre[3], Lars Eckmann[6], Giorgio Trinchieri[5] & Michael Karin[1]

Cell PRESS

Promotion of Hepatocellular Carcinoma by the Intestinal Microbiota and TLR4

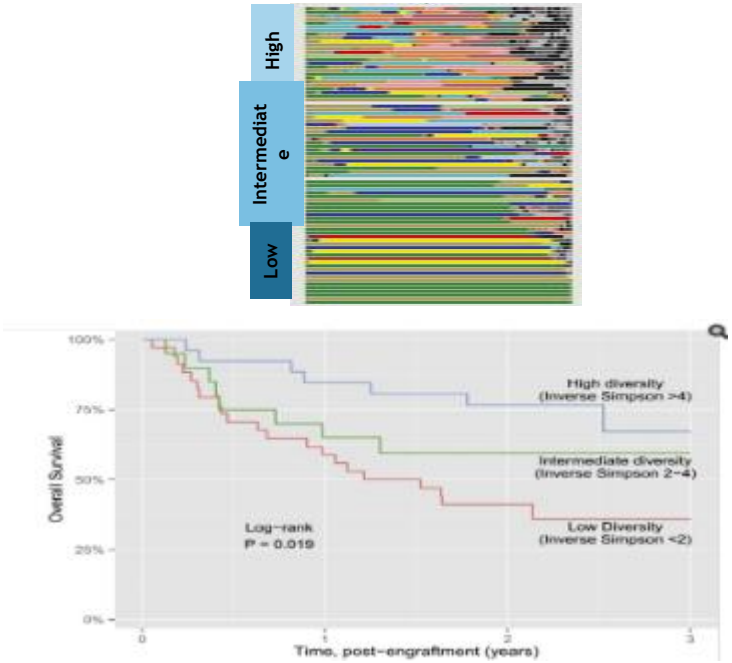
Dianne H. Dapito,[1,2,10] Ali Mencin,[3,10] Geum-Youn Gwak,[1,7,10] Jean-Philippe Pradere,[1,10] Myoung-Kuk Jang,[1] Ingrid
Jay
and
Dapito, Ali Mencin, Geum-Youn Gwak, Jean-Philippe Pradere, Myoung-Kuk Jang, Hossein Khiabanian, Adebowale Adeyemi, Ramon Bataller

Chronic Active Hepatitis and Associated Liver Tumors in Mice Caused by a Persistent Bacterial Infection With a Novel *Helicobacter* Species

*Jerrold M. Ward, James G. Fox, Miriam R. Anver, Diana C. Haines, Cathi V. George, Michael J. Collins, Jr., Peter L. Gorelick, Kunio Nagashima, Matthew A. Gonda, Raymond V. Gilden, Joseph G. Tully, Robert J. Russell, Raoul E. Benveniste, Bruce J. Paster, Floyd E. Dewhirst, John C. Donovan, Lucy M. Anderson, Jerry M. Rice**

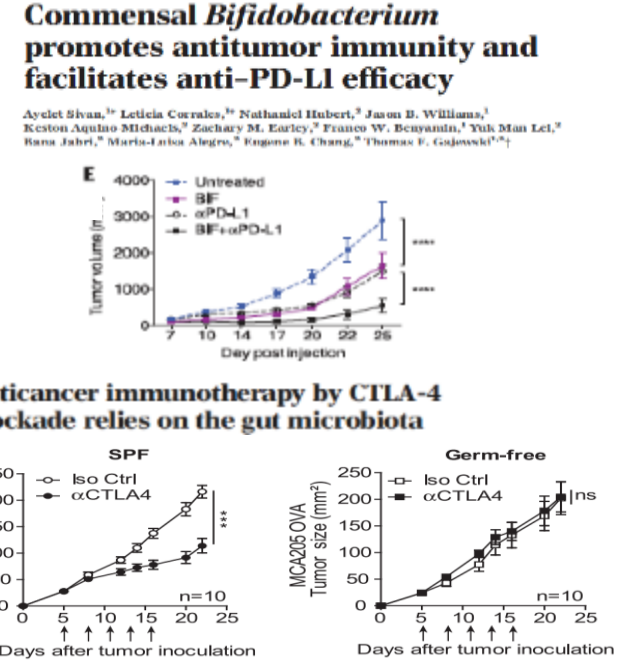
The microbiome may also influence responses to cancer immunotherapy

Diversity of the gut microbiome is associated with differential outcomes in the setting of stem cell transplant in patients with AML



Taur…Pamer Blood 2014

Composition of the gut microbiome is associated with differential responses to checkpoint blockade in murine models



Sivan…Gajewski Science 2015, Vetizou…Zitvogel Science 2015

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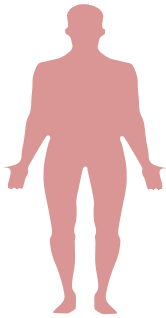
Based on this evidence, we wanted to better understand the role of the gut microbiome in response to checkpoint blockade in patients with melanoma

Hypothesis

- Differential bacterial “signatures” exist in responders versus non-responders to immune checkpoint blockade
- Favorable signatures will be associated with an enhanced anti-tumor immune response (with increased CD8+ T cells, as well as evidence of an enhanced innate immune response)
- Insights gained could lead to strategies to enhance responses to therapy (through modulation of the microbiome)

