

## Supplemental Information

**Figure S1:** Study design. K001 and K002 are randomized, open-label, three-cohort studies. The study product is FOS in K001 and PDX in K002. Subjects were randomized on Day 0 to one of three cohorts with different feeding amounts. The study began with 2 weeks of Run-In, 2 weeks of feeding followed by 2 weeks of feeding at same or higher dose, and 4 weeks of Washout. K003 is a randomized, double-blind, two-cohort study. Subjects were randomized on Day 0 to one of two cohorts. The study began with 2 weeks of Run-In, then 2 weeks of product 1 feeding followed by 4 weeks of Washout. Then subjects received product 2 for 2 weeks followed by another 4-week Washout.

**Figure S2:** Study product exposure. For each subject along the feeding periods, the intended dose of product consumption is colored in cyan and the actual dose is colored in red. The cyan and red dots overlapped on most study days for most subjects, indicating a good compliance.

**Figure S3:** Baseline microbiome characterization. (A) Alpha (Shannon) diversity of baseline samples in each cohort of the FOS and PDX studies. (B) Community composition at the phylum level for each subject in the FOS and PDX studies. (C) Multidimensional scaling (MDS) analysis on baseline microbiome samples in the FOS and PDX studies.

**Figure S4:** Species differentially abundant between baseline and feeding periods in each cohort receiving FOS or PDX.

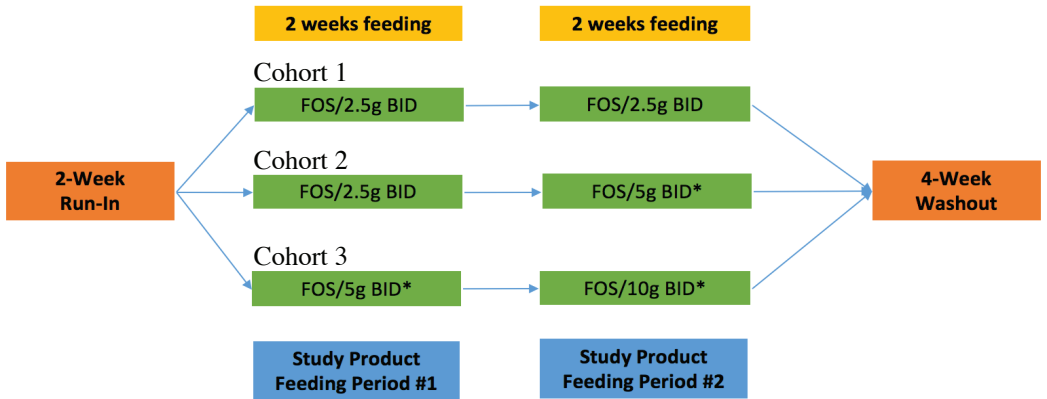
**Figure S5:** Microbiome responses in the FOS-PDX crossover study. (A) Percent changes in alpha (Shannon) diversity between baseline and later periods (Feeding1, Washout1, Feeding2, and Washout2) in each cohort receiving FOS or PDX. (B) Genera differentially abundant between baseline and FOS feeding periods in cohorts that either received FOS as the first or second compound. (C) Genera differentially abundant between baseline and PDX feeding periods in cohorts that either received PDX as the first or second compound.

**Figure S6.** Differentially abundant genes encoding CAZymes for PDX. For each CAZyme gene, we compared the difference in the distributions of fold-change (baseline versus combined feeding periods) of aggregated abundances of taxa in participants' microbiomes with the gene, and taxa without the gene (using reference genomes to make this determination.) Statistical testing was performed using the Wilcoxon rank-sum test (with  $p$ -values adjusted for multiple hypothesis testing using the Benjamini-Hochberg method and  $FDR < 0.01$ .) CAZymes are organized using the CAZy database structure, which contains five enzyme classes as well as carbohydrate-binding modules. Genes are sorted by  $p$ -values within each enzyme class.

**Figure S7:** Histogram of inferred onset times. Onset times for those species which responded (Bayes factor  $> 100$ ) across at least 25% of participants are shown. (A) FOS and (B) PDX.

