Microbiome

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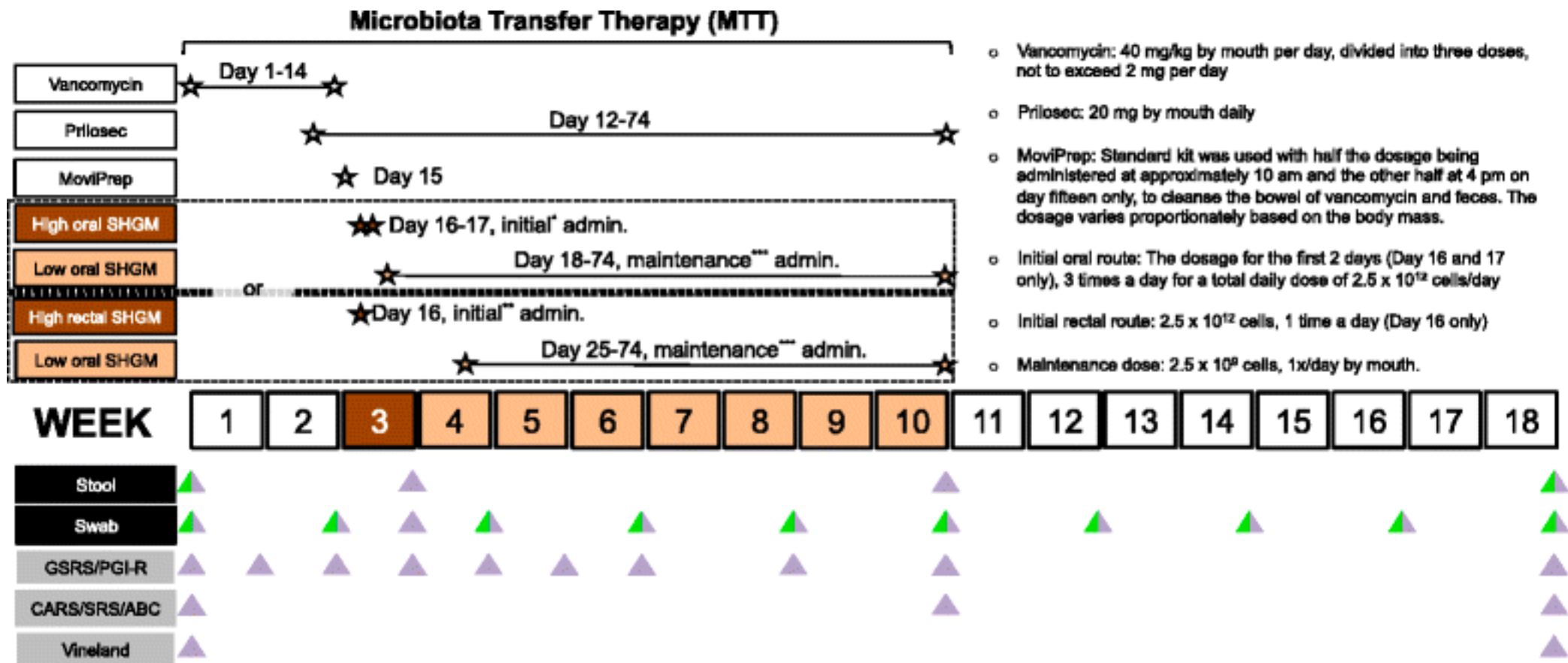
Microbiota Transfer Therapy alters gut ecosystem and improves gastrointestinal and autism symptoms: an open-label study

Dae-Wook Kang[1†], James B. Adams[2†], Ann C. Gregory[3,15†], Thomas Borody[4], Lauren Chittick[5,15], Alessio Fasano[6], Alexander Khoruts[7,8,9], Elizabeth Geis[2], Juan Maldonado[1], Sharon McDonough-Means[10], Elena L. Pollard[2], Simon Roux[5,15], Michael J. Sadowsky[8,11], Karen Schwarzberg Lipson[12], Matthew B. Sullivan[3,5,15,16*], J. Gregory Caporaso[12,13*] and Rosa Krajmalnik-Brown[1,14*]

Microbiota Transfer Therapy (MTT)

| | WEEK | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |

Vancomycin — Day 1-14

Prilosec — Day 12-74

MoviPrep — Day 15

High oral SHGM — Day 16-17, initial* admin.