Oral and gut microbiome were studied in a large cohort of patients with metastatic melanoma going onto systemic therapy



n = 233 patients

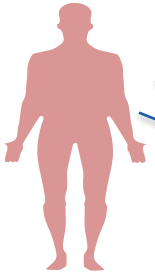
Initial oral & gut microbiome sampling

Tumor biopsy

Start of therapy

Clinical assessment & restaging

Repeat oral & gut microbiome sampling

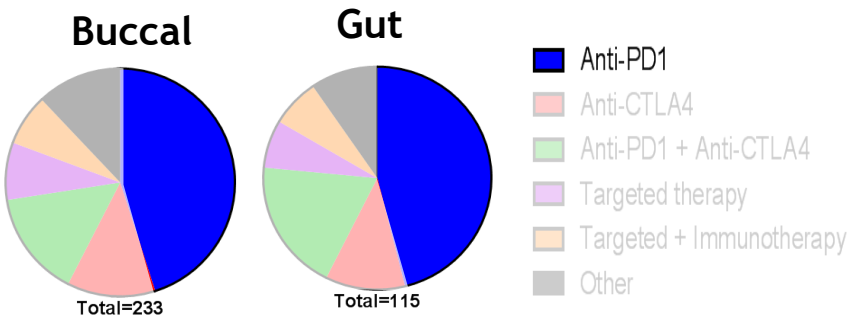


Patients on aPD-1 (n=113)

RECIST at 12 weeks and PFS assessed

Responder CR, PR, SD (≥ 6mos)

Non-Responder PD, SD (< 6mos)



Microbiome sequencing

16S sequencing
Whole genome sequencing

Molecular Profiling

Whole Exome Sequencing

Immune Profiling

Immunohistochemistry
Flow cytometry
T cell Receptor Sequencing
Cytokine Analysis

Gopalakrishnan et al, Science 2018

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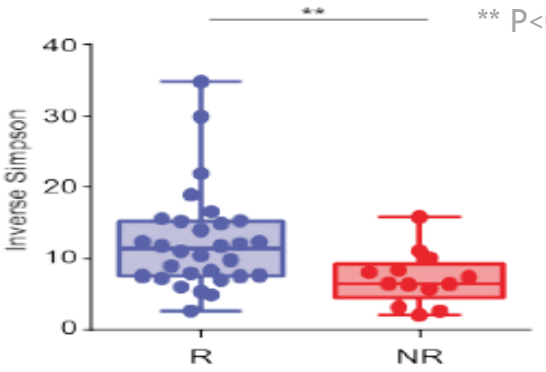
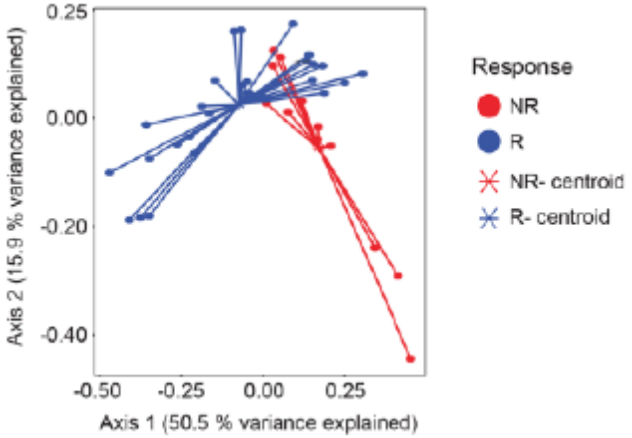
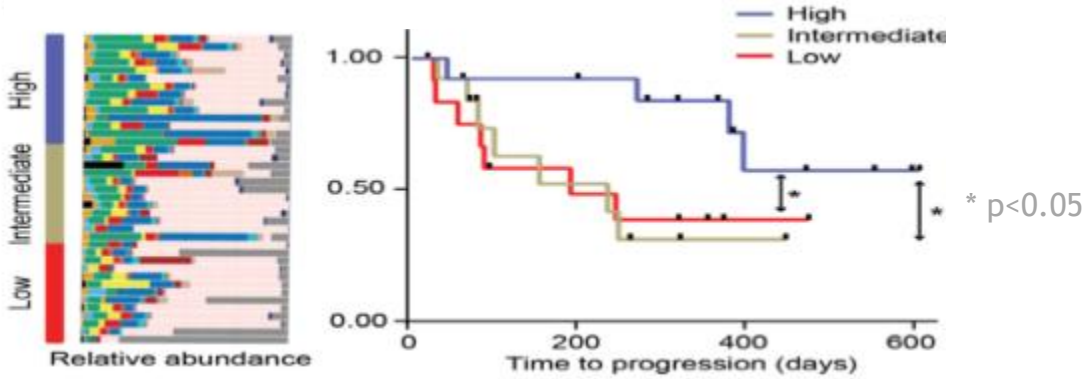
Responders to anti-PD1 had a significantly higher diversity of bacteria in the gut microbiome, and clustered separately from non-responders