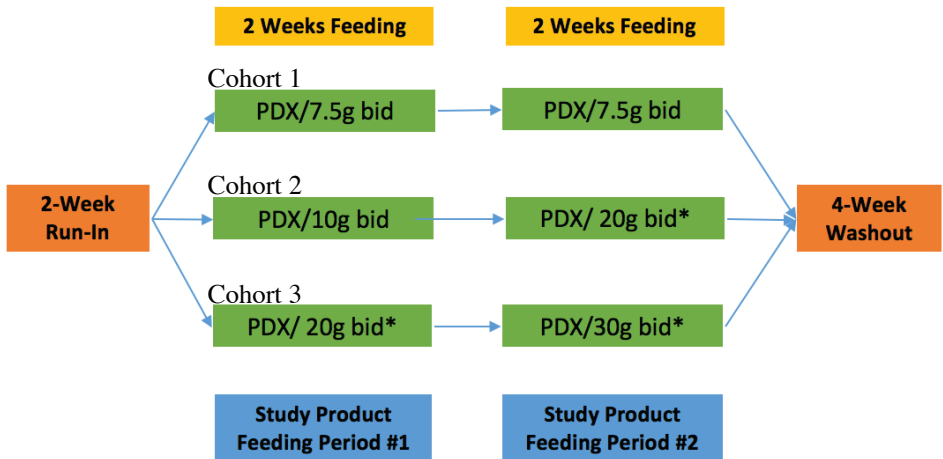
**Table S1:** Demographic characteristics of participants in each study.

## K001 Fundamental FOS Study



\*Or lower until individual maximal tolerable amount is reached.