Low oral SHGM — Day 18-74, maintenance*** admin.

or

High rectal SHGM — Day 16, initial** admin.

Low oral SHGM — Day 25-74, maintenance*** admin.

- Vancomycin: 40 mg/kg by mouth per day, divided into three doses, not to exceed 2 mg per day
- Prilosec: 20 mg by mouth daily
- MoviPrep: Standard kit was used with half the dosage being administered at approximately 10 am and the other half at 4 pm on day fifteen only, to cleanse the bowel of vancomycin and feces. The dosage varies proportionately based on the body mass.
- Initial oral route: The dosage for the first 2 days (Day 16 and 17 only), 3 times a day for a total daily dose of 2.5×10^{12} cells/day
- Initial rectal route: 2.5×10^{12} cells, 1 time a day (Day 16 only)
- Maintenance dose: 2.5×10^{9} cells, 1x/day by mouth.

Stool · Swab · GSRS/PGI-R · CARS/SRS/ABC · Vineland

14 days of oral vancomycin
Bowel prep + 1-day fast
One day of high dose SHGM
Follow-up low-dose, oral SHGM every day for 7/8 weeks

PPI from end of vanco until the end of SHGM treatment

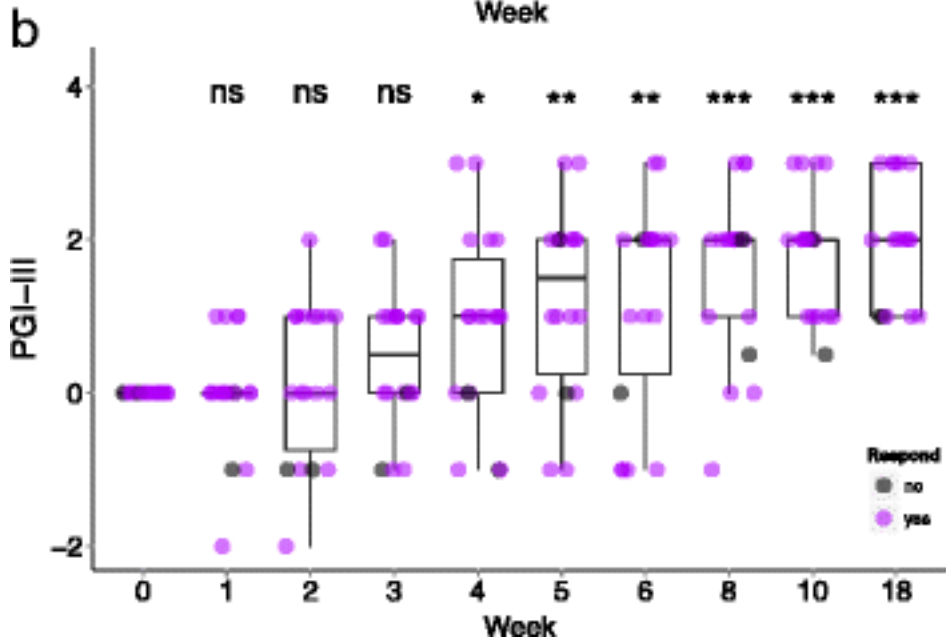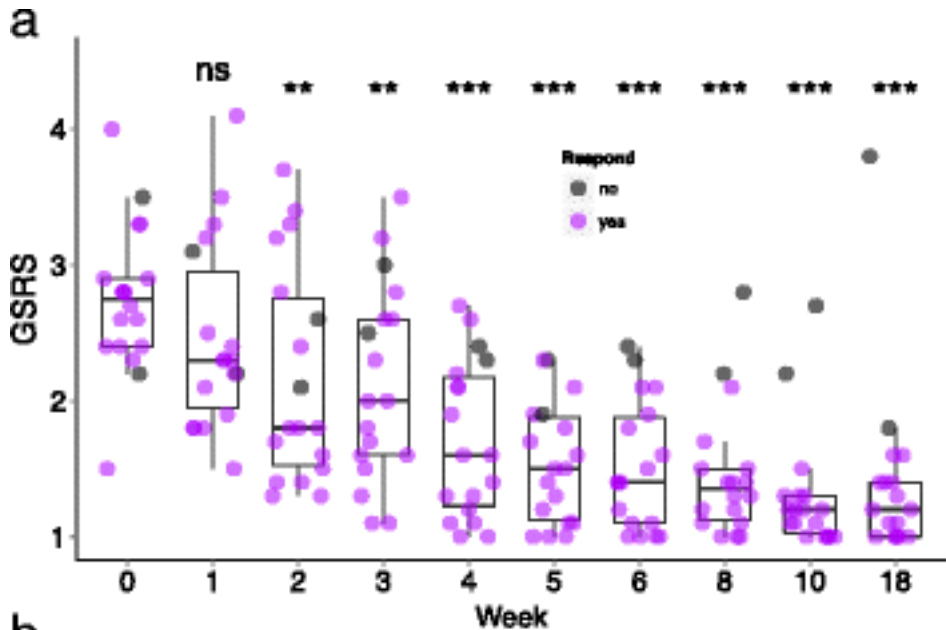18 ASD + 20 neurotypical. Everything open-labeled to everyone.