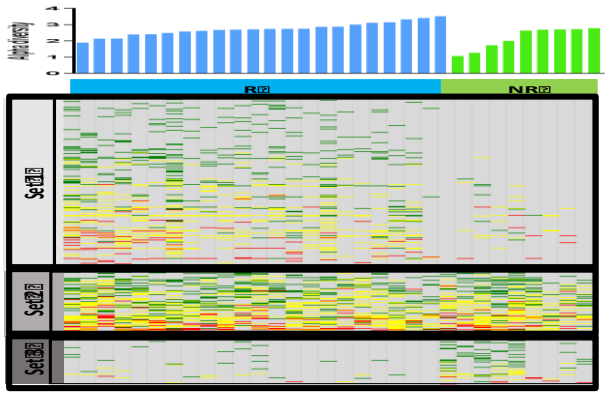


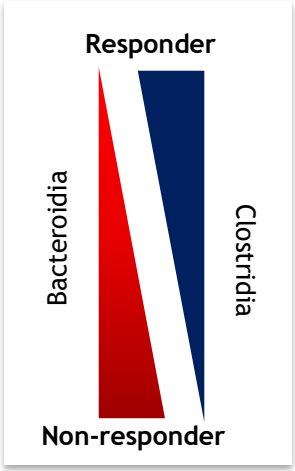


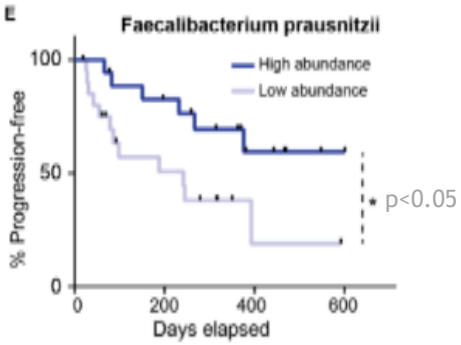


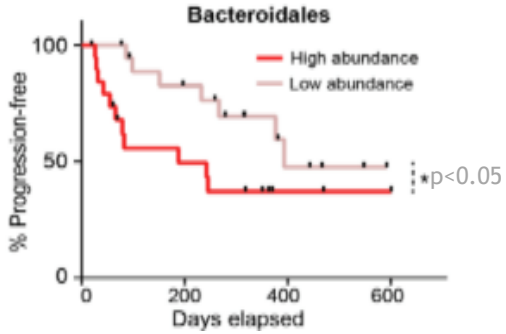
Higher diversity of the gut microbiome was associated with improved PFS on anti-PD-1 therapy

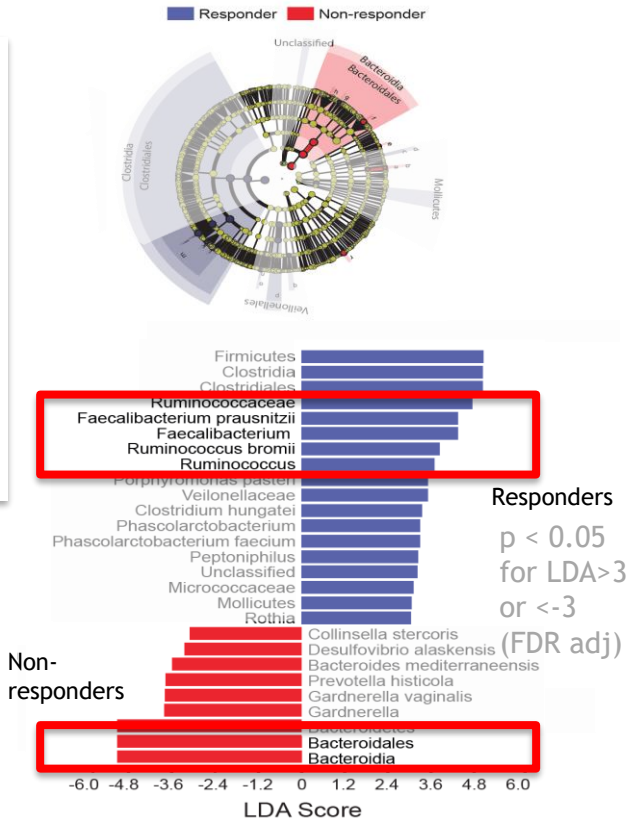
Compositional differences in the gut microbiome were also noted in responders versus non-responders to PD-1 blockade