## K002 Fundamental PDX Study



\*or lower until individual maximal tolerable dose is reached

## K003 Fundamental FOS - PDX Crossover Study

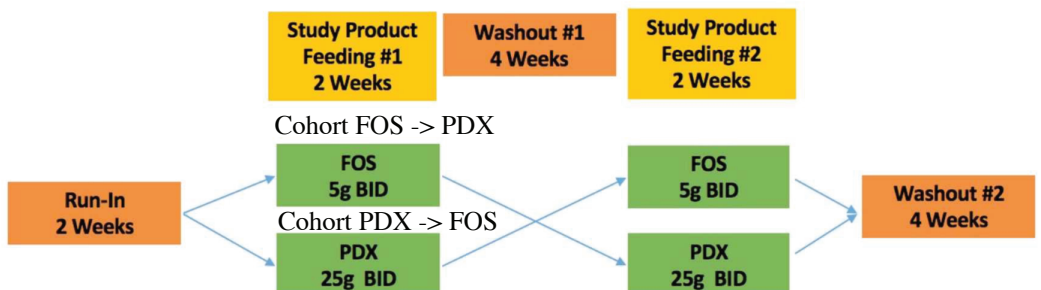
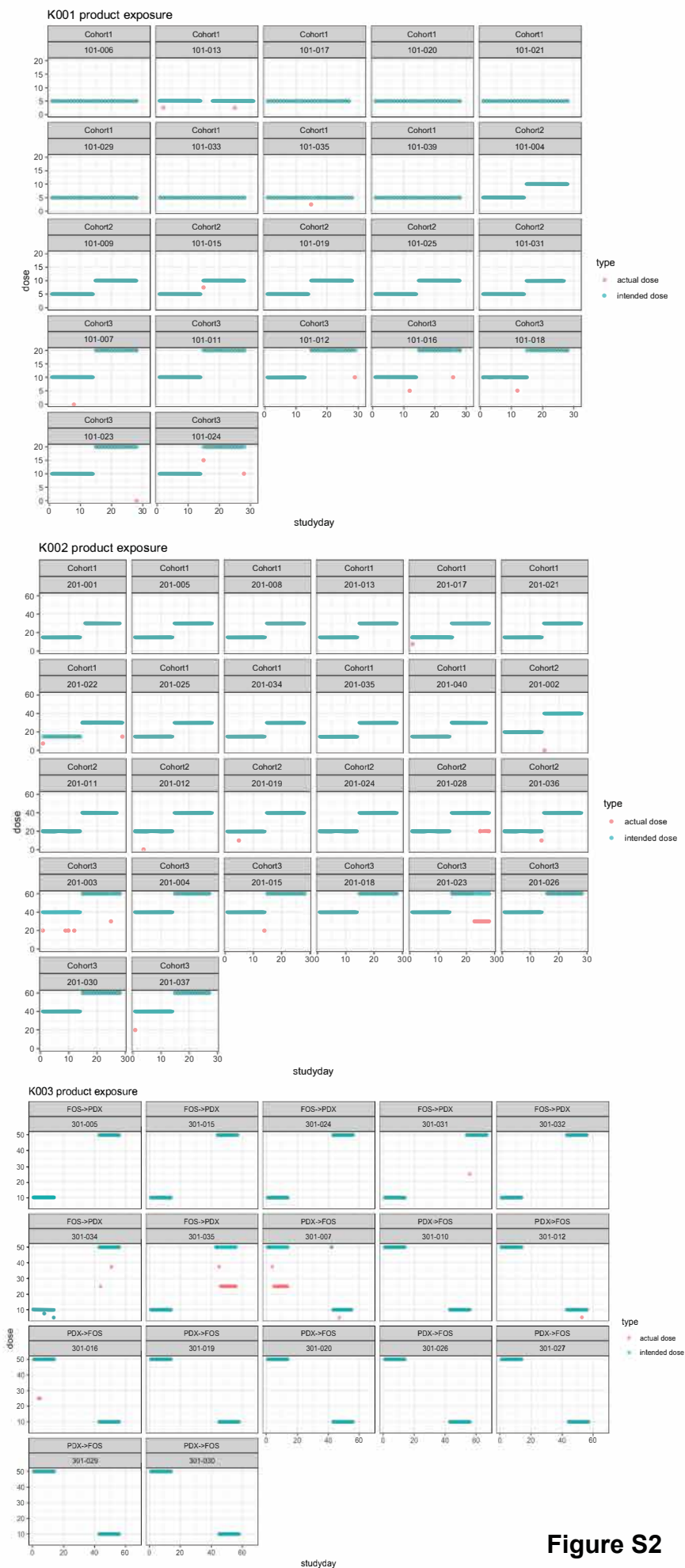
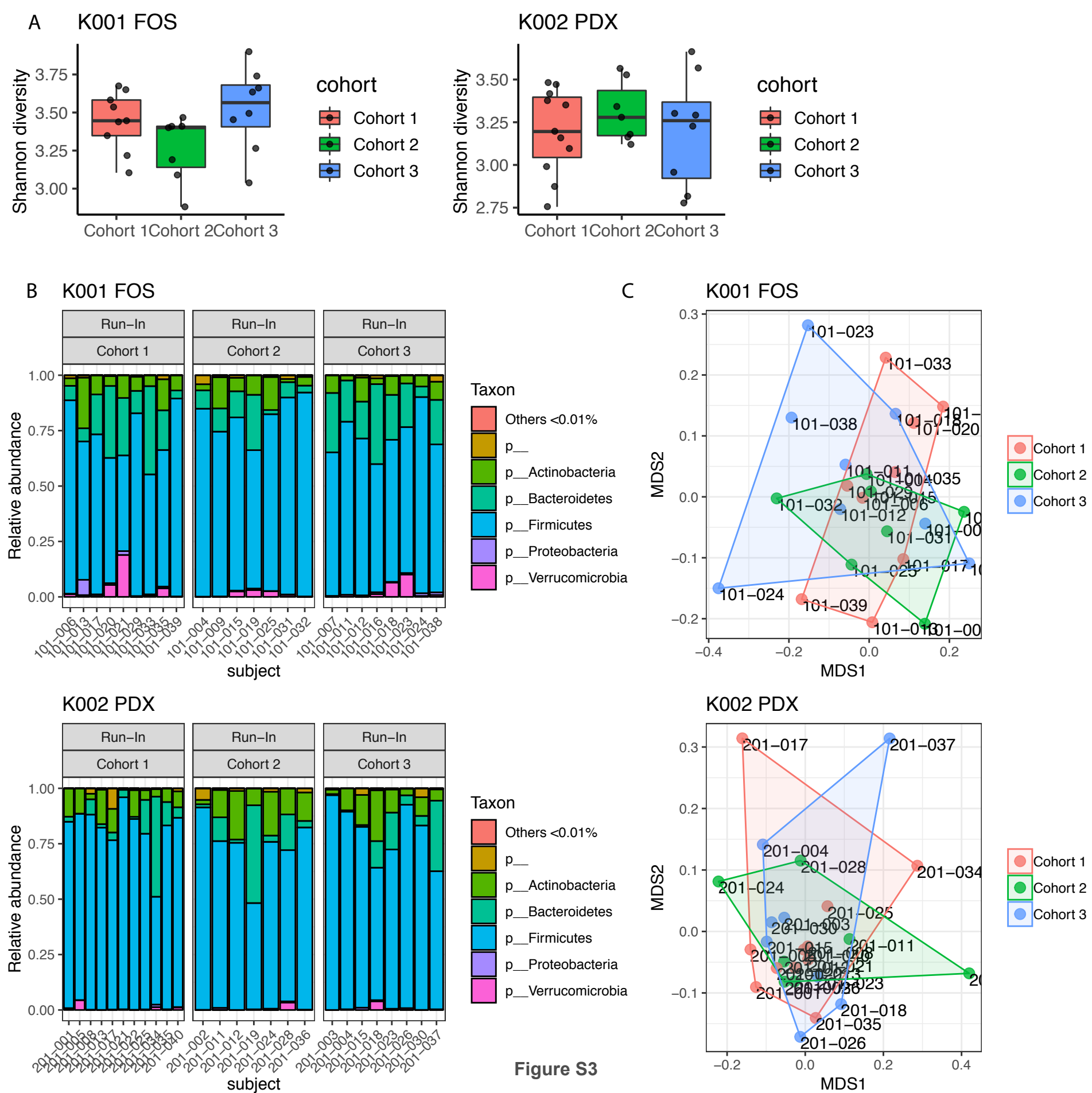


