

## Review

# Is GPR39 the natural receptor of obestatin?

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#### ABSTRACT

he famil f G GPR39, an han ece bel nging ein-c led ece . a iginall e ed be he ece f be a in.H e e ecenl,n me е ha e e i ned hi c ncl i n. In mammal, GPR39 a e ed be in l ed in he eg lain fga in e inal and he me ab licfncin. In hia icle, a la e and biefe ie n he ece famil, c e, di ib i n and h i l gicalf nc i n f GPR39 ha been e ed.

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## 1. Introduction

The G ein-c led ece 39 (GPR39) i an han membe f a famil incl ding he ece f gh elin and m ilin [30]. GPR39 h a high deg ee f c n i i e ignaling h gh he e m e n e elemen (SRE) a h a [20]. In 2005, GPR39 a e ed be he ece f a e idefagmen f m heghelin ec named be a in, hich a ed beag h m ne ha ing he i e effec nf d in ake and GI- ac f nc i n gh elin [52]. The eafe, he GPR39 ignaling a aciaed b incin

 $(Zn^{2+})$  h gh he G  $\alpha$ -PLC a h a [48]. H e e, Cha el e al. [8] gge ed ha be a in did n ac i a e GPR39; he ef e, he na al ligand f GPR39 i nce ain fa. In hi a icle, e mma i ed he ece famil, c e, di ib i n and h i l gical f nc i n f GPR39.

#### 2. Receptor family of GPR39

In 1996, he g h h m ne ec e ag g e - ece (GHS-R) gene a cl ned and h n enc de a ni e G ein-



Fig. 1 – The receptor family of GPR39. (A) Schematic phylogenic tree of the receptor family of GPR39. The constitutively active receptors are highlighted with red color. (B) A model of human GPR39. GPR39-1a is the full length 7-transmenbrane (TM) receptor, and GPR39-1b is a truncated form of GPR39-1a lacking after 5-TM [12,41]. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

ihaded ced led ece ein e ence ha C а 96% iden ical in h man and a [22]. Beca e f he h i l gical im ance f he GHS-R, a ea ch f famil a hen ini ia ed and i m lec la e l i n a membe in e iga ed. McKee e al. iginall indica ed ha GPR38 and GPR39 ha ed a igni can amin acid e ence iden ical i h he GHS-R. ne medin U ece and he ne en in ece (Fig. 1A). Fl e cence in situ h b idi aindem n a ed ha GPR38 and GPR391 cali ed a e a a e

ch m me and e e di inc f m he gene enc ding he GHS-R and NT-R e 1 [30].

GPR38 a enc ded b a ingle gene e e ed in he h id gland, mach, and b ne ma , and i i n kn n be he ece f m ilin, hich mainl eg la e ga in e inal (GI) c n ac i n and g m ili [13]. GPR39 a e e ed in he b ain and he e i he al i e [30]. The GHS-R gene a la e indica ed be he ece f he GI- ac h m ne gh elin in l ed in a la ge a a f



Fig. 2 – Alignment of amino acid sequences of human, mouse, rat, chicken, quail and pig GPR39. Transmembrane regions were represented as red letters; the gene sequences are quoted from GenBank accession (nos. NM001508, NM001114392, ENSRNOG00000021586, NM001080105, EF375709, and EU669821). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

h i l gical f nc i n incl ding he eg la i n f f d in ake, b d eigh, GI m ili and h halamic and h h eal h m ne ec e i n [18,27,33,49]. O he membe f he GPR39 ece famil a e ne medin U ece and ne en in ece . Ne medin U and ne en in b h ha e been im lica ed in he c n l f f d in ake and GI f nc i n [21,54].

## 3. Structure and distribution of GPR39

## 3.1. Structure of the GPR39 receptor

The GRP39 ece bel ng he cla f h d in-like ece famil incl ding GHS-R and m ilin ece (GPR38) [20,30]. The amin acid e ence f GPR39 in h man, a, m e, ail, chicken and ig a e h n in Fig. 2.

The m lec la eigh f h man GPR39 i 52 kDa [14]. The hmanGPR39genecni fen eaaedbae ima el 200 kb [36]. PCR anal i lage in nfa eiedhen in ha GPR39 a e edb lice a ian , namel GPR39-1a, c e nding hef ll leng h7an menb ane (TM) ece , and GPR39-1b, c e nding a nca ed f m f GPR39-1a lacking af e 5-TM (Fig. 1B) e al. [46,47] e ed he amin acid [12]. Yamam e ence and gene c e f chicken and ail GPR39. Chicken and ail GPR39 b h enc de a 462-amin acid ein, ihhigh e encehmlg h man, a and e GPR39. The ail GPR39 cDNA c n i ed f 354 b f5'm UTR, 1484 b f 3'-UTR and 1389 b f c ding egi n [47]. The chicken GPR39 genei c m ed feneaaedban in n, HNF-1, GCb and CCAATb , b n can nical TATA b a f nd in he chicken GPR39 gene [46]. Recen l, e de e mined he ig GPR39 cDNA enc ding a 465-amin acid ein (Fig. 2).

GPR39 [52]. M echa e al. [31] and Zhang e al. [50] gge ed ha be a in a a h m ne ca able f binding GPR39 eg la e hef nc i n f di e e ga in e inal and adi e i e.F he die indica ed ha be a in a in l ed in inhibi ing hi and an ie [37], im ing mem [6], affec ing cell life a i n [5,53], c n lling id h me a i [38] and inc ea ing he ec e i n f anc ea ic j ice en me [25]

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