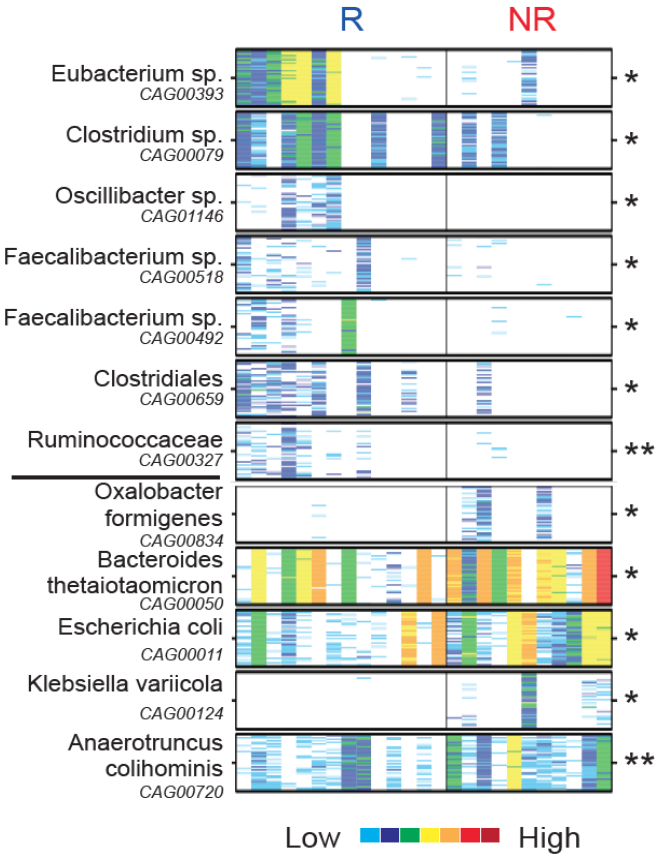


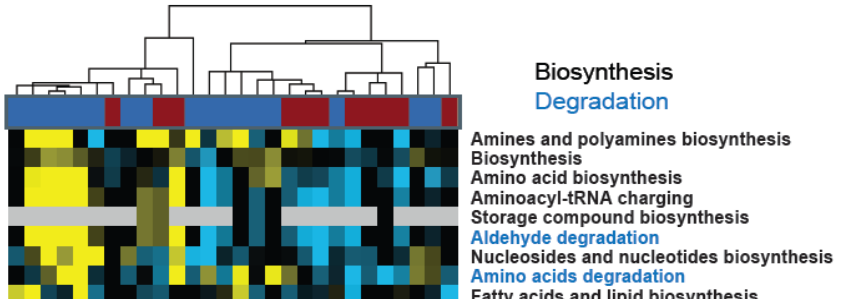




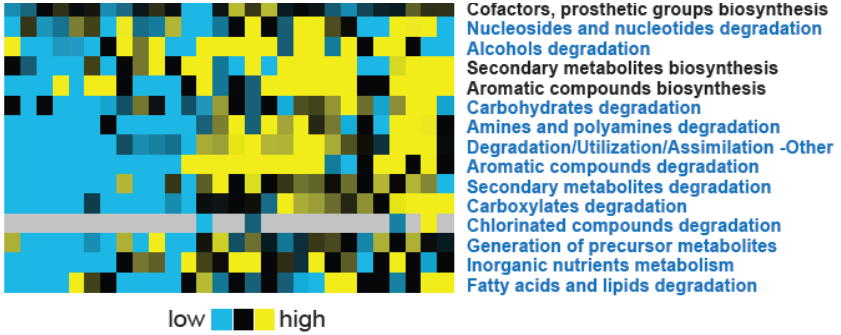
Gopalakrishnan et al, Science 2018

Metagenomic sequencing confirmed taxonomic differences, and also revealed differences in metabolomic profiles of responders (R) versus non-responders (NR)





Enrichment of biosynthetic pathways in R and degradative pathways in NR



Gopalakrishnan et al, Science 2018

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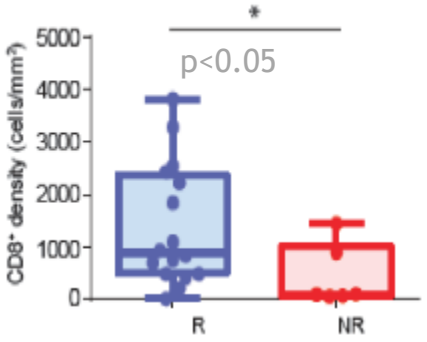
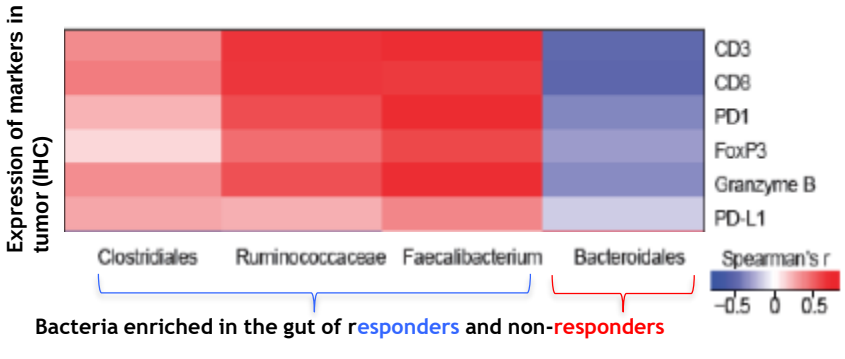
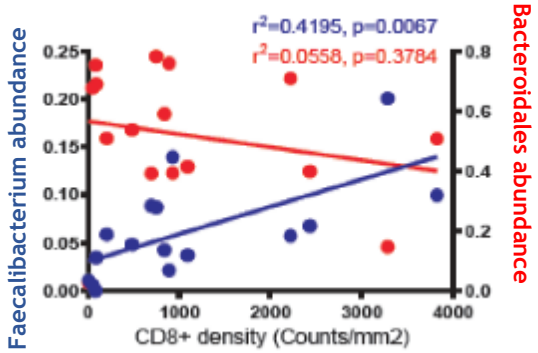
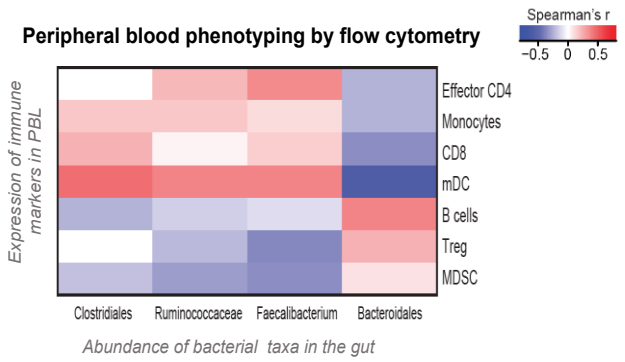
Anti-tumor immune responses were assessed and were compared to the composition of the gut microbiome in patients on anti-PD-1

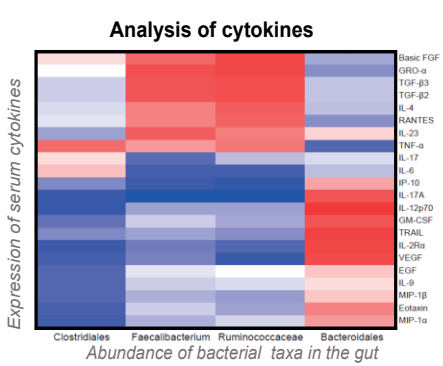


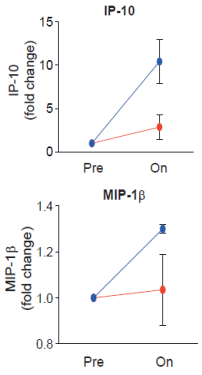


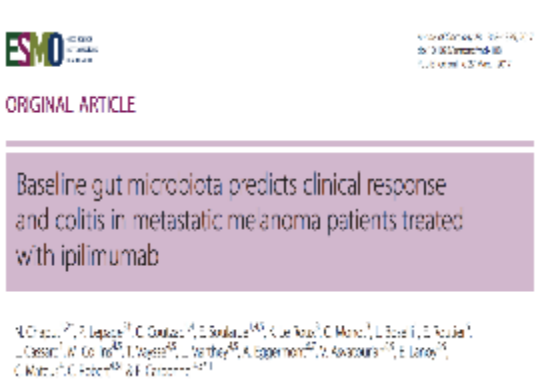


High abundance of Ruminococcus & Faecalibacteria in gut associated with cytotoxic T cells in tumor microenvironment









Differences were also noted in the periphery, with more effector T cells and improved cytokine responses