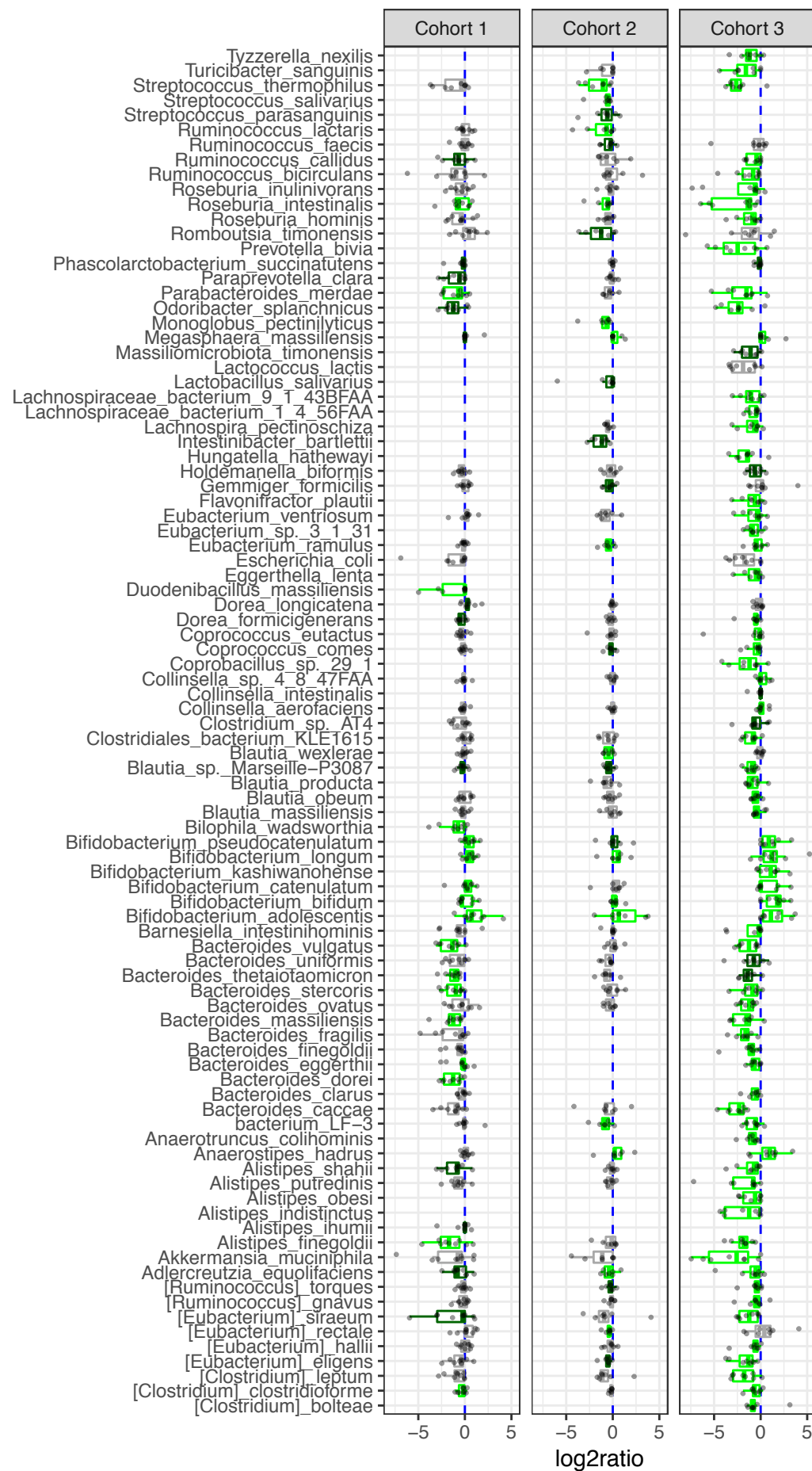
Figure S1





**Figure S3**

K001 FOS



K002 PDX

