The VGF derived peptide TLQP-21: Functional dissection and structural analysis of a new pro-lipolytic and anti-obesity molecule

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Epidemiological evidence demonstrates that obesity is rising exponentially to pandemic levels in the western societies. Obesity is a major risk factor for type 2 diabetes and cardiovascular disease. Obesity is often associated with lipolytic catecholamine resistance in adipocytes which results in a failure of to increase lipolysis despite sustained sympathetic tone (1). We recently identified an anti-obesity 21 amino acid peptide encoded by the Vgf gene named TLQP-21 (2). VGF is part of the granin family of peptides (chromogranins, secretogranins and additional related proteins such as 7B2, NESP55, proSAAS, and VGF) which subserve essential roles in the regulated secretory pathway and their processed peptides function prominently in metabolic and glucose homeostasis, and blood pressure supporting the current utility of granins and granin-derived peptides as disease biomarkers and target for drug discovery (3). TLQP-21 is the first granin peptide for which a pro-lipolytic role was demonstrated and that can oppose lipolytic catecholamine resistance in obese subjects and decrease adiposity (4).

**Background**

**Our working model**

TLQP-21 is released by nerve terminals, binds a receptor in adipocytes membranes, increases lipolysis downstream of βARs

**Absence of any significant secondary structure**

In the absence of cells, TLQP-21 is present in equilibrium among several unfolded conformations, likely arising from Pro-18 and Pro-19 isomerization

**Chemical shift perturbation in presence of its putative receptor**

Free state TLQP-21 no cells

Receptor bound state TLQP-21 with 3T3L1

**Solid State NMR of TLQP21 in presence of target cells**

**References**