Gopalakrishnan et al, Science 2018

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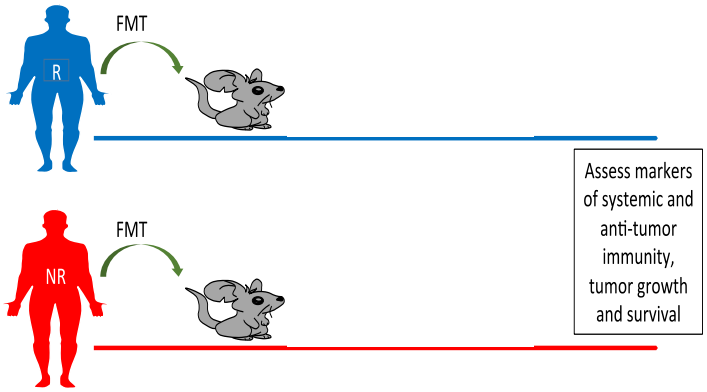
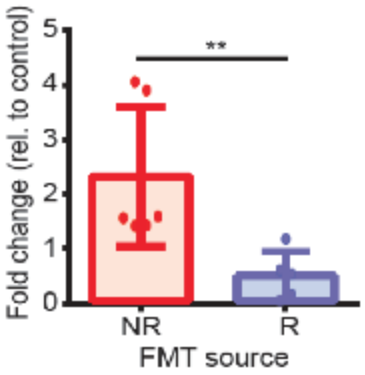
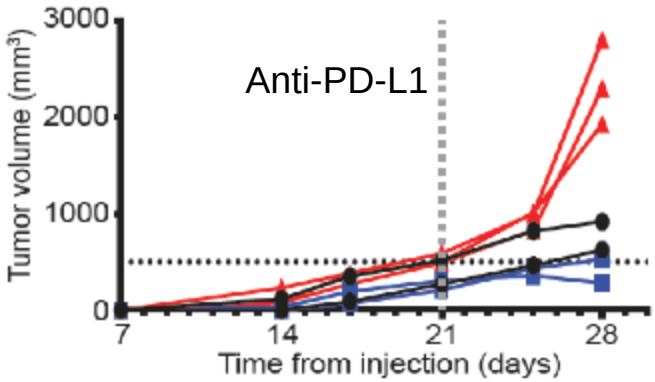
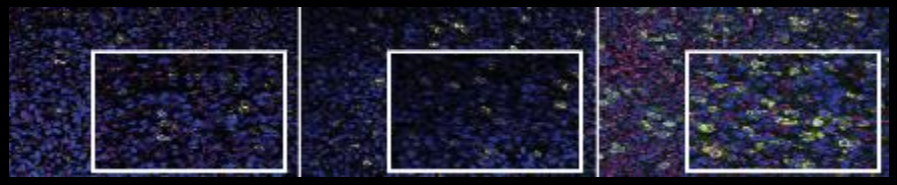
Mechanistic studies in murine models demonstrated a link between the gut microbiome and response to anti-PD-1 based therapy





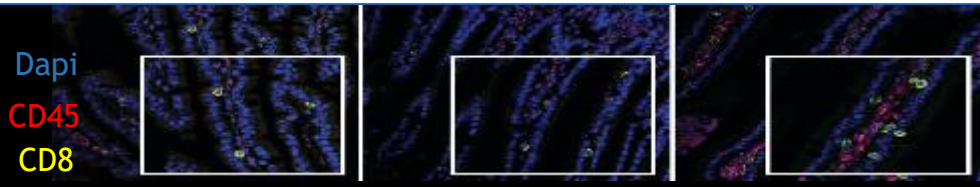


Germ-free mice receiving FMT from responders have delayed tumor growth and enhanced response to anti-PD-L1