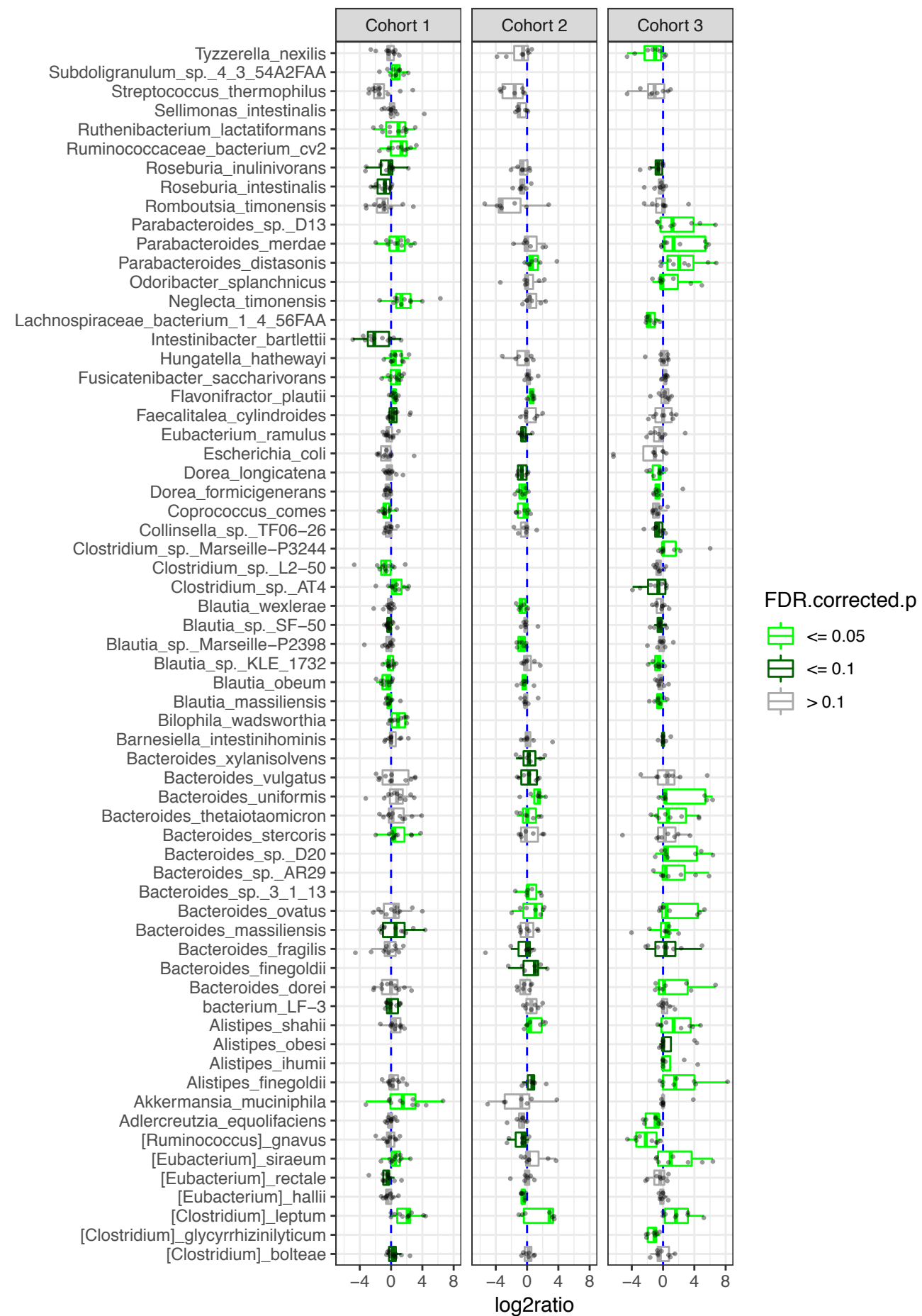
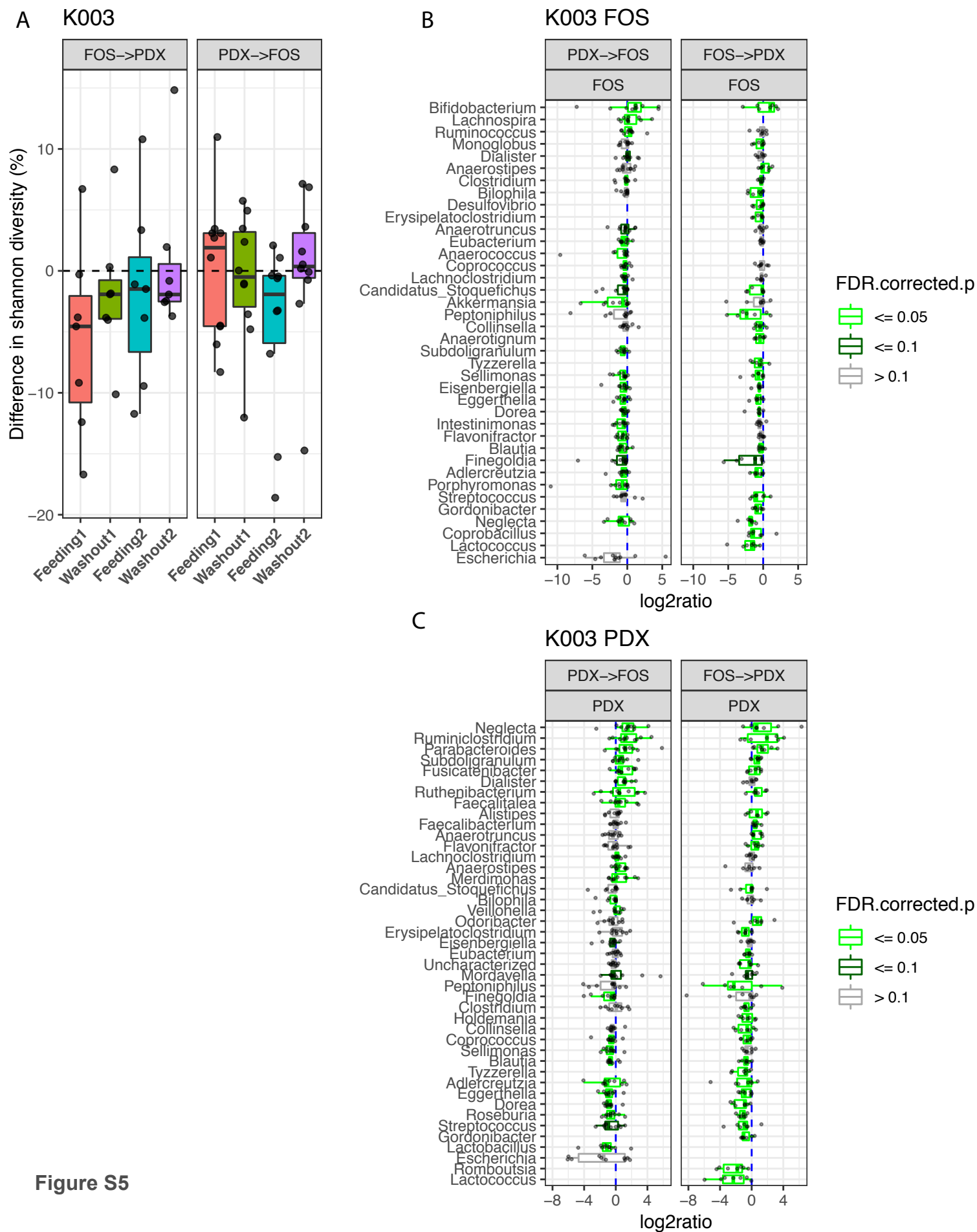


