

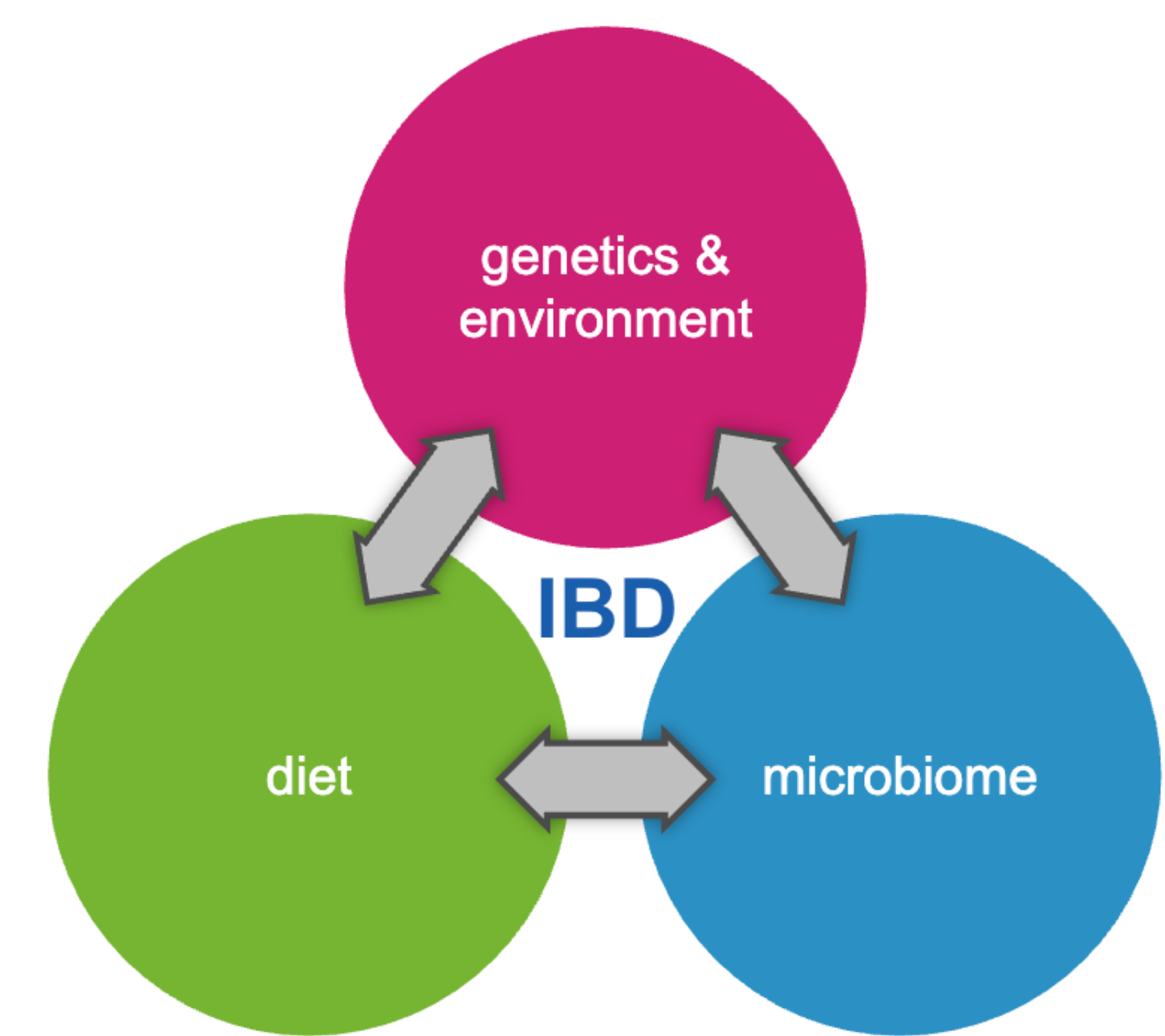
**IBD AND THE MICROBIOME**

IBD is a complex disease, with multiple potential factors leading to the expression of disease symptoms.

