

# Hypothalamic Lin28a shows role in glucose homeostasis

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(HealthDay)—An experimental study supports a TANK-binding kinase

1 (TBK-1)-dependent role for Lin28a in the hypothalamic ventromedial nucleus in glucose homeostasis. The study was published online May 26 in *Diabetes*.

Jung Dae Kim, Ph.D., from the Yale University School of Medicine in New Haven, Conn., and colleagues examined the central function of the Lin28a/*Let-7* axis. Noting that Lin28a is highly expressed in the hypothalamus and that its expression is associated with positive energy balance, the authors targeted the hypothalamic ventromedial nucleus (VMH) to selectively overexpress (*Lin28aKI<sup>VMH</sup>*) or downregulate (*Lin28aKD<sup>VMH</sup>*) Lin28a expression in mice.

The researchers found that body weight and [glucose homeostasis](#) were not affected in *Lin28aKI<sup>VMH</sup>* or *Lin28aKD<sup>VMH</sup>* mice on a standard chow diet. No differences in body weight and composition were observed on high-fat diet, although compared with their controls, *Lin28aKI<sup>VMH</sup>* mice showed improved glucose tolerance and insulin sensitivity. In contrast, [glucose intolerance](#) and insulin resistance were seen in *Lin28aKD<sup>VMH</sup>*. There were no associations seen for changes in VMH AKT (protein kinase B) activation of diet-induced obese *Lin28aKI<sup>VMH</sup>* or *Lin28aKD<sup>VMH</sup>* mice and alterations in *Let-7* levels or insulin receptor activation. Expression of TBK-1, which was a direct Lin28a target mRNA, was altered. In diet-induced obese mice, VMH-specific inhibition of TBK-1 impaired [glucose metabolism](#) and AKT activation.

"Altogether, our data show a TBK-1- dependent role for central Lin28a in glucose homeostasis," the authors write. "This pathway may represent a mechanism that functions to alter peripheral [insulin sensitivity](#) in response to changes in circulating [glucose levels](#)."

**More information:** [Abstract/Full Text \(subscription or payment may be required\)](#)

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