Figure S4



Glycoside Hydrolases

( $\beta/\alpha$ )<sub>8</sub> (GH-A) — GH5  
( $\beta/\alpha$ )<sub>8</sub> (GH-A) — GH30  
GH57  
GH145  
GH67  
( $\alpha/\alpha$ )<sub>6</sub> (GH-O) — GH116  
GH144  
GH108  
GH117  
GH141  
( $\alpha/\alpha$ )<sub>6</sub> (GH-L) — GH15  
6-fold  $\beta$ -propeller (GH-E) — GH93  
( $\beta/\alpha$ )<sub>8</sub> (GH-A) — GH147  
GH66  
GH142  
GH137  
( $\beta/\alpha$ )<sub>8</sub> (GH-A) — GH1  
GH138  
GH99  
GH143  
( $\beta/\alpha$ )<sub>8</sub> (GH-A) — GH26  
( $\alpha/\alpha$ )<sub>6</sub> (GH-O) — GH52  
GH139  
( $\beta/\alpha$ )<sub>8</sub> (GH-A) — GH35  
GH75  
GH150  
GH25  
GH38  
GH126  
GH47  
 $\beta$ -helix (GH-N) — GH49  
GH112  
GH106  
( $\alpha/\alpha$ )<sub>6</sub> (GH-G) — GH125  
GH55  
GH76

Glycosyl Transferases

GT3  
GT10  
GT25  
GT70  
GT82  
GT74  
GT102  
GT80  
GT30  
GT45  
GT20  
GT90  
GT9  
GT94  
GT7  
GT31  
GT35  
GT76  
GT17  
GT6  
GT92