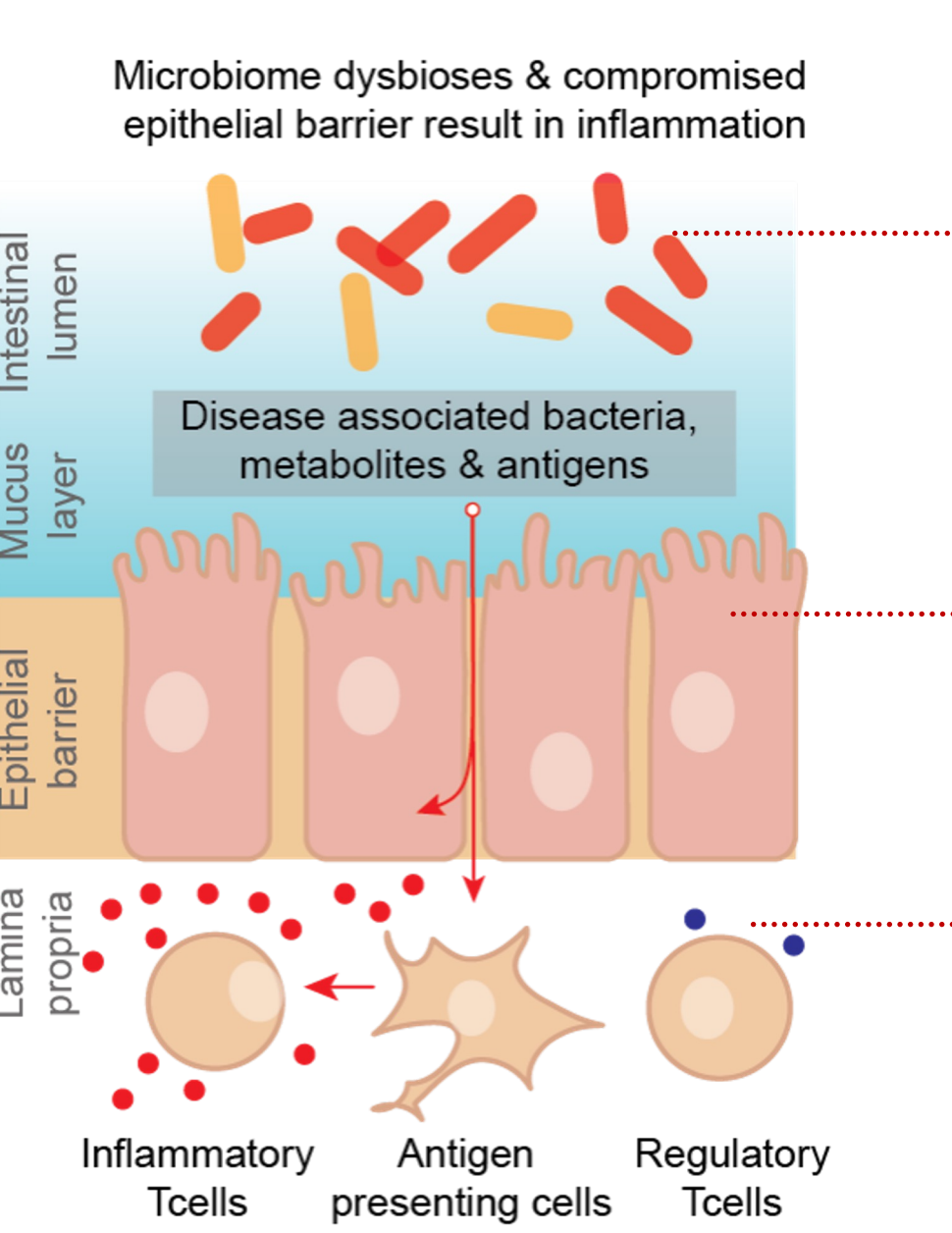
The microbiome has been hypothesized to play a causal role in disease in some patients, acting as a source of inflammation.

