Variations in gene expression may underlie increased food intake in obesity

11 April 2016

Large-scale genetic studies have identified a number of variations in genes that increase an individual's susceptibility to obesity.

An allelic variant in the intronic region of a gene called fat mass and obesity-associated (*FTO*) is strongly linked to increased food intake and body weight in humans, but it is unclear how the variant causes these effects.

In this month's issue of the *JCI*, a research team led by Rudolph Leibel at Columbia University examined how the obesity-risk allele alters the regulation of nearby genes to promote obesity.

Liebel's group found that the allele was associated with reduced expression of *FTO* and a nearby gene called *RPGRIP1L*, which encodes a component of the primary cillium. In mice, altered expression of *Rpgrip1l* was linked to increased food intake and weight gain.

Further, the researchers found that reduced expression of *Rpgrip1l* in neurons produced deficits in the brain's response to leptin, a hormone that signals satiety, which may produce the observed increases in food intake.

Collectively, this study suggests that the obesity-risk allele mediates its effect in part through changes in expression to neighboring genes and provides new insights into the mechanisms underlying genetic predisposition to obesity in humans.

More information: George Stratigopoulos et al. Hypomorphism of Fto and Rpgrip1l causes obesity in mice, *Journal of Clinical Investigation* (2016). DOI: 10.1172/JCI85526

Provided by Journal of Clinical Investigation

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