European Crohn's and Colitis Organisation

Gut microbial variations in patients with quiescent Crohns disease predict subsequent disease flare

Yael Haberman, MD, PhD

Sheba Medical Center, Israel

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Disclosures:

Conflict of interest:

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Dysbiosis likely contribute to CD pathogenesis and is not just secondary to inflammation or medications

Based on Murine studies
Based on treatment naïve early onset cohort (no meds)
Based on gut segments with no inflammation

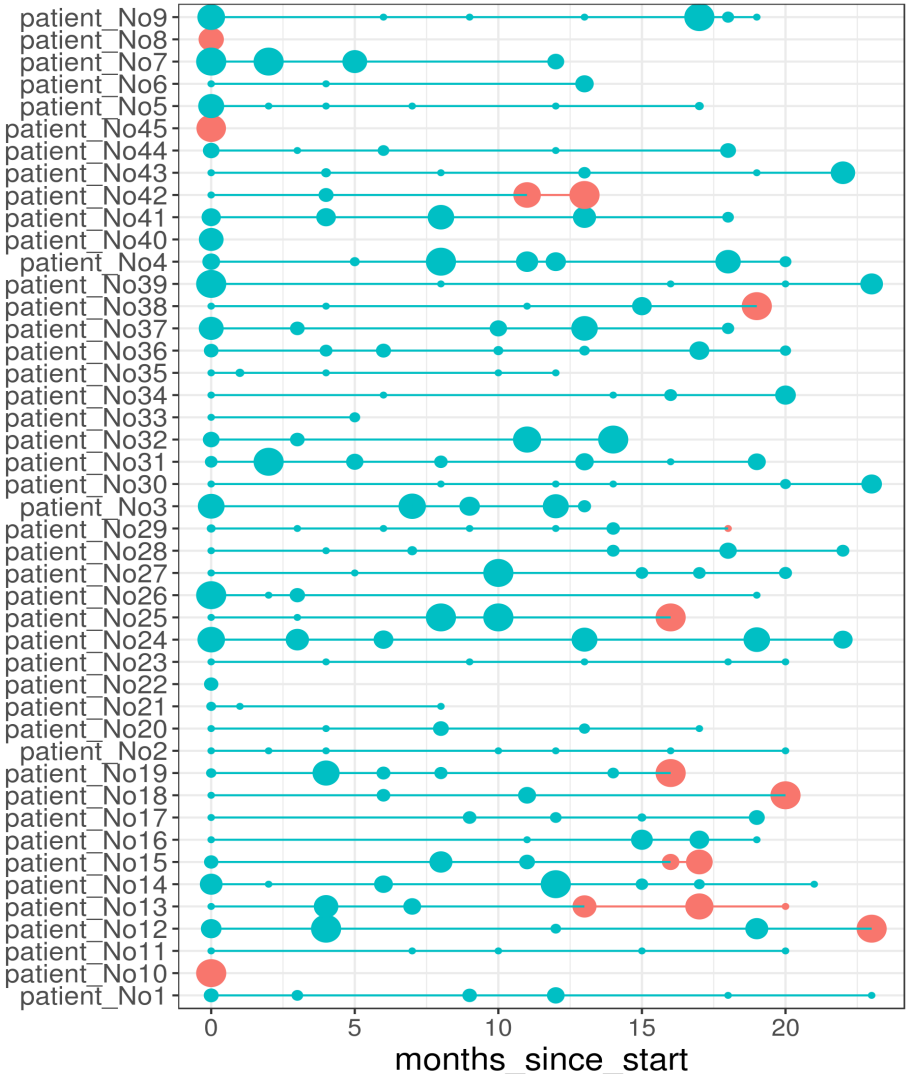
- Hypothesis I: CD patients in disease remission still show microbial dysbiosis

- Hypothesis II: changes in longitudinal clinical and microbial data may precede disease flare

Importance: If dysbiosis persist in the absence of inflammation and changes precede disease flare it is probably a primary driver of pathogenesis.

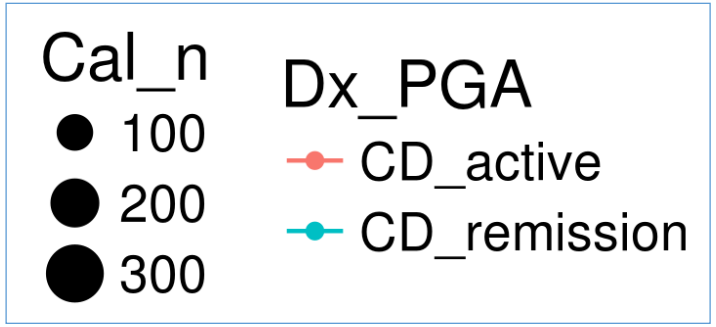
➢This mandate attention in regards to overall treatment goals
➢This may be used as a prognostic marker

