GEPHE SUMMARY

Gephebase Gene

GPRC6A (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^GPRC6A^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001670

Main curator

Prigent

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Cell signaling (membrane receptor activity) (https://www.gephebase.org/search-criteria?/and+Trait=^Cell signaling (membrane receptor activity)^#gephebase-summary-title)

Trait State in Taxon A

WT

Trait State in Taxon B

Intracellular retention lacking signaling function

Ancestral State

Taxon A

Taxonomic Status

Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)

Taxon A

Latin Name

Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)

Common Name

human

Synonyms

human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent

Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID

9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon A an Infraspecies?

Yes

Taxon A Description

Human. NCBI & 1000 Genomes phase III (1KG) & Inter99 datasets. 30% of African population 0.1-4% of other populations. (Also bonobo and mouse)

Taxon B

Latin Name

Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)

Common Name

human

Synonyms

human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent

Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID

9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon B an Infraspecies?

Yes

Taxon B Description

Human. NCBI dataset

GENOTYPIC