Primary endpoint: resolve GI symptoms
Secondary endpoint: improve ASD symptoms

same professional evaluator assessed the ADI-R (original dx) and the CARS
parents assessed the GSRS, PGI-III, ABC, and SRS

GI Symptoms

Gastrointestinal Symptom Rating Scale
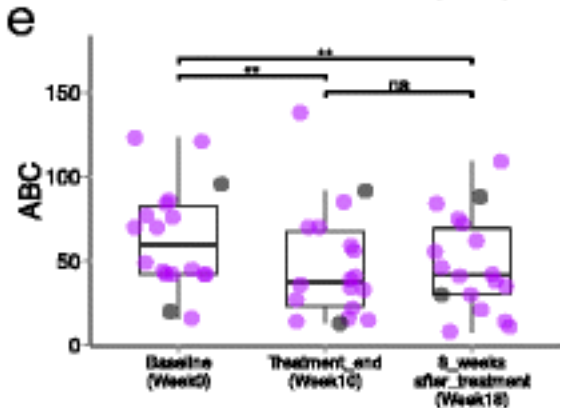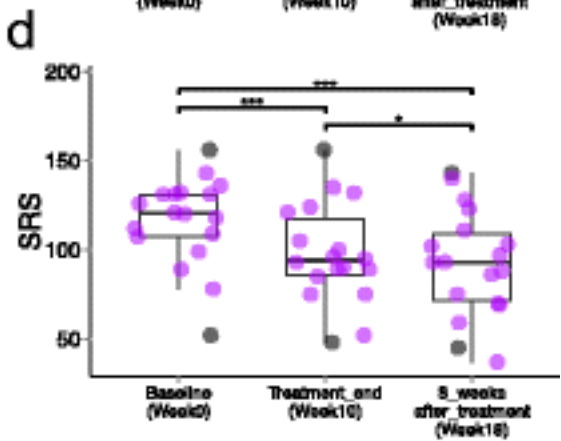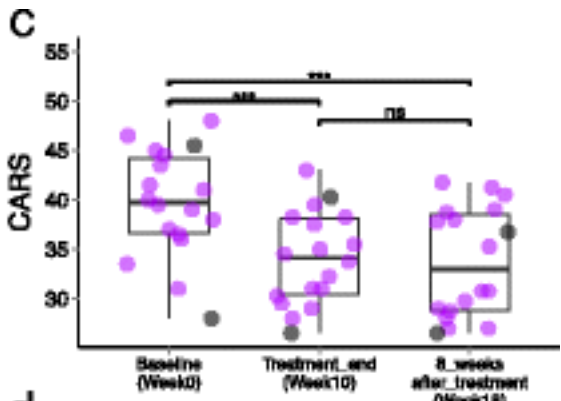
Non-responders defined based on this

