Supplementary Methods

Processing of Urine and Stool Samples

Stool samples were first emulsified with saline. From each stool sample four vials, each consisting of 1.8mL of stool plus 0.2mL of glycerol, were collected and stored at -80^{o}C. Urine samples were aliquoted into four vials and stored at -80^{o}C.

Lactulose Breath Test (LBT)

Patients fasted for 10 hours overnight and ingested 30 ml of antiseptic mouthwash immediately before the test to eliminate lactulose fermentation by oropharyngeal bacteria. A baseline breath sample was collected and patients then ingested the test meal consisting of a packet of Kristalose (Cumberland Pharmaceuticals, Nashville, Tennessee, USA), containing 10 g lactulose and 0.3 g galactose/lactose (caloric content = 0.5 calorie). Subjects were instructed to avoid cigarette smoking before and during the test and to continue fasting for the 5 hour test period. End expiratory breath samples were collected at 15 min intervals and analyzed for H_2 and CH_4 concentration in parts per million (ppm) using the Quintron 12i Microlyzer (Quintron Instrument Company, Milwaukee, Wisconsin, USA).

Statistical Analysis of Urine Metabolites

These levels were additionally normalized using logarithmic transformation and pareto scaling. Multivariate statistical analysis was performed using partial least squares discriminant analysis (PLS-DA). Metabolites with a p-value less than 0.2 (using univariate analysis after the intervention concentrations) were selected for generating the logistic regression model. A 10-fold cross-validation technique was used to ensure that the logistic regression models were robust. Permutation analysis using random resampling (n=1000) of the two diet groups was conducted to

determine the probability that the observed separation was a result of chance or not and a p-value that represents the probability of a random finding was generated. Important metabolites responsible for the discrimination between metabolomic profiles of patients in the two diet groups were selected based on variable importance in projection (VIP) values. The VIP value indicates the contribution of each feature to the regression model. The MetaboAnalyst 3.0 was used for metabolomic-related statistical analysis.

FODMAP Diet Scoring System

A FODMAP scoring system was designed based on the five main categories of FODMAPs: fructose, lactose, fructans, galacto-oligosaccharides, and polyols (modified from (1)). Based on our experience, there is a wide variation in wheat consumption. Therefore, fructans were broken down into subcategories: vegetables/fruit, gluten, and inulin (Supplementary Table 1). Patients in the high FODMAP group who did not wish to eat a high amount of wheat were encouraged to eat fiber bars that were high in inulin if they were in the high FODMAP group. Fructose was scored based on consumption of fructose content and not fructose in excess of glucose. Each category was given a score of 0 to 2. The score was based on the dietician's experience of frequency of consumption of the foods in each category. If one food contained 2 categories of FODMAPs (i.e. contained lactose and gluten), it was counted for each category.

As an initial validation step, the dietician scored the FODMAP content based on her FODMAP diet scoring system in the first 6 patients where she was blinded to the diet. The score was calculated by examining the food diary of each patient from day 13 to day 19 of the study. For these patients, she then unblinded herself and the score was then

compared to the diet to which each patient had been assigned. The score correlated well with patient assignment (i.e. high FODMAP patients had higher scores and low FODMAP patients had low scores). Thus, the remaining patients were given a FODMAP diet score in a similar manner.

Supplementary References

1. Gibson PR, Shepherd SJ. Evidence-based dietary management of functional gastrointestinal symptoms: The FODMAP approach. J Gastroenterol Hepatol. 2010;25(2):252-8.