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Targeting Trends

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Deletion of NPY/AGRP and POMC Neurons in the Arcuate Nucleus by Leptin-Saporin Produces Hyperphagia, Obesity and Changes in Diurnal Feeding Patterns in Rats

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Leptin is a fat tissue-derived hormone with widespread actions in brain and peripheral tissues. Leptin's actions are mediated by the long isoform of the leptin receptor, OB-Rb, which has a lengthy intracellular region containing several motifs required for signal transduction via the JAK2/STAT3 pathway. Leptin profoundly influences food intake and body weight, in large part by its actions on OB-Rb receptors in the arcuate nucleus (Arc) in the basomedial hypothalamus. Two populations of neurons in the Arc that are importantly involved in these functions are neuropeptide Y (NPY) and agouti gene-related protein (AGRP) co-expressing neurons and pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) co-expressing neurons. The majority of both NPY/AGRP and POMC/CART neurons are OB-Rb-positive. Exogenous administration of leptin excites and increases phospho-STAT3 expression in POMC/CART neurons and inhibits NPY neurons in the Arc.

In the present study, we used a novel leptin-saporin conjugate (Lep-SAP), a targeted toxin developed recently by Advanced Targeting Systems, to lesion OB-Rb-expressing NPY/AGRP and POMC/CART neurons in Arc.

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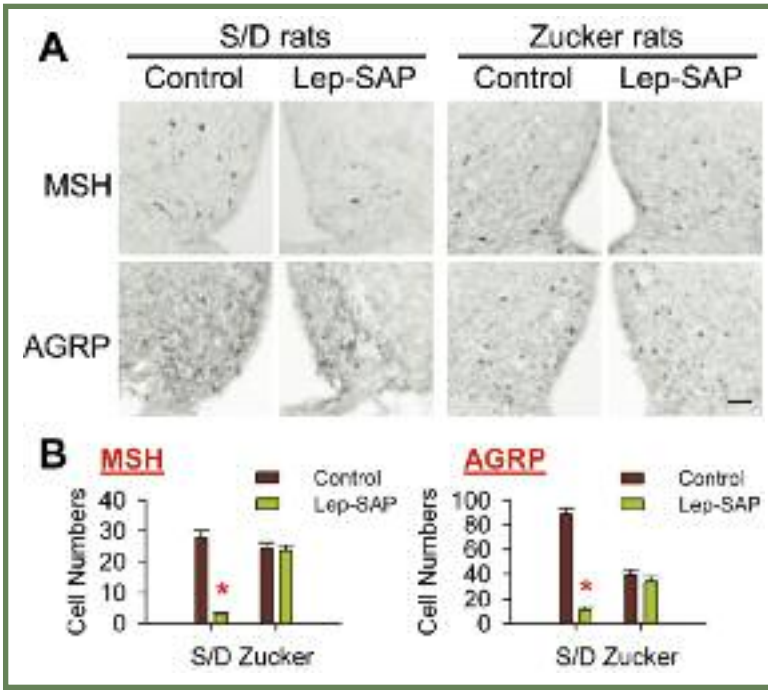

Figure 1.
Effects of unilateral Lep-SAP injection into Arc on α-MSH and AGRP expression.
(A) Representative photomicrographs of α-MSH and AGRP cell bodies after unilateral injection of Lep-SAP into Arc in Sprague Dawley (S/D) or Zucker *fa/fa* (Zucker) rats.
(B) Numbers of α-MSH- and AGRP-positive cell bodies in the Arc of S/D and Zucker rats ipsilateral and contralateral to Lep-SAP injection. In S/D rats, but not Zucker *fa/fa* rats, Lep-SAP significantly decreased the numbers of α-MSH- and AGRP-positive cells in Arc on the injected side, compared to the uninjected side.
* $P < 0.01$; unpaired t-test vs. control non-injection side.
Calibration bar = 100 µm.

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Denise Higgins, Editor

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