There are many unanswered questions:

- What features of the microbiome impact IBD?
- How does the microbiome of patients with IBD impact response to therapy?
- Can we proactively identify patients based on their microbiome to inform treatment?

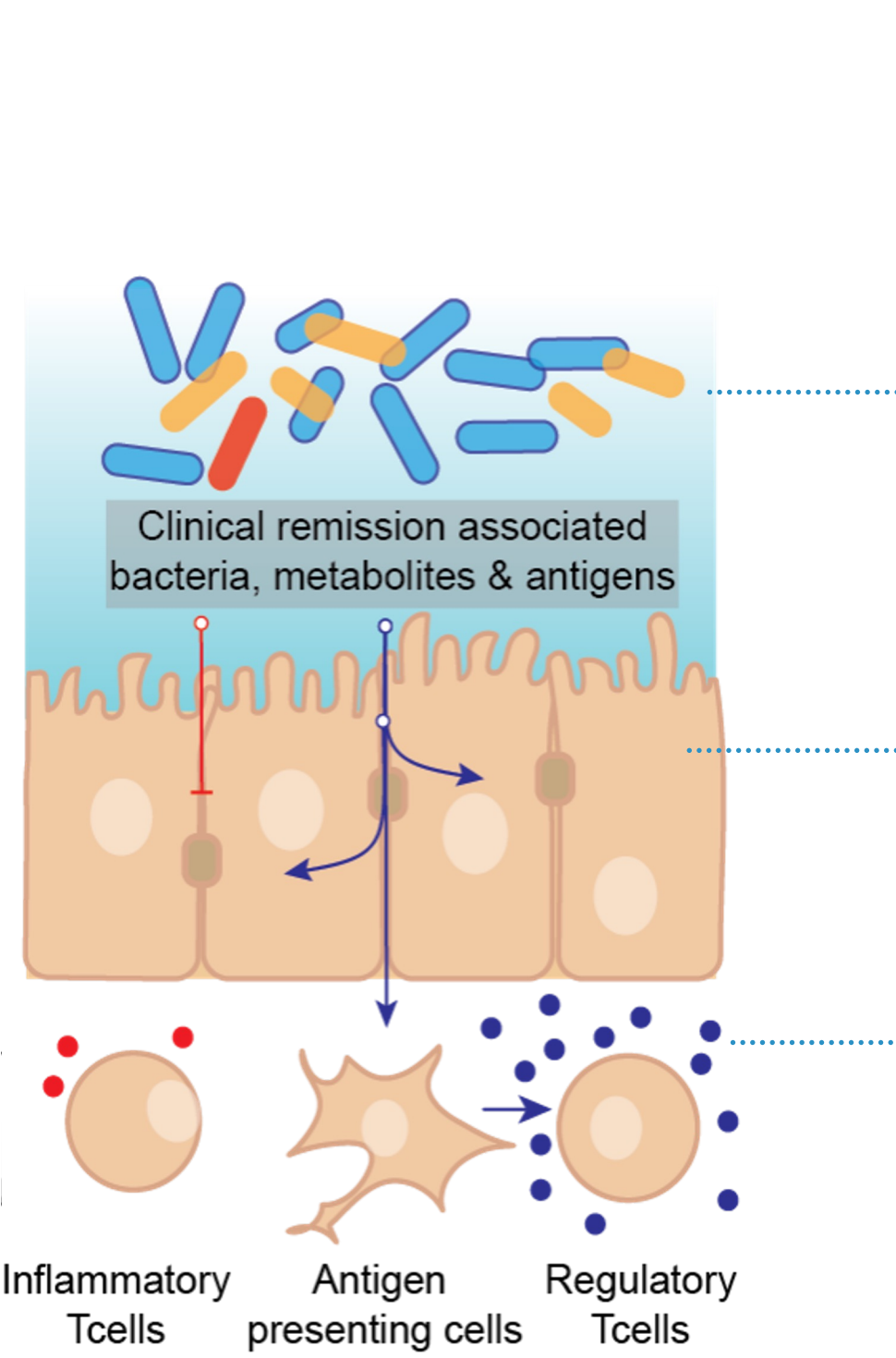


**HOW MIGHT THE DISRUPTED MICROBIOME IMPACT IBD?**



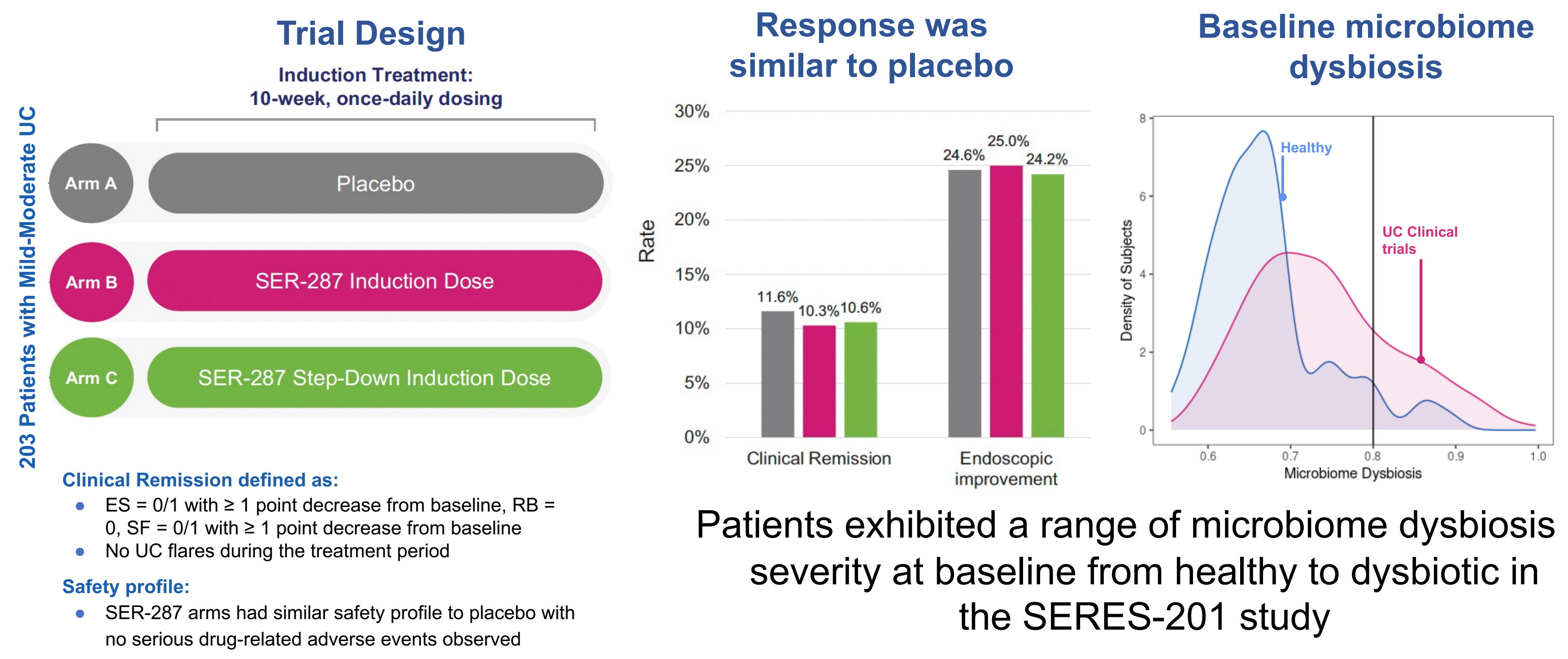
- (1) The presence of pro-inflammatory bacteria may drive disease through activation of cell receptors along the epithelial layer
- (2) The absence of beneficial bacteria may deprive host cells of needed nutrients to maintain an intact epithelial barrier
- (3) The combination of these two phenomena may enable inflammatory bacteria and bacterial products to enter surrounding GI tissue, driving inflammation