Polysaccharide Lyases

PL5  
PL20  
PL8  
PL13  
PL6  
PL22  
PL27  
PL1  
PL15  
PL9  
PL17  
PL10  
PL14

Carbohydrate Esterases

CE11

Auxiliary Activities

AA5  
AA3

Carbohydrate-Binding Modules

CBM38  
CBM62  
CBM69  
CBM20  
CBM9  
CBM47  
CBM44  
CBM27  
CBM72  
CBM57

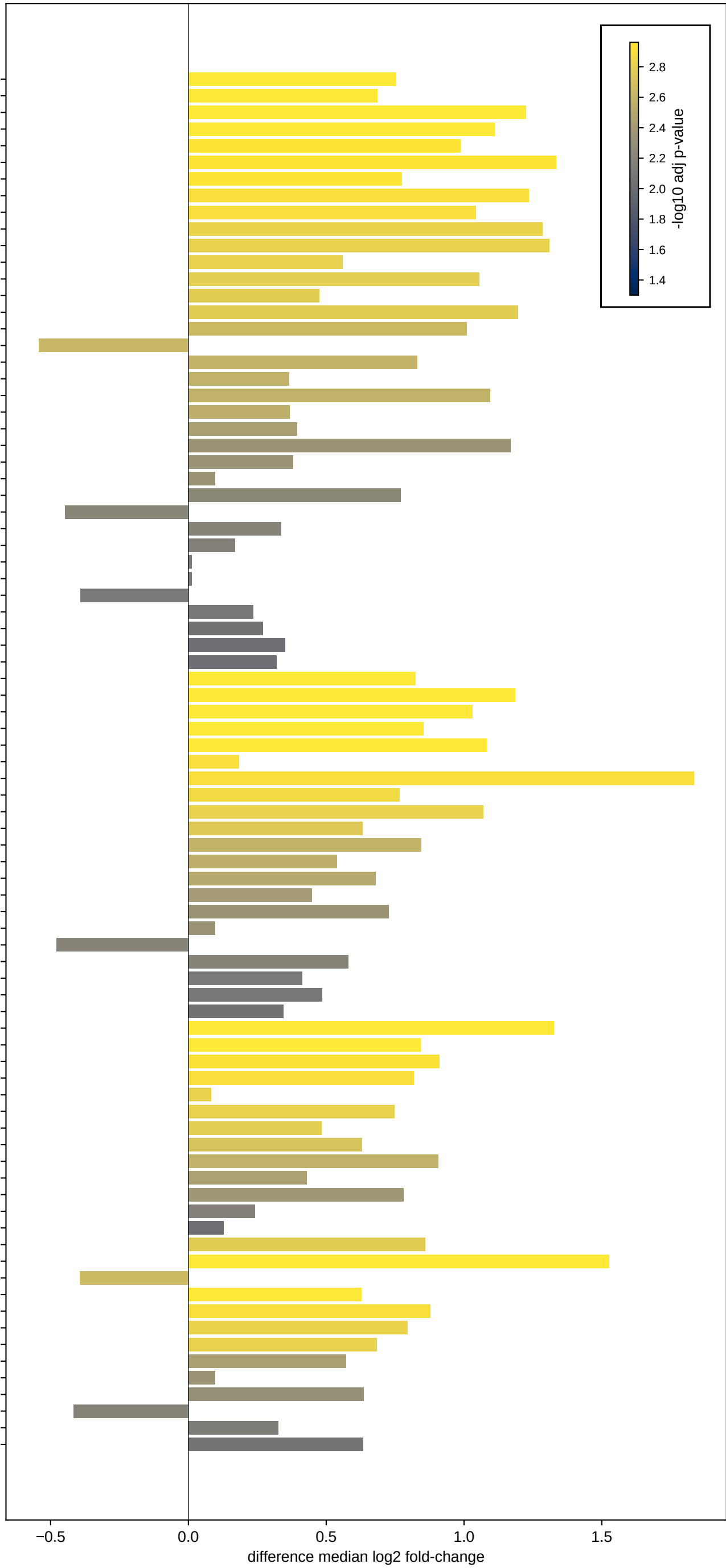
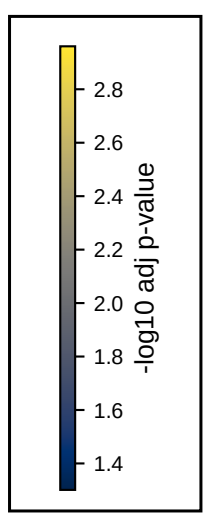
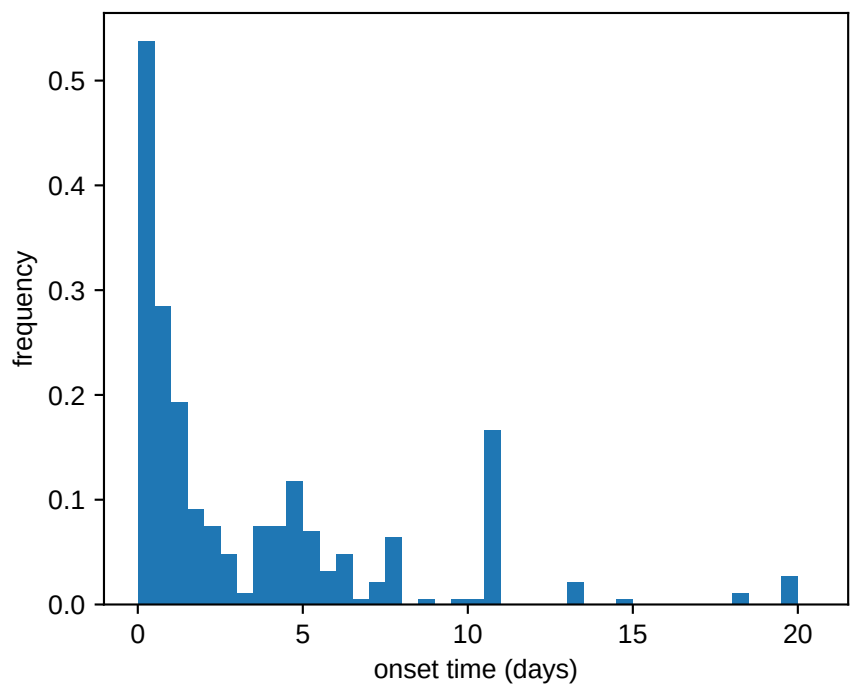


