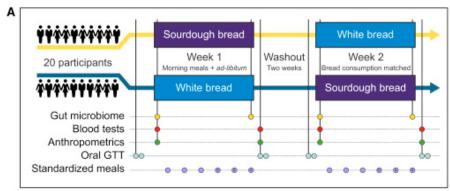
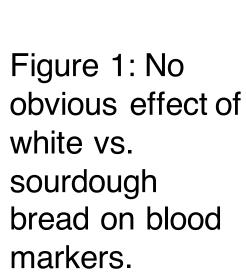
Clinical and Translational Report

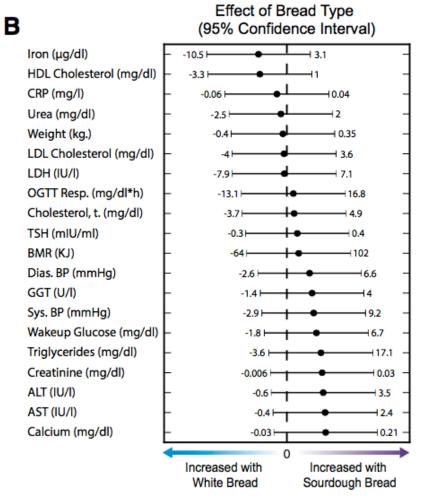
Cell Metabolism

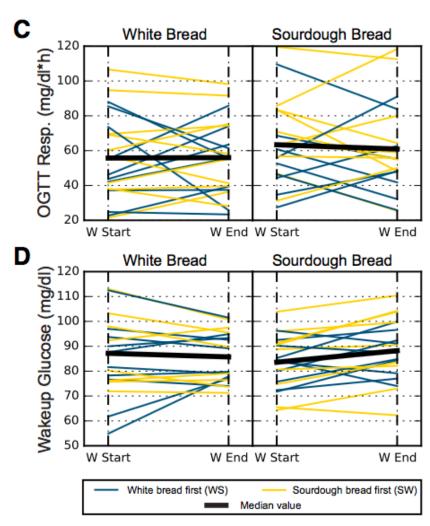
Bread Affects Clinical Parameters and Induces Gut Microbiome-Associated Personal Glycemic Responses

Tal Korem⁷, David Zeevi⁷, Niv Zmora, Omer Weissbrod, Noam Bar, Maya Lotan-Pompan, Tali Avnit-Sagi, Noa Kosower, Gal Malka, Michal Rein, Jotham Suez, Ben Z. Goldberg, Adina Weinberger, Avraham A. Levy ✓ —, Eran Elinav ✓ —, Eran Segal⁸ ✓









D Α Ε Calcium В **AST GGT** LDH Magnesium Iron 20 60 p<0.01 p<0.001 p<0.005 p<0.005 p<0.01 p<0.01 30 -15 10 40 0.4 0.4 20 10 20 0.2 (lp/gm) 1/Md 0.0 0.2 (lb/grl) LWD_-20 (mg/dl) 0.0 10 (IUI) 100 0 5 ΔW1 ΔW1 ₩_{-0.2} -5 -10-0.4-20 -0.4-40-10 -15-0.6-30-0.6Κ Cholesterol, t. H LDL Cholesterol | **ALT** Creatinine CRP L HDL Cholesterol 30 p<0.05 p<0.05 p<0.05 p<0.05 p<0_05 n.s. 20 10 0.2 20 0.05 10 10 0.1 OW1 (mg/dl) (mg/dl) (mg/dl) (mg/dl) (mg/_{0.0} **DW1 (IUI) √** ₩₋₁₀, ΔW1 ΔW1 ₽ M -0.1 -5 -10 -0.05 -20 -0.2-20-10-30-20White bread consumer Sourdough bread consumer 95% confidence interval

Figure 2: Looking at both breads together, some blood markers do change, but not by much.

"Anecdotally, one subject was enrolled in both studies (colored yellow and green, Figure 3E) and retained similar microbiota composition despite the prolonged time passed between studies (over 18 months)."

n.s.