ASD Symptoms

Parent Global Impressions-III

Ask parents directly about observed changes

18 different scores, one of which is "GI symptoms"

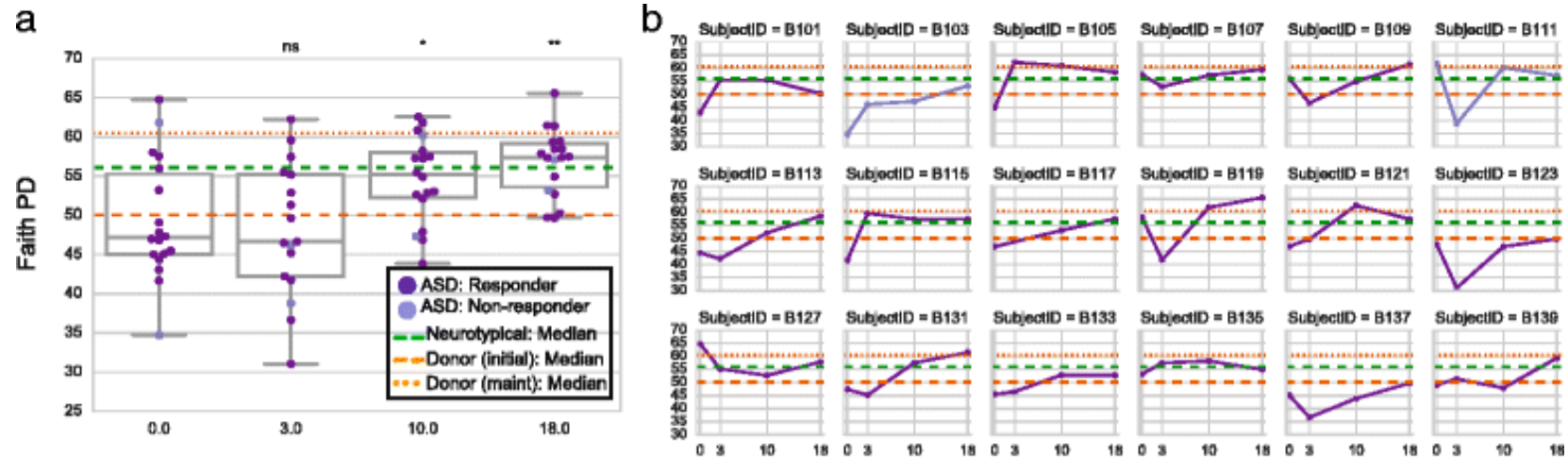**Childhood Autism Rating Scale**

15-item scale

