

A variant near *MTNR1B* is associated with increased fasting plasma glucose levels and type 2 diabetes risk.

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In genome-wide association (GWA) data from 2,151 nondiabetic French subjects, we identified rs1387153, near *MTNR1B* (which encodes the melatonin receptor 2 (MT2)), as a modulator of fasting plasma glucose (FPG; $P = 1.3 \times 10^{-7}$).

In European populations, the rs1387153 T allele is associated with increased FPG ($\beta = 0.06$ mmol/l, $P = 7.6 \times 10^{-29}$, $N = 16,094$), type 2 diabetes (T2D) risk (odds ratio (OR) = 1.15, 95% CI = 1.08–1.22, $P = 6.3 \times 10^{-5}$, cases $N = 6,332$) and risk of developing hyperglycemia or diabetes over a 9-year period (hazard ratio (HR) = 1.20, 95% CI = 1.06–1.36, $P = 0.005$, incident cases $N = 515$). RT-PCR analyses confirm the presence of MT2 transcripts in neural tissues and show MT2 expression in human pancreatic islets and beta cells.

Our data suggest a possible link between circadian rhythm regulation and glucose homeostasis through the melatonin signaling pathway.