Presence and functional actions of In1-1-qhrelin splicing variant reveals a potentially relevant pathophysiological role in human pituitary adenomas

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Introduction

Pituitary adenomas comprise a heterogeneous group of tumors causing serious comorbidities, which would benefit from identification of novel, common molecular/cellular biomarkers and therapeutic targets. The ghrelin system encompasses a complex molecular family with multiple functions, and some of its components have been linked to development of various endocrine-related cancers. In this work, we aim to better delineate the pathophysiological significance of the ghrelin regulatory system in pituitary tumors, by pursuing two specific objectives:

1) To analyze the presence of key components of the ghrelin system in pituitary tumors: native ghrelin, the recently discovered splicing variant In1-1-qhrelin; ghrelin receptors GHSR1A (full-length) and GHSR1B (truncated variant), and MBOAT4 (GOAT), the enzyme responsible for ghrelin acylation.

2) To compare the direct effects of native ghrelin and In1-1-qhrelin variant administration on selected functional parameters in cell cultures derived from the main types of pituitary adenomas.

Materials & Methods

In1-1-qhrelin derived peptides and native ghrelin induced differential intracellular signaling activation in pituitary adenoma cells

Functional assays

Expression profile

Conclusions

Altogether, our results indicate that ghrelin system components are present and markedly altered in human pituitary tumors, where In1-1-qhrelin variant, particularly, could play a relevant functional role in the regulation of adenoma pathophysiology, which paves the way for using In1-1-qhrelin variant as a new tool to explore novel diagnostic/prognostic biomarkers and/or therapeutic targets in these human tumors.