

Novel approaches to the prevention and treatment of type 2 diabetes

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All metabolic processes, from single cell substrate oxidation to complex behaviors, are under the control of specific CNS circuits, aiming to maintain homeostasis. Afferent signals include gut hormones, adipokines and nutrient components, while efferent information primarily originates from the hypothalamic nuclei and involves components of the autonomic nervous system as well as the classic endocrine axes. We recently observed that diet-induced metabolic diseases, such as obesity and type 2 diabetes, are associated with (and preceded by) pathological processes in these hypothalamic control centers. Such pathophysiology concerns the hypothalamic cell matrix beyond key neuronal populations and includes astrocytosis, microgliosis, hypervascularisation as well as increased presence of pro-inflammatory cytokines. Specific targeting of such “hypothalamic inflammation” using novel gut-peptide based delivery of glucocorticoids to key metabolic disease regions improved both local

pathophysiology and systemic metabolic health. Such a novel unimolecular dual agonism and steroid delivery approach may not only offer superior therapeutic option for at least some patient subpopulations, but also suggests a pathogenetic relevance for this novel hypothalamic syndrome.