IIRN Crohn Disease cohort in remission
45 cases with prospectively collected 217 samples



45 cases

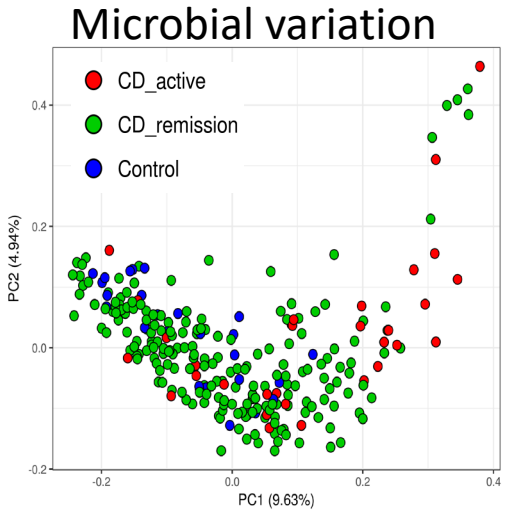
12 flared (27%)

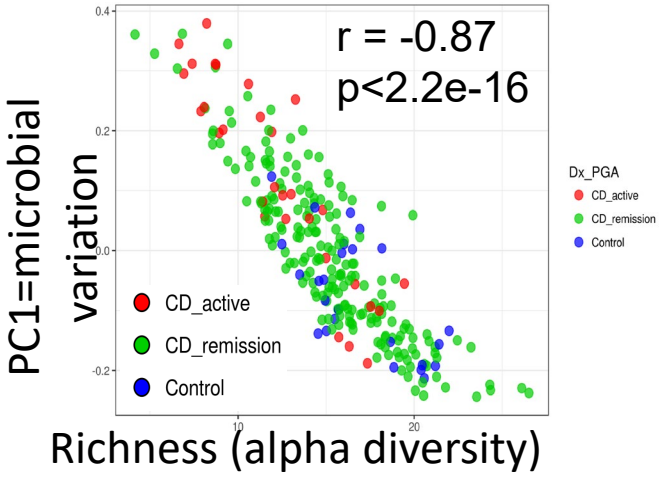


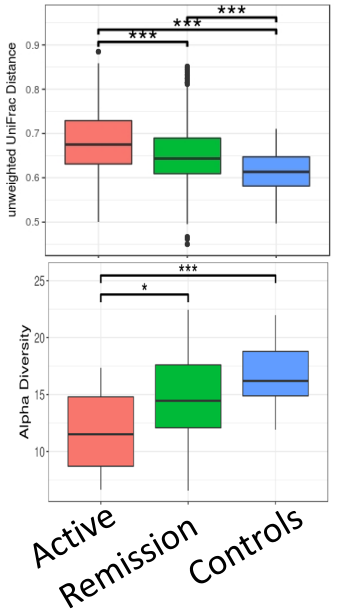
	Ctl (n=22)	CD active (n=17)	IIRN (n=45)
Age (years) mean[SD]	40[16]	39 [14]	33 [10]
Gender M	55%	70%	60%
Fecal Calprotectin median(IQR)	-	588 (151,729)	43.5 (30,121)

Braun & Haberman et al. Am J of Gastro, 2019

Crohn patients in clinical, biomarker, and mucosal remission show microbial variation in between active disease patients and controls



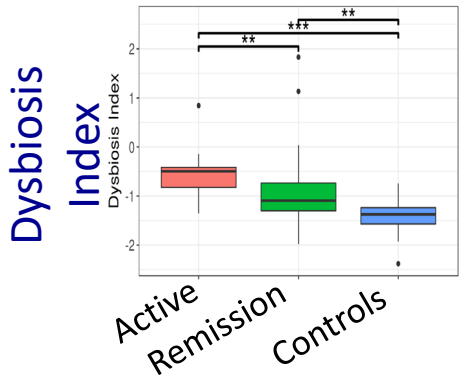




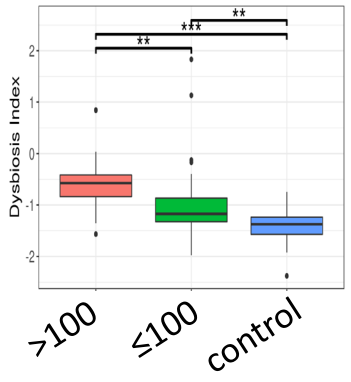
Microbial variation

Microbial richness

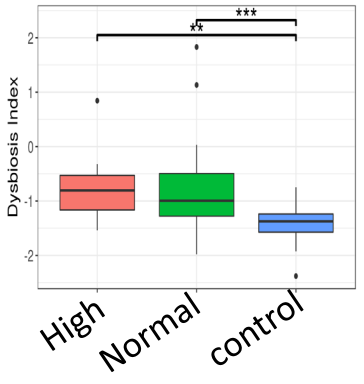
Clinical severity (PGA)