Social Responsiveness Scale

65-item scale assesses social impairments

Aberrant Behavior Checklist

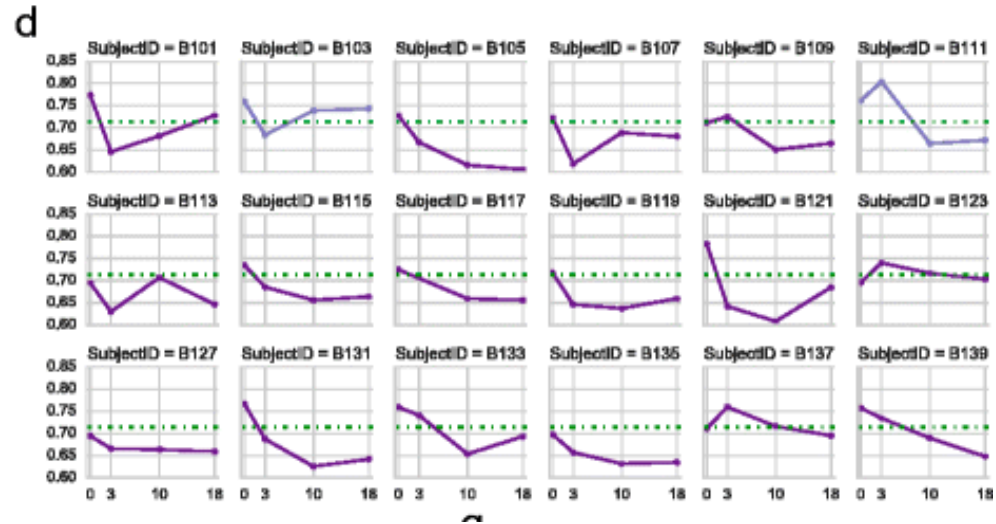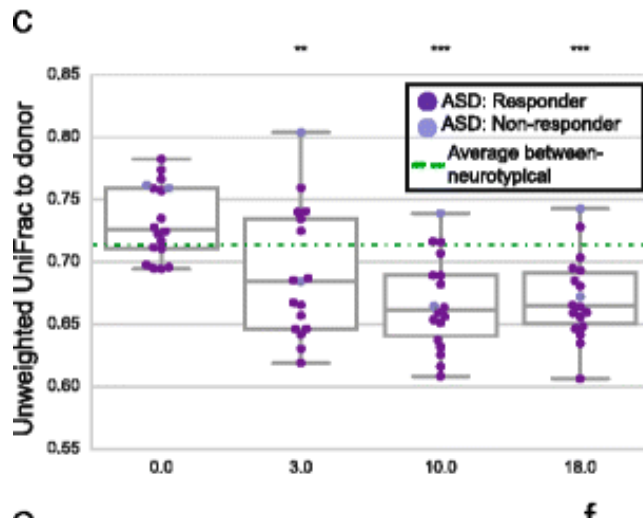irritability, lethargy, stereotypy, hyperactivity, and inappropriate speech