**Oral Microbiome Therapeutics: consortia of commensal bacteria designed to restore GI microbiome function and improve health**

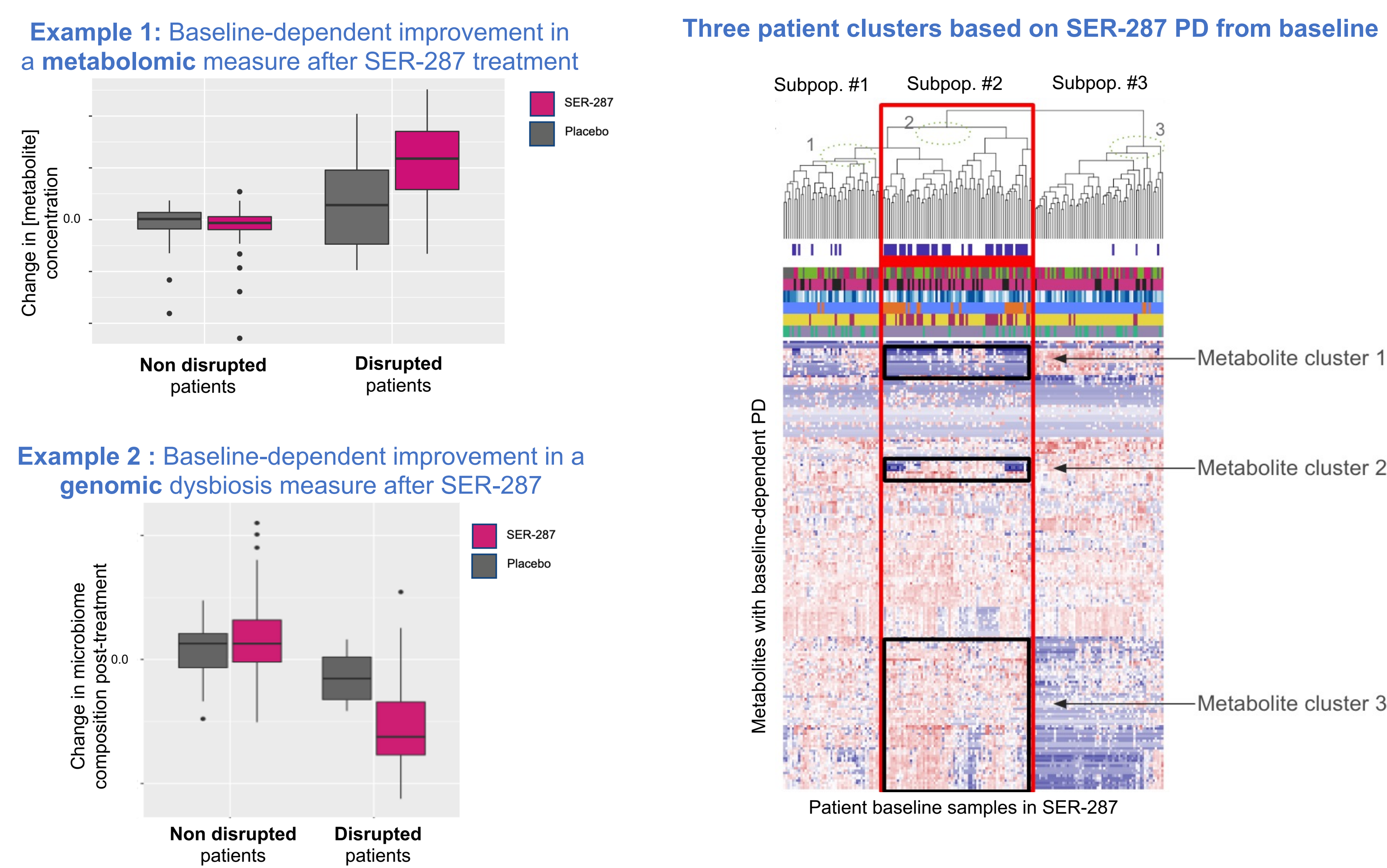


- (1) Displace and decolonize pro-inflammatory bacteria with healthy commensal microbes, removing inflammatory stimuli
- (2) Re-introduce and boost the production of bacterial metabolites that fuel epithelial cell function
- (3) Reduce the escape of bacteria and bacterial products into the surrounding tissue

**A SUBSET OF IBD PATIENTS HAVE A HIGHLY DISRUPTED MICROBIOME**



**SER-287 HAS MORE FAVORABLE PHARMACODYNAMICS IN PATIENTS WITH A DISRUPTED BASELINE MICROBIOME**



- Taxonomic and metabolic features were evaluated for baseline dependent effects on SER-287 pharmacodynamics (PD)
- >150 metabolites were identified with baseline-dependent PD
- Three clusters of SER-287 patients were identified by baseline dependent metabolites and 4 metabolites and 2 taxonomic markers were selected that best differentiate the cluster with the highest levels of baseline disruption

