

## Variations in *PPARD* Determine the Change in Body Composition during Lifestyle Intervention: A Whole-Body Magnetic Resonance Study

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**Context:** We recently demonstrated that single-nucleotide polymorphisms (SNPs) in the peroxisome proliferator-activated receptor- $\delta$  gene (*PPARD*), *i.e.* rs1053049, rs6902123, and rs2267668, affect the improvement of mitochondrial function, aerobic physical fitness, and insulin sensitivity by lifestyle intervention (LI).

**Objective:** The objective of the study was to determine whether the aforementioned *PPARD* SNPs influence the change in body composition and ectopic fat storage during LI.

**Design:** A total of 156 subjects at an increased risk for type 2 diabetes were genotyped for rs1053049, rs6902123, and rs2267668 and participated in a LI program. Body fat depots, ectopic liver fat, and muscle volume of the leg were quantified using magnetic resonance spectroscopy and imaging.

**Results:** With regard to body composition, carriers of the minor SNP alleles displayed reduced responses to LI, *i.e.* LI-induced reduction in adipose tissue mass (nonvisceral adipose tissue: rs1053049,  $P = 0.02$ ; rs2267668,  $P = 0.04$ ; visceral adipose tissue: rs1053049,  $P = 0.01$ ) and hepatic lipids (rs1053049,  $P = 0.04$ ; rs6902123,  $P = 0.001$ ; independent of changes in adiposity) as well as LI-induced increase in relative muscle volume of the leg (rs1053049,  $P = 0.003$ ; rs2267668,  $P = 0.009$ ) were less pronounced in homo- and heterozygous carriers of the minor alleles as compared with homozygous carriers of the major alleles.

**Conclusion:** SNPs rs1053049, rs6902123, and rs2267668 in *PPARD* affect LI-induced changes in overall adiposity, hepatic fat storage, and relative muscle mass. Our findings provide a mechanistic explanation for the involvement of these genetic variations in the development of insulin resistance and type 2 diabetes. (*J Clin Endocrinol Metab* 93: 1497–1500, 2008)