Baseline ASD have lower diversity than neurotypical
Alpha diversity increased after treatment and stayed high
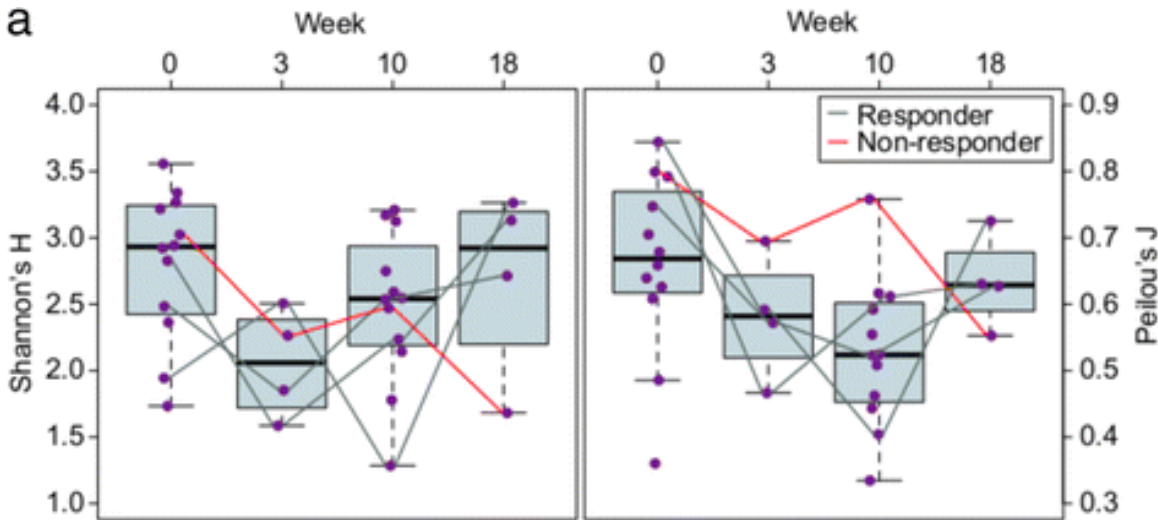
Recipients became more similar to the donor community
After treatment, the distance between the recipient and the donor was less than normal interpersonal variation
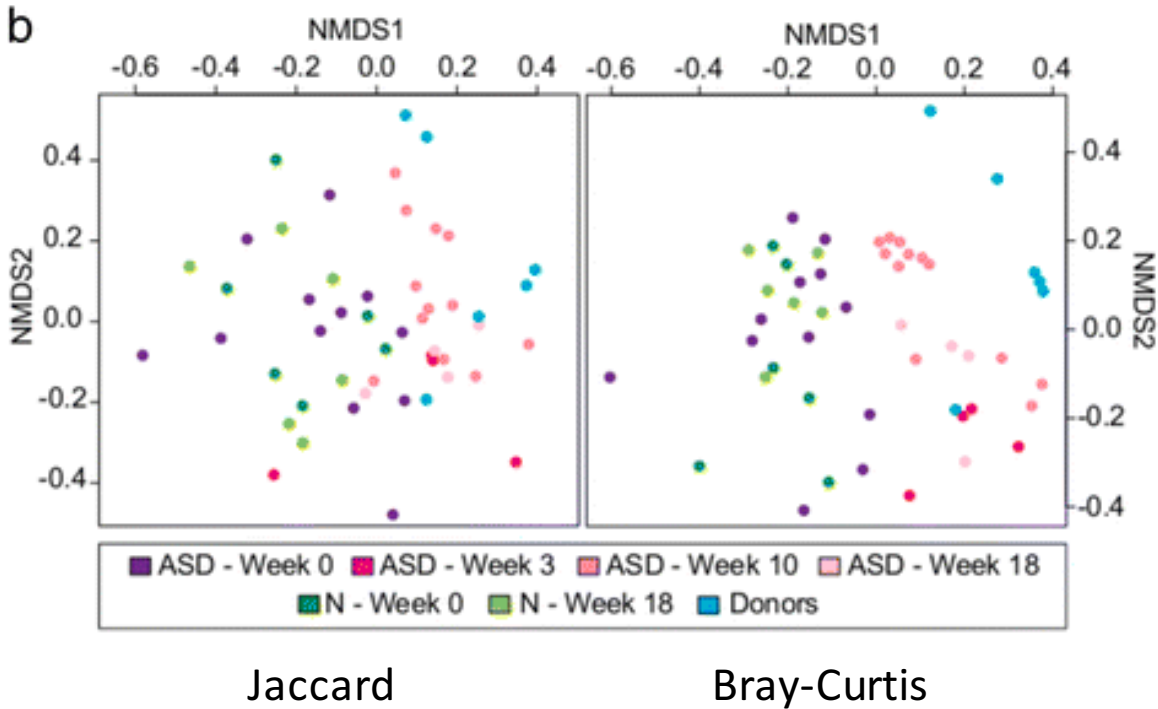*"These signatures of engraftment suggest that MTT overcame "colonization resistance""*