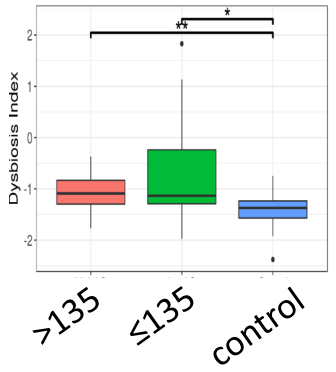
Mucosal inflammation (Fecal calprotectin)



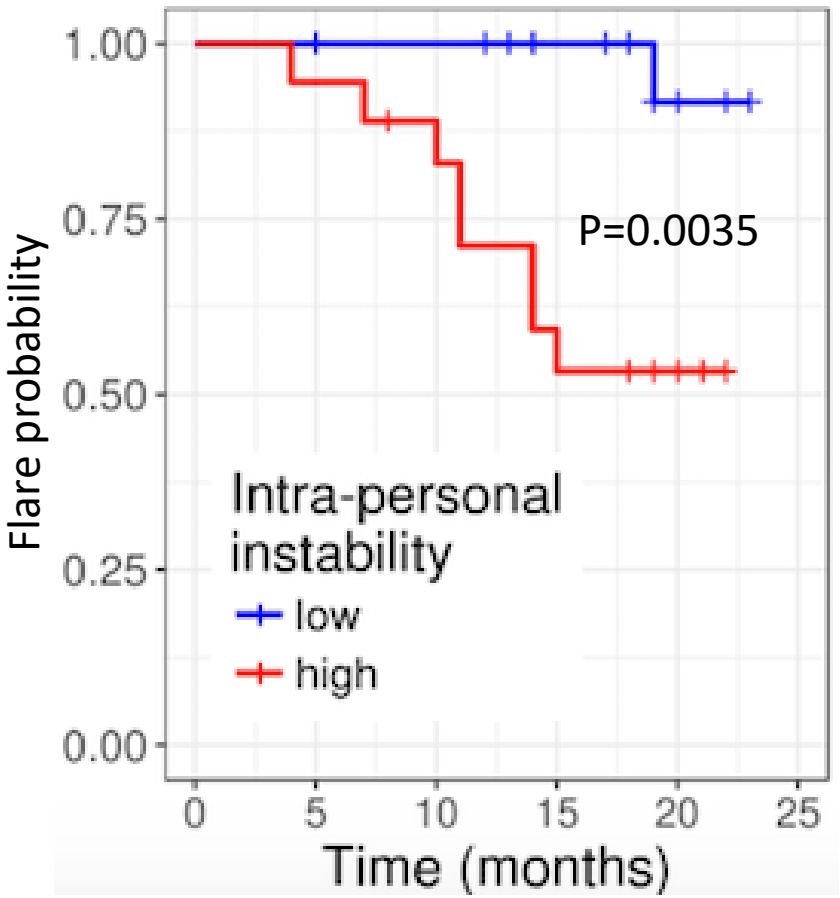
Systemic inflammation (CRP)



Mucosal inflammation (highest Lewis score)



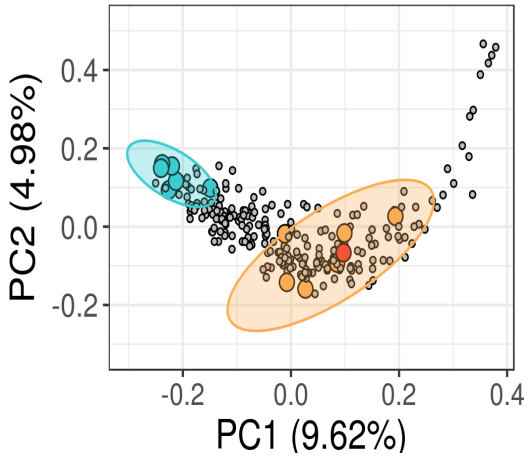
Microbiome changes during remission may be the cause or a reporter of the inflammatory process pre-flare that subsequently lead to a disease flare



