



## Abstract Comparative Evaluation of a Dietary Fiber Mixture in an Intestinal Screening Platform and a Crossover Intervention Study<sup>+</sup>

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Abstract: In personalized nutrition, specific recommendations are often based on extensive phenotyping. In the world of microbiome research, classification is often based on the bacteriological composition of gut microbiota and enterotypes. We investigated if there is a possibility of translating outcomes from an intestinal screening platform to an intervention study that makes use of phenotyping. A 12-week double-blind, randomized, placebo-controlled, crossover intervention study (8-week wash-out period) with a dietary fiber mixture of acacia gum and carrot powder (ratio 3.33:1) was performed in healthy volunteers (N = 54, 45–70 years, BMI 27.3  $\pm$  1.4) to modulate their microbiome. Fecal samples were collected every 4 weeks during the 32-week study period. Before and after the intervention a standardized mixed meal challenge was performed and plasma samples were taken (0, 30, 60, 120, and 240 min). Postprandial responses were used for sub-group cluster analysis to identify the metabolic phenotype. The individual participants' samples were cultured anaerobically for 24 h with the mixture and the individual fibers. Compositional 16s rRNA data of exposed in vitro (24 h) and in vivo samples (4, 8, and 12 weeks) was compared and linked to the metabolic cluster analysis. The comparison between the clinical intervention's effect on microbiota composition after 12 weeks and a single 24 h exposure in vitro showed a statistically significant association in microbiome effects between in vivo and in vitro exposures (p < 0.05) for the fiber intervention. Analysis of the metabolic postprandial responses revealed a division between improvement and deterioration in response to the fiber intervention indicating two distinct clusters (metabolic phenotypes). Cluster 1 contained the lowest triglycerides-, total cholesterol-, and non-esterified fatty acids responses, while cluster 2 contained the highest triglycerides- and total cholesterol responses. Interestingly, the beta diversity of the microbiota was linked to these two clusters, resembling two different responses to the fiber intervention. Our study in healthy individuals demonstrates that a short-term in vitro exposure of individual microbiome samples to the fiber mixture is predictive of a long-term in vivo effect and relates to a distinct phenotypic cluster. This paves the way for using the in vitro platform as a pre-screen for intervention studies.

Keywords: microbiome; postprandial; health; phenotyping; mixed-meal challenge test

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