Control FMT from NR FMT from R

Tumors in mice receiving R FMT are more infiltrated



Control FMT from NR FMT from R

The gut of mice receiving R FMT is also more infiltrated

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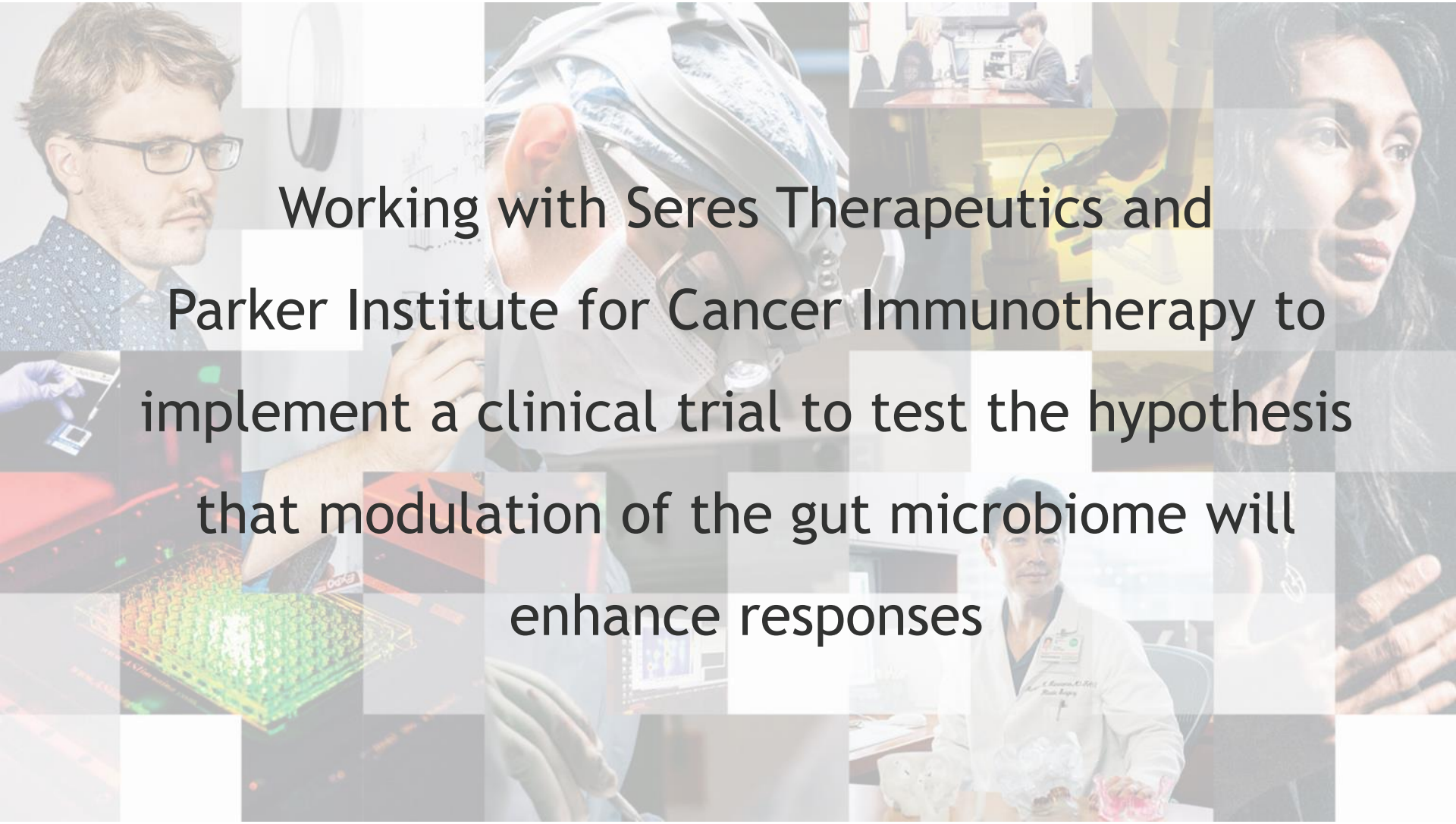
Can we modulate the gut microbiome to enhance responses to immunotherapy?



Working with Seres Therapeutics and Parker Institute for Cancer Immunotherapy to implement a clinical trial to test the hypothesis that modulation of the gut microbiome will enhance responses

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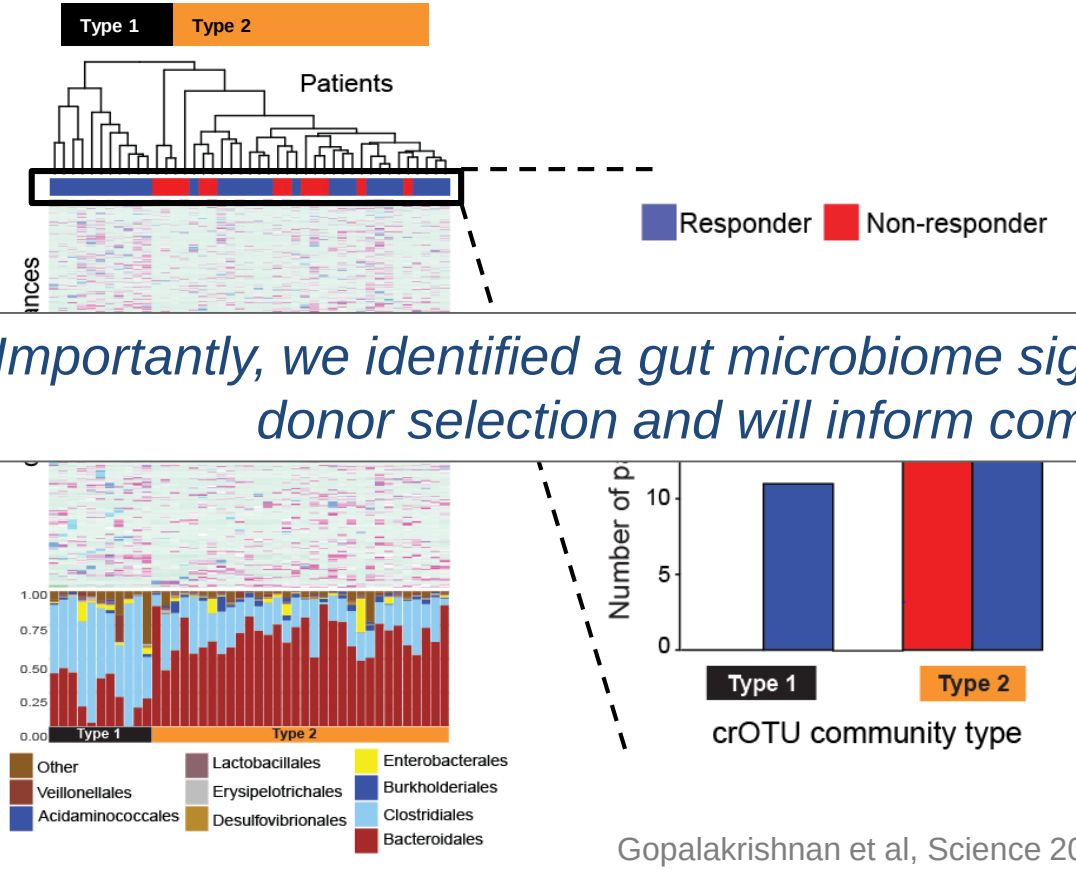
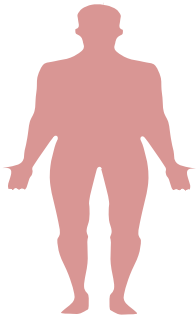
Importantly we identified a gut microbiome signature that can help us with CR donor selection, and will inform composition of SER-401



Importantly, we identified a gut microbiome signature that can help us with CR donor selection and will inform composition of SER-401