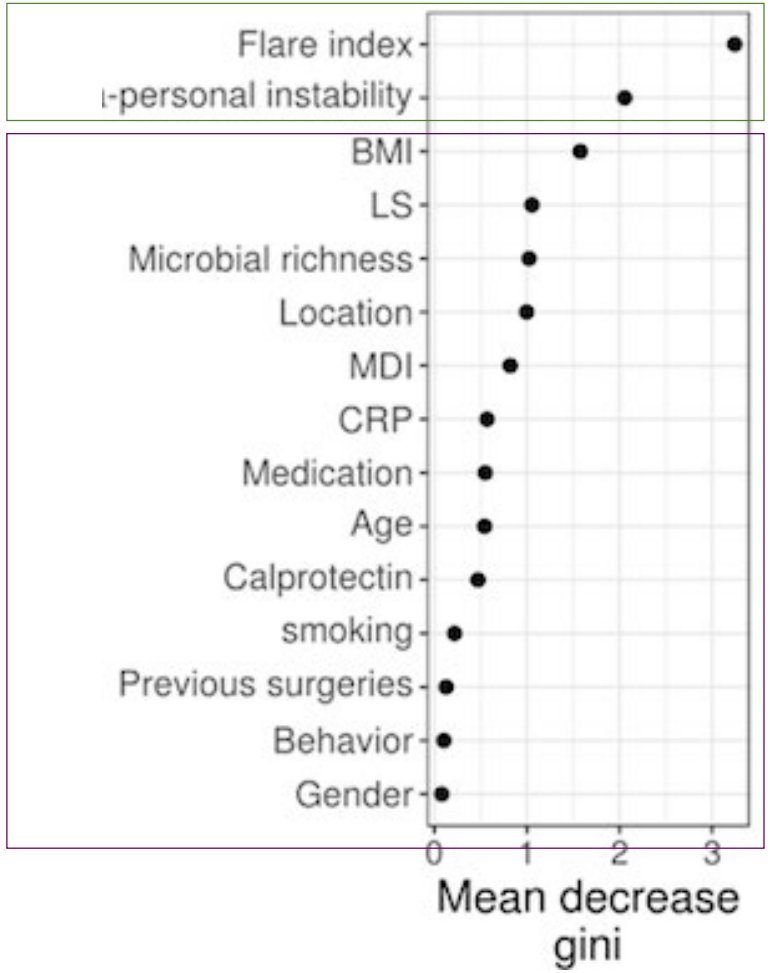
Patient X with persistent remission

Patient Y in remission with a subsequent flare

Patient Y flare



Prioritization of contributing factors based on machine learning classifier



Conclusions– Crohn dysbiosis

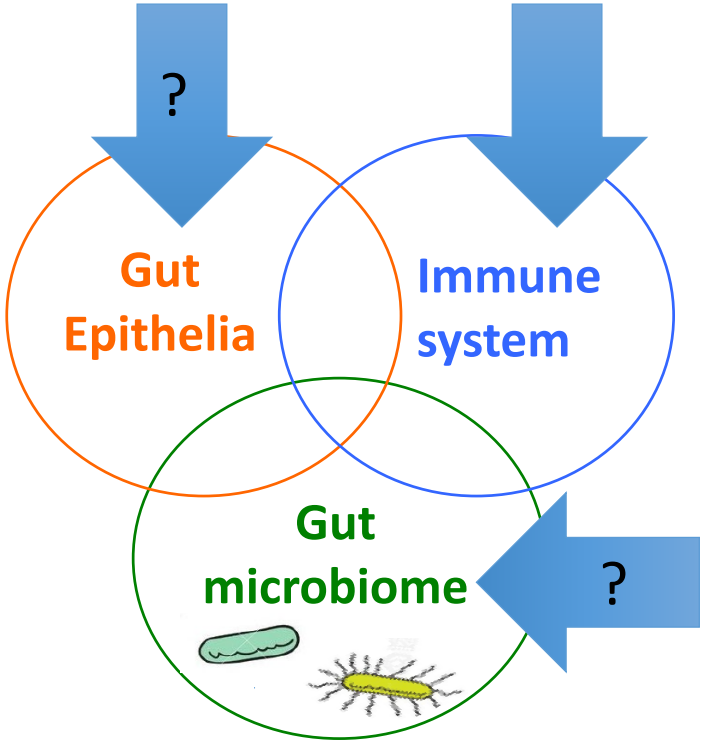
- Crohn patients in deep remission and in the absence of mucosal ileal inflammation still show significantly higher microbial dysbiosis index

- Specific taxa ("flare index") and intra-personal instability are associated with and can predict a subsequent flare

Implications

- CD dysbiosis like genetics is a primary intrinsic component of the pathogenesis that is not currently addressed by therapeutic approaches.

- However, as opposed to genetics that is harder to manipulate, future therapeutic and nutritional interventions should aim to target the microbiota to improve CD natural history.



Acknowledgments

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