Reference

Cohort (No

Intervention)

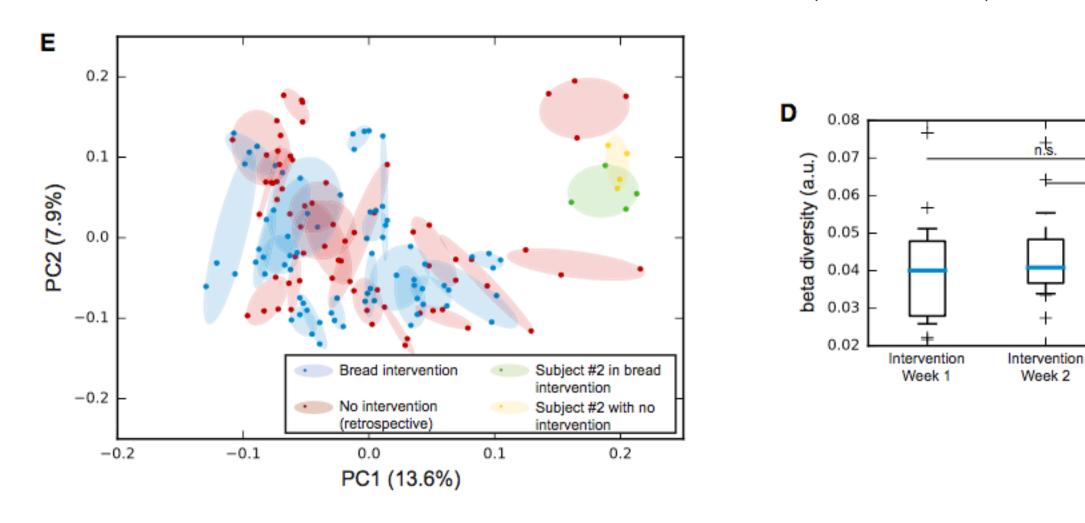


Figure 3: People cluster with themselves

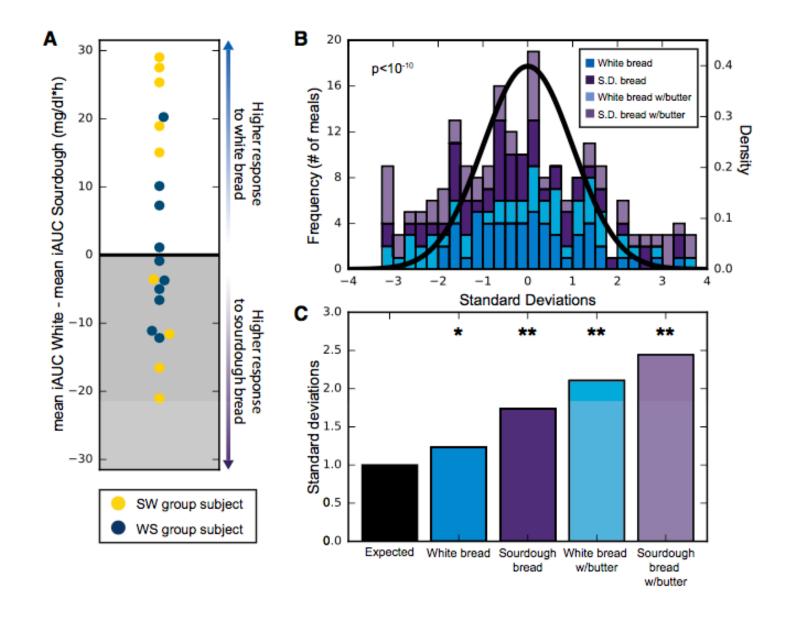


Figure 4: People have individualized responses to different foods.

Analysis of treatment effect in the crossover trial and calculation of 95% confidence interval was done using linear mixed models as recommended (Mehrotra, 2014), using SAS version 9.4, estimating treatment effect with fixed effects for period, sequence group, the difference between baseline measurements at both intervention periods, and interaction between that difference and the period. No other co-variates were included in the model. For the effect of bread on the gut microbiome (Figures 1E, 1F, and <u>\$3</u>), only instances (e.g., genus, module) with abundance above capping level observed in both weeks in at least 15 subjects were included in the analysis. Results were corrected for multiple hypothesis testing using FDR of 0.1 for each phylogenetic or functional level separately. Analysis of general bread consumption effect was performed using Wilcoxon signed-rank test, with results corrected for multiple hypothesis testing using FDR of 0.1.