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IN BRIEF

METABOLISM

Brain PPAR-γ promotes obesity and is required for the insulin-sensitizing effect of thiazolidinediones

Lu, M. *et al. Nature Med.* **17**, 618–622 (2011)

A role for central nervous system PPAR-γ in the regulation of energy balance

Ryan, K.K. *et al. Nature Med.* **17**, 623–626 (2011)

Thiazolidinediones (TZDs) — drugs widely used to treat type 2 diabetes — have an unwanted side effect: weight gain. Because these compounds are known to activate peroxisome proliferator-activated receptor-γ (PPARγ), an orphan receptor expressed in the brain as well as in peripheral tissues, the authors proposed that this receptor might mediate their effects on energy balance. Indeed, they found that deleting or inhibiting the activity of CNS PPARγ increased energy expenditure, improved leptin sensitivity, reduced food intake and attenuated weight gain in animals exposed to a high fat diet or treated with the TZD rosiglitazone. PPARγ was also required for the therapeutic insulin-sensitizing effects of rosiglitazone. Conversely, activating CNS PPARγ increased food intake and weight gain. These findings demonstrate that PPARγ is an important target of TZDs and highlight its role in regulating energy balance.

STRESS

Hippocampal neuronal nitric oxide synthase mediates the stress-related depressive behaviors of glucocorticoids by downregulating glucocorticoid receptor

Zhou, Q-G. *et al. J. Neurosci.* **31**, 7579–7590 (2011)

Elevated glucocorticoid levels, which are associated with stress, and dysfunction of hippocampal glucocorticoid receptors have been linked to hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis and depression. However, the molecular mechanisms underlying this connection were unknown. Here, the authors show that neuronal nitric oxide synthase (nNOS) is required for the promotion of depression-like behaviour by glucocorticoids in an animal model. They reveal a mechanism through which glucocorticoids increase hippocampal nNOS levels, triggering activation of a molecular pathway that results in the downregulation of glucocorticoid receptor expression and an increase in HPA axis output.

SENSORY SYSTEMS

An epigenetic signature for monoallelic olfactory receptor expression

Magklara, A. *et al. Cell* **145**, 555–570 (2011)

Mammalian olfactory receptor (OR) neurons each express a single OR and repress the expression of the thousands of other OR alleles. How they do so is unclear, although a feedback mechanism triggered by OR protein translation has been proposed. Here, the authors show that OR sequences are enriched for markers of chromatin-mediated silencing. The transcription of a single OR allele seems to occur through removal of this repression. Thus, gene silencing occurs before OR expression, implying that an OR protein-triggered feedback mechanism is not involved in the regulation of OR expression.