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Ghrelin receptor (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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Abstract

The ghrelin receptor (**nomenclature as agreed by the NC-IUPHAR Subcommittee for the Ghrelin receptor [18]**) is activated by a 28 amino-acid peptide originally isolated from rat stomach, where it is cleaved from a 117 amino-acid precursor (*GHRL*, Q9UBU3). The human gene encoding the precursor peptide has 83% sequence homology to rat prepro-ghrelin, although the mature peptides from rat and human differ by only two amino acids [70]. Alternative splicing results in the formation of a second peptide,[des-Gln^{14}]ghrelin with equipotent biological activity [48]. A unique post-translational modification (octanoylation of Ser^{3}, catalysed by ghrelin O-acyltransferase (*MBOAT4*, Q96T53) [127] occurs in both peptides, essential for full activity in binding to ghrelin receptors in the hypothalamus and pituitary, and for the release of growth hormone from the pituitary [56]. Structure activity studies showed the first five N-terminal amino acids to be the minimum required for binding [4], and receptor mutagenesis has indicated overlap of the ghrelin binding site with those for small molecule agonists and allosteric modulators of ghrelin function [43]. In cell systems, the ghrelin receptor is constitutively active [44], but this is abolished by a naturally occurring mutation (A204E) that results in decreased cell surface receptor expression and is associated with familial short stature [88].

Contents

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