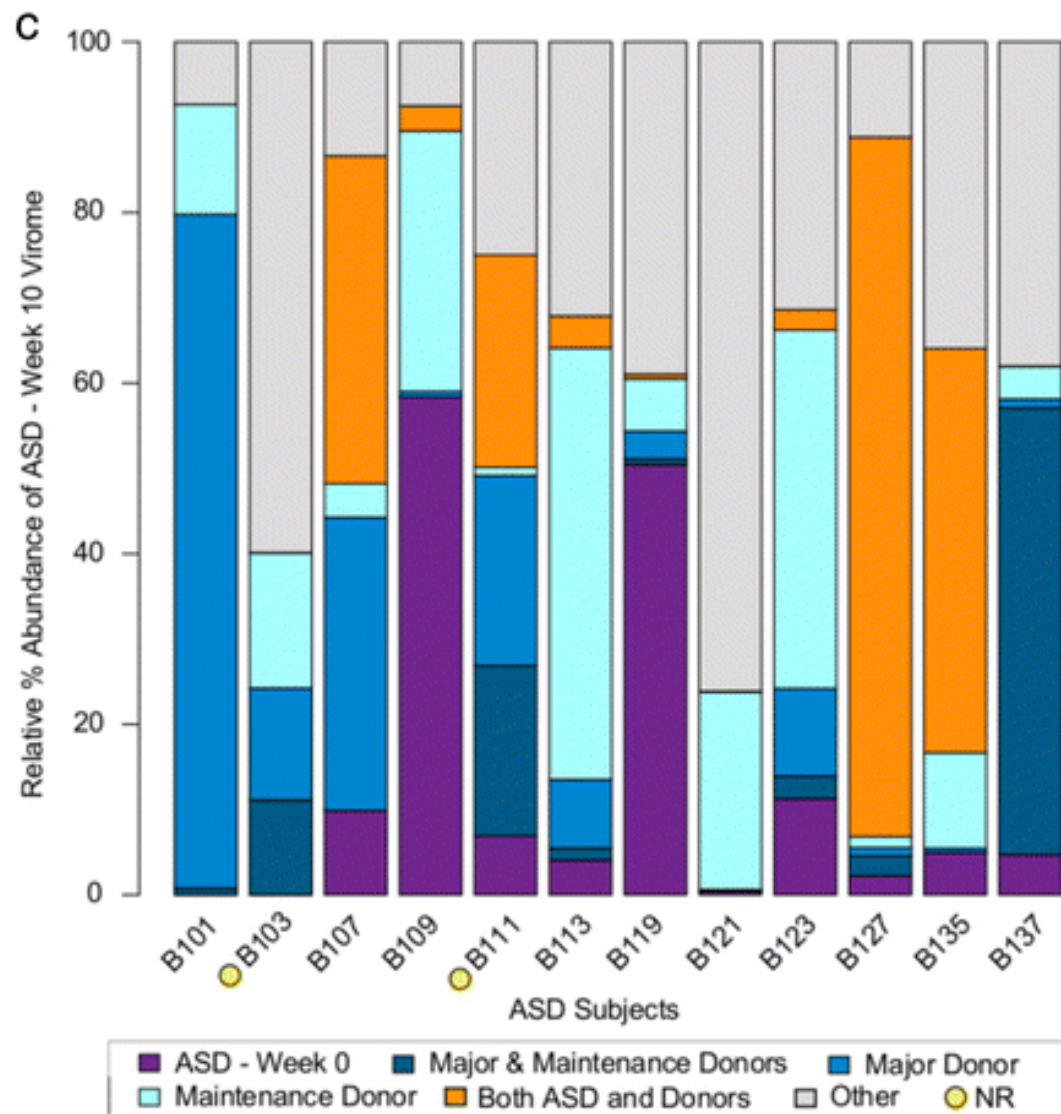4 patients had longitudinal phage samples: 3 responders, 1 non-responder

Phage diversity decreased during vanco and
bounced back after microbial transfer
Non-responder diversity did not bounce back

ASD gut bacteriophage communities are
more similar to donor communities after
SHGM doses

AKA Pink dots are closer to blue dots

Jaccard   Bray-Curtis

At week 10, majority of phage community is from a donor (all blue bars)

Also, less than 20% of the community at week 10 is from baseline (purple)

Yellow dot = non-responders