Gopalakrishnan et al, Science 2018

SER-401 Phase 1b study design



Patients with metastatic cancer (melanoma) going onto immune checkpoint blockade (anti-PD-1)

Arm A
Fecal microbiota (FM) from complete responders anti PD-1 (n=20)

Arm B
SER-401 (n=20)

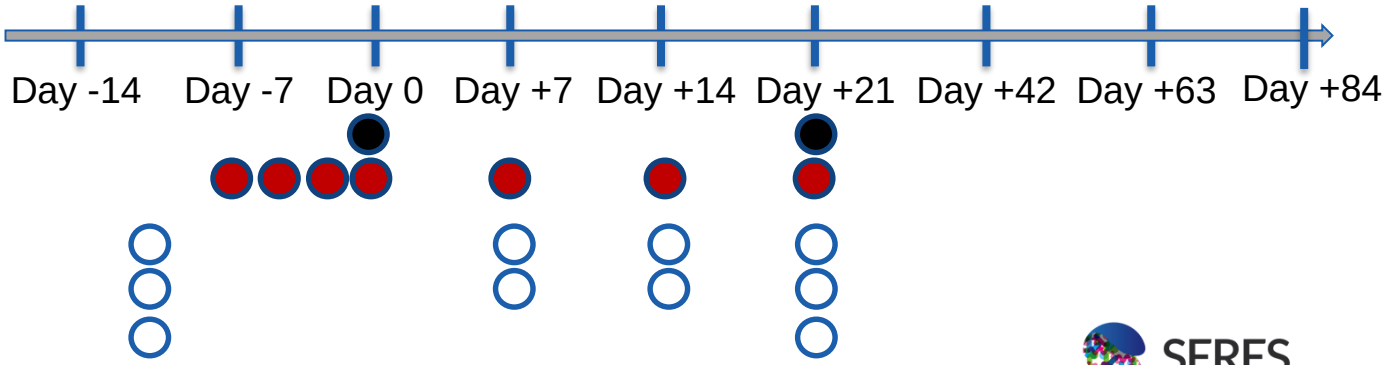
Arm C
Placebo (n=20)

Study objectives

All patients = CT scans with RECIST week 12

Primary endpoint = safety and tolerability

Secondary endpoints: engraftment, response and correlative studies (immune correlates in blood and tumor, metabolites)



Treatment: **anti-PD-1: Pbo/401/FM**

Biospecimens: **Blood Stool Biopsy**

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Acknowledgements

Patients and their families

Seres R&D Day Attendees / Supporters

Seres Therapeutics

- Roger Pomerantz MD
- Dave Cook PhD
- Lata Jayaraman PhD
- John Aunins PhD
- Matt Henn PhD
- Michele Trucksis MD PhD
- Jennifer Wortman PhD
- Jennifer Mahoney PhD

Parker Institute for Cancer Immunotherapy

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- Fred Ramsdell PhD
- Theresa LaValle PhD
- Marcy Kravet PhD
- Leigh Feigenbaum PhD
- Stephanie Liva JD PhD
- Melinda Griffith JD

Laboratory Investigation (Wargo lab members)

- Vancheswaran Gopalakrishnan PhD
- Christine Spencer PhD
- Alexandre Reuben PhD
- Miles Cameron Andrews MD PhD
- Luigi Nezi PhD
- Beth Helmink MD PhD
- Sangeetha Reddy MD PhD
- Liz Burton MBA

MDACC Collaborators

- Isabella Glitza MD, Hussein Tawbi MD PhD
- Jim Allison PhD, Pam Sharma MD PhD
- Michael Davies MD PhD, Jeff Gershenwald MD
- Patrick Hwu MD, other Melanoma Med Onc Facutly / Staff
- Jeff Lee MD, Merrick Ross MD, other Surg Onc Faculty / Staff
- Robert Jenq MD PhD, other MDACC faculty / staff

Philanthropic/Grant Support

- MRA, BSF, AACR-SU2C, PICI, R01 (PQ 10) Sabin Family Foundation
- Melanoma Moon Shot Program

Agenda

8:00-8:10 a.m.
Opening remarks
Roger Pomerantz, M.D., Seres President, CEO and Chairman

8:10-8:20 a.m.
The microbiome as a new therapeutic modality
Will Dere, M.D., Seres Board Member

ULCERATIVE COLITIS
8:20-8:40 a.m.
Pathology and role of the microbiome
Alan Moss, M.D., Beth Israel Deaconess Medical Center

8:40-9:05 a.m.
SER-287 Phase 1b results and continued late stage development
Shelley Trucksis, Ph.D., M.D., Seres Executive Vice President and Chief Medical Officer and Matthew Henn, Ph.D., Seres Executive Vice President, Microbiome Research and Development

9:05-9:25 a.m.
Microbiome therapeutic development
Stephen Hanauer, M.D., Northwestern University

9:25-9:30 a.m.
Break

IMMUNO-ONCOLOGY
9:30-9:40 a.m.
Rationale for microbiome drug development in cancer
David Cook, Ph.D., Seres Executive Vice President of R&D and Chief Scientific Officer

9:40-10:00 a.m.
Microbiome therapeutics and immuno-oncology – Charting a path forward
Jennifer Wargo, M.D., MD Anderson Cancer Center

10:00-10:30 a.m.
Q&A Session

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Appendix

Demographics

Characteristic	PBO/PBO (N=11)	PBO/SER-287 qWk (N=15)	Vanco/SER-287 qWk N=17	Vanco/SER-287 qD (N=15)
Mean age (years)	45.8	46.5	47.9	47.8
Disease location				
Left-sided colitis	72.7%	66.7%	70.6%	60.0%
Extensive colitis	27.3%	33.3%	29.4%	40.0%
Severity of UC				
Mild	27.3%	40.0%	52.9%	40%
Moderate	72.7%	60.0%	41.2%	60%
Mean years since dx	11.5	12.4	11.8	12.7

