

# Abstract

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## Lipoprotein lipase is a gene for insulin resistance in Mexican Americans.

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**BACKGROUND:** The insulin resistance syndrome is increasingly recognized as a risk factor for cardiovascular disease. Lipoprotein lipase (LPL) is a candidate gene for components of the syndrome. A small number of studies have demonstrated association of single nucleotide polymorphisms within LPL and indirect or surrogate measures of insulin resistance, largely based on glucose and insulin values obtained in the fasting state or during an oral glucose tolerance test.

**OBJECTIVE AND METHODS:** To test directly whether LPL is an insulin resistance gene, we performed the hyperinsulinemic-euglycemic clamp in a large family-based population of Mexican Americans who were genotyped at six polymorphisms in LPL that define the most common haplotypes in the population.

**RESULTS:** LPL haplotypes showed linkage to the glucose infusion rate (GINF), a direct physiologic measurement of insulin sensitivity ( $P = 0.034$ ). In addition, significant associations with GINF were demonstrated for the most common haplotype ( $P = 0.031$ ) and the fourth most common haplotype ( $P = 0.007$ ). Haplotype 1 was associated with insulin sensitivity (mean GINF for haplotype 1 carriers = 383.0 mg/min) and haplotype 4 with insulin resistance (mean GINF for haplotype 4 carriers = 344.3 mg/min).

**CONCLUSIONS:** This haplotype-based genetic analysis provides compelling evidence that variation in the LPL gene plays a role in determining insulin resistance in this ethnic group with a high prevalence of the insulin resistance syndrome.

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