

## OBSERVATIONS

## Dietary Fiber Intake Modulates the Association Between Variants in *TCF7L2* and Weight Loss During a Lifestyle Intervention

Single nucleotide polymorphisms (SNPs) within the transcription factor 7-like 2 (*TCF7L2*) gene are well known risk variants for type 2 diabetes (1). The best studied SNP is rs7903146, which is additionally associated with insulin secretion (2) and BMI (3). We furthermore reported that this variant influenced weight loss during the Tübingen Lifestyle Intervention Program (TULIP) such that carriers of the nonrisk CC alleles lost more weight than carriers of XT alleles (4). The TULIP program consists of exercise and diet intervention with decreased intake of fat and increased intake of fibers (participants were instructed to eat at least 15 g fiber per 1,000 kcal). However, a recent report (1) from the Diabetes Prevention Program (DPP) failed to replicate the association of *TCF7L2* SNP rs7903146 with successful weight loss during lifestyle intervention. The authors speculated that this might be because increased fiber intake was not part of DPP, and dietary fibers may be important for *TCF7L2* because they may alter the association between *TCF7L2* and diabetes (5). We therefore investigated if fiber intake influences the association between *TCF7L2* SNP rs7903146 and weight loss during TULIP lifestyle intervention.

Details on the TULIP intervention program as well as on genotyping and clinical characteristics are reported in ref. 4. We analyzed data of 304 subjects for which food diaries were available. Of these, 144 carried the CC alleles and 160 carried XT alleles. The cohort was divided in two groups by the median daily fiber intake during lifestyle intervention

(25 g/day). Each participant provided multiple 3-day food diaries. Food diaries documenting a caloric intake <600 kcal/day were considered nonrepresentative and not analyzed. Nutrient intake was analyzed using a validated computer program (DGE-PC 3.0; Deutsche Gesellschaft für Ernährung). Data are given as means  $\pm$  SD. Statistical analyses were conducted using JMP 8.0. Differences in weight loss were tested in a multivariate linear regression analyses with adjustment for BMI, sex, and age at baseline.

The mean dietary fiber intake before lifestyle intervention was  $23.2 \pm 7.5$  g/day and increased to  $26.0 \pm 7.2$  g/day during the 9 months of participation that were analyzed. Fiber intake was not different between *TCF7L2* genotypes, either before or during the program ( $P \geq 0.2$ ). In the group with low dietary fiber intake ( $20.4 \pm 3.1$  g/day), there was no association of genotype with weight loss during lifestyle intervention ( $\Delta$ BMI  $-0.6 \pm 1.3$  vs.  $-0.6 \pm 1.6$ ,  $P = 0.7$ ). By contrast, the nonrisk CC alleles were associated with significantly greater weight loss in participants with high fiber intake ( $31.4 \pm 5.8$  g/day;  $\Delta$ BMI  $-1.6 \pm 1.6$  vs.  $-0.8 \pm 1.4$ ,  $P = 0.0018$ ).

Thus, the speculation of McCaffery et al. (1) is true for participants of TULIP: variation in *TCF7L2* becomes important for successful weight loss when high fiber intake is present. Associations between genotype and weight loss may therefore be undetectable in studies with lower fiber intake, such as DPP.

Besides diabetes risk (5), there is also *TCF7L2* gene-diet interaction in regard to successful weight loss during lifestyle intervention. This knowledge can help to individualize and optimize such programs.

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