Figure S6

# A. FOS



# B. PDX

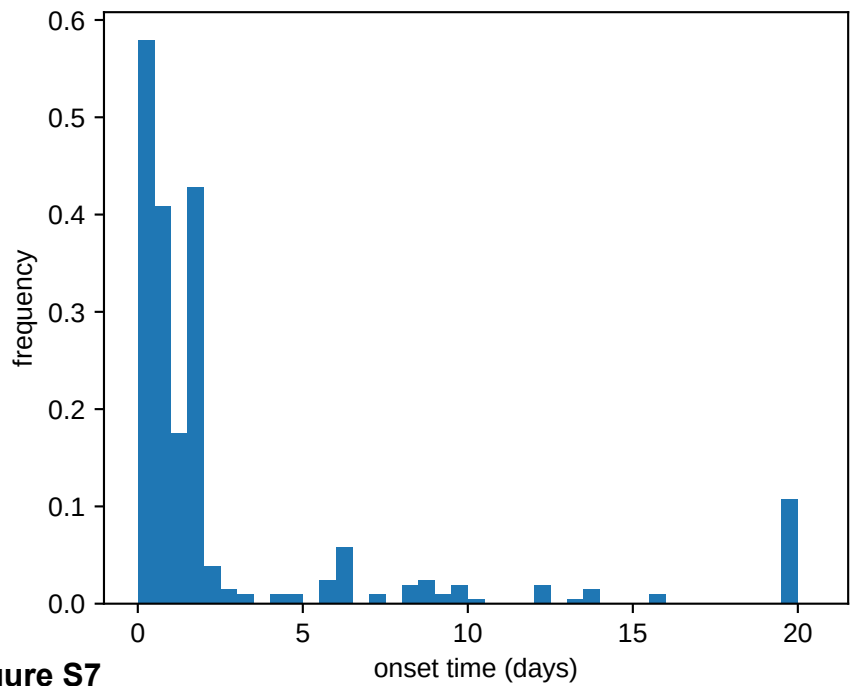


Figure S7



**Table S1**

K001 demographic characteristics			
	Cohort1 n = 9	Cohort2 n = 6	Cohort3 n = 7
Gender			
Female	3 (33.3%)	4 (66.7%)	5 (71.4%)
Male	6 (66.7%)	2 (33.3%)	2 (28.6%)
Age (years)	31.9(± 11.5)	34.5(± 10.7)	38.1(± 13.1)
Race			
Asian	0 (0.0%)	1 (16.7%)	0 (0.0%)
Black or African American	0 (0.0%)	0 (0.0%)	2 (28.6%)
White	9 (100.0%)	5 (83.3%)	5 (71.4%)
Ethnicity			
Hispanic or Latino	6 (66.7%)	3 (50.0%)	4 (57.1%)
Not Hispanic or Latino	3 (33.3%)	3 (50.0%)	3 (42.9%)

K002 demographic characteristics			
	Cohort1 n = 11	Cohort2 n = 7	Cohort3 n = 8
Gender			
Female	5 (45.5%)	4 (57.1%)	1 (12.5%)
Male	6 (54.5%)	3 (42.9%)	7 (87.5%)
Age (years)	31.9(± 10.0)	33.6(± 13.0)	31.2(± 9.6)
Race			
Asian	2 (18.2%)	1 (14.3%)	2 (25.0%)
Black or African American	0 (0.0%)	1 (14.3%)	1 (12.5%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)	1 (14.3%)	0 (0.0%)
White	9 (81.8%)	4 (57.1%)	5 (62.5%)
Ethnicity			
Hispanic or Latino	5 (45.5%)	2 (28.6%)	2 (25.0%)
Not Hispanic or Latino	6 (54.5%)	5 (71.4%)	6 (75.0%)

K003 demographic characteristics		
	FOS->PDX n = 7	PDX->FOS n = 10
Gender		
Female	6 (85.7%)	6 (60.0%)
Male	1 (14.3%)	4 (40.0%)
Age (years)	41.4(± 14.9)	34.2(± 9.9)
Race		
Black or African American	1 (14.3%)	4 (40.0%)
White	6 (85.7%)	6 (60.0%)
Ethnicity		
Hispanic or Latino	1 (14.3%)	0 (0.0%)
Not Hispanic or Latino	6 (85.7%)	10 (100.0%)