## High-fat, low-carbohydrate diet was associated with unfavourable impact on colonic luminal microenvironment

We thank Ardalan *et al* for their interest and comments[1] on our 6-month randomised controlled feeding trial, in which we have investigated the effects of dietary fat on gut microbiota and faecal metabolites, and their relationship with cardiometabolic risk factors.[2] They indicated that the differences in microbial structure, faecal short-chain fatty acids concentrations and protein fermentation observed in our trial could be explained by the change in carbohydrates, especially the non-digestible carbohydrates like resistant starch (RS) and fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs), in company with the change in dietary fat due to the isocaloric design.

Our trial was designed based on the notion that the prevalence of obesity and type 2 diabetes had increased dramatically in parallel with a transition from the traditional low-fat, high-carbohydrates diet to a diet relatively high in fat and reduced in carbohydrates.[3 4] Thus, we designed three diets with different dietary fat to carbohydrate ratios (20% fat and 66% carbohydrate in the low-fat diet; 30% fat and 56% carbohydrate in the moderate-fat diet; 40% fat and 46% carbohydrate in the high-fat diet) to represent macronutrients change in China.[5 6] To exclude the influence of energy intake, the three diets were kept isocaloric by replacing a proportion of energy derived from carbohydrates, white rice and wheat flour (the most consumed carbohydrate sources in Asia) with soybean oil (the most widely used edible oil in Asia). Under isocaloric and constant protein intake, an increase in dietary fat must lead to a reduction in carbohydrates.

We agree that alterations in non-digestible carbohydrates like RS when increasing carbohydrates intake to 66% of total energy in the low-fat diet compared with 46% for the high-fat diet could play a role, we have discussed this issue in discussion section in the article. However, it should be noted that the absolute difference in non-digestible carbohydrates among the three dietary groups was not as large as the documented levels that was able to change microbial structure with differences of around 40 g/d of RS or 20 g/d of FODMAPs comparing intervention diets with control diets.[7 8] In our study, take the 1-day sample menu (table 2 in Wan *et al*, 2017[6]) as an example. The low-fat diet group had 85 g white rice and 10 g wheat flour more than those in the high-fat group. RS has been reported to be present in 3% of white rice and 2% of wheat flour, while FODMAPs is undetectable in white rice and around 1.6% in wheat flour, leading to a difference of 2.8 g RS and 0.16 g FODMAPs between low-fat and high-fat diet groups.[9 10] Such difference was much less than those reported in previous trials.[7 8] Though we agree that attention should also be paid to the altered non-digestible carbohydrates in our trial, how much difference RS and FODMAPs can make is well worth reconsideration.

Furthermore, it cannot be denied that the high-fat content could affect the colonic luminal microenvironment as well, reflected by the enrichment in lipopolysaccharide biosynthesis and arachidonic acid metabolism pathway after high-fat diet intervention. Arachidonic acid was the precursor of eicosanoids and other lipid mediators involved in the inflammation process. Consistent with the altered predicted pathways, faecal concentration of arachidonic acid and plasma concentration of thromboxane $B_2$ (one type of eicosanoids) were increased in the group consuming a high-fat, low-carbohydrate diet. In summary, we agree with the possible effects of non-digestible carbohydrates on gut microbiota and microbial metabolites when achieving dietary fat distribution with altering the carbohydrates content. However, a diet with high-fat, low-carbohydrate seems to be undesirable owing to unfavourable changes in colonic luminal microenvironment and circulating markers of subclinical inflammation.

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