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Adverse Events Incidence by Treatment and Organ Class

	Pbo/PBO (N = 11) n (%)	Pbo/SER-287 Wkly (N = 15) n (%)	Vanco/SER-287 Wkly (N = 17) n (%) E	Vanco/SER-287 Daily (N = 15) n (%)	SER-287 Overall (N = 47) n (%)
Gastrointestinal disorders	5 (45.5)	7 (46.7)	8 (47.1)	2 (13.3)	17 (36.2)
General disorders and administration site conditions	1 (9.1)	0	3 (17.6)	1 (6.7)	4 (8.5)
Immune system disorders	0	0	1 (5.9)	0	1 (2.1)
Infections and infestations	3 (27.3)	1 (6.7)	6 (35.3)	4 (26.7)	11 (23.4)
Injury, poisoning and procedural complications	2 (18.2)	0	0	0	0
Investigations	0	0	1 (5.9)	0	1 (2.1)
Metabolism and nutrition disorders	0	0	1 (5.9)	1 (6.7)	2 (4.3)
Musculoskeletal and connective tissue disorders	0	3 (20.0)	1 (5.9)	2 (13.3)	6 (12.8)
Nervous system disorders	0	0	1 (5.9)	3 (20.0)	4 (8.5)
Psychiatric disorders	1 (9.1)	0	0	1 (6.7)	1 (2.1)
Reproductive system and breast disorders	0	0	1 (5.9)	0	1 (2.1)
Respiratory, thoracic and mediastinal disorders	0	1 (6.7)	2 (11.8)	1 (6.7)	4 (8.5)
Skin and subcutaneous tissue disorders	0	0	1 (5.9)	3 (20.0)	4 (8.5)

SER-287 treatment arms compare favorably with PBO arms with most efficacious arm showing a significant reduction in GI AEs compared to placebo - independent evidence for efficacy as GI AEs likely represent disease activity.

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Key inclusion and exclusion criteria

Inclusion Criteria

- Active mild-to-moderate UC:
  - Total Modified Mayo Score (TMMS) 4-10
  - ESS >1, with evidence of mucosal lesions
  - ≥ 15 cm of disease from anal verge

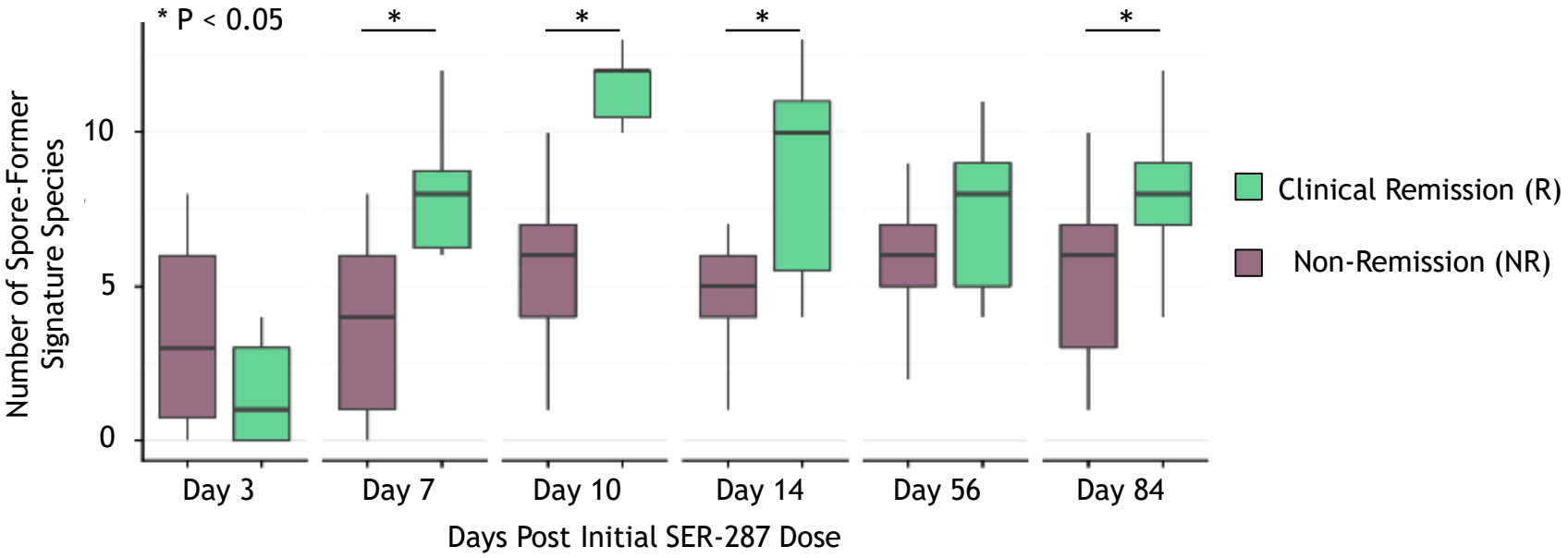
Permitted medications

- ASAs
- Immunomodulators (e.g. azathioprine)
- Prednisone ≤15mg
- Budesonide ≤6mg or Budesonide MMX ≤9mg

Exclusion Criteria

- Subjects taking cyclosporine
- Subjects taking biologic therapy currently or within 3 months prior to randomization
- Known allergy or intolerance to oral vancomycin
- Unable to stop the following medications before screening visit:
  - Probiotics
  - Steroid enemas or suppositories
  - Mesalamine enemas or suppositories

Engraftment of remission-associated spore-former species is greater in subjects with clinical remission across all study arms



- 14 of 19 species signature identified as positively associated with clinical remission in the Vancomycin pre-tx / SER-287 daily arm are spore-formers
- Engraftment of these 14 SER-287 spore-formers was significantly more prevalent in subjects with clinical remission vs non-remission starting at 7 days post treatment with SER-287

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