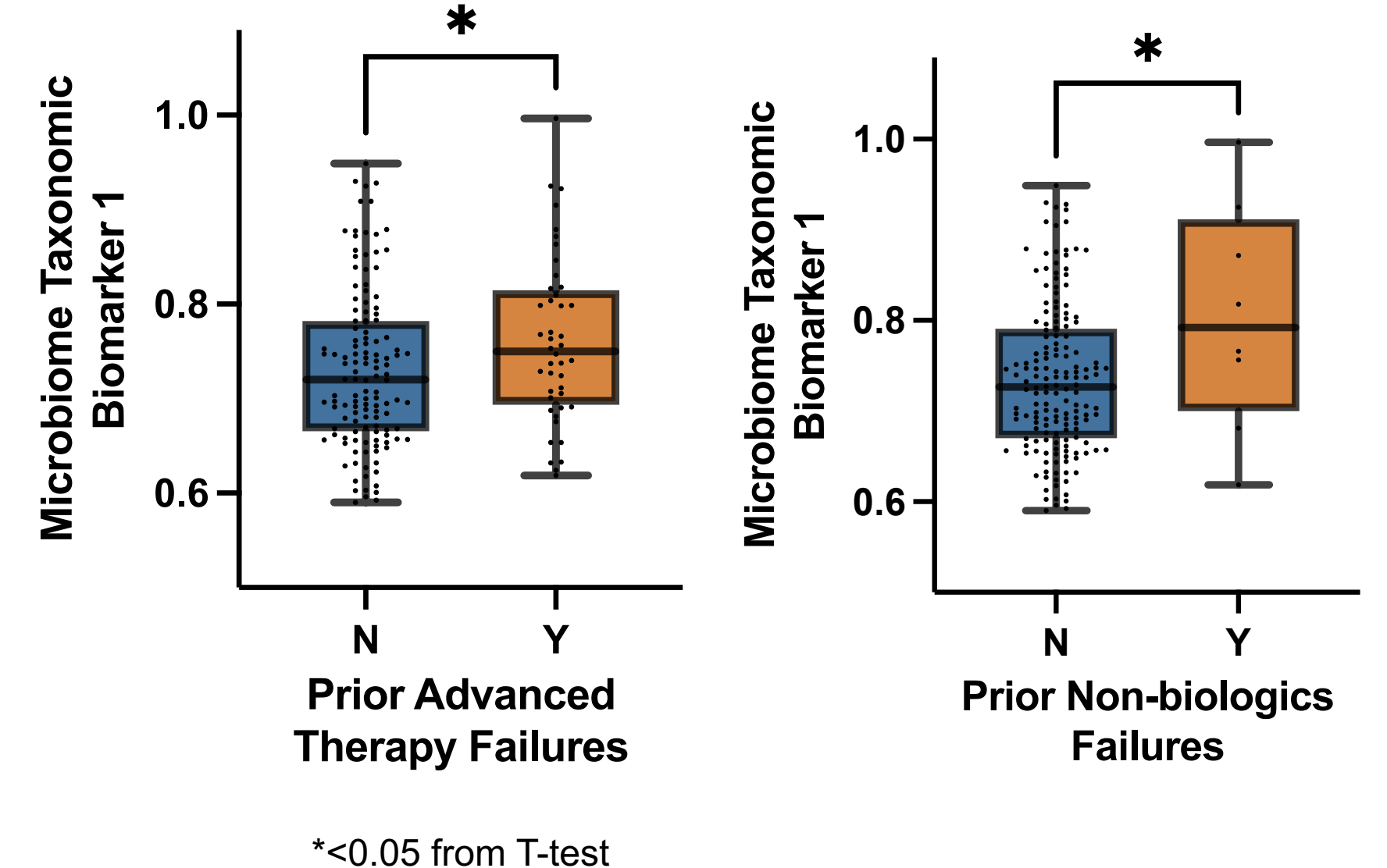
**MICROBIOME BASED PREDICTIVE BIOMARKERS ENRICH FOR CLINICAL REMISSION**

Population	N	Baseline endoscopic subscore (%)			Clinical remission (%)	
		ES=1	ES=2	ES=3	Placebo	SER-287
All patients	203	21.7	42.9	35.5	11.6	10.5
Microbiome taxonomic biomarker 1	39	23.1	38.5	38.5	0	6.7
Microbiome taxonomic biomarker 2	50	26.0	40.0	34.0	0	8.6
Microbiome metabolite biomarker 1	55	25.5	38.2	36.4	0	10.8
Microbiome metabolite biomarker 2	34	20.6	26.5	52.9	0	8.3
Microbiome metabolite biomarker 3	18	27.8	16.7	55.5	0	14.3
Microbiome metabolite biomarker 4	33	18.2	33.3	48.5	0	4.8
Any of the above	94	22.34	38.30	39.36	0	8.7

Baseline-dependent biomarkers populations based on baseline samples of have increased rate of clinical remission compared to placebo

**PATIENTS FAILING PAST ADVANCED THERAPY HAVE HIGHER BASELINE MICROBIOME TAXONOMIC BIOMARKER 1**

**Microbiome taxonomic biomarker 1 in patients failing past advanced therapy**



- The "prior advanced therapy failures" group included patients who previously failed biologic (e.g., anti-TNF, anti-integrin) or small molecule (e.g., anti-JAK) therapy.
- Microbiome taxonomic biomarker 1 showed a statistically significant increase in patients with all prior advanced therapy failure
- Specifically, the non-biologic (small molecule) failures were statistically significant while other subsets (anti-TNF and anti-integrin) showed an increase but did not reach significance due to limited population size

**Conclusion:**

- A post-hoc analysis of data from the Phase 2b trial of SER-287 ("SERES-201", NCT03759041) has identified potential microbiome based predictive biomarkers of clinical response.
- These data are consistent with a growing appreciation that a subset of IBD patients have a disrupted gut microbiome suggesting the microbiome is a driver of inflammation in these patients.
- Use of microbiome-based predictive biomarkers may enable identification of patients with a disease etiology linked to the microbiome and predict response to advanced therapies that would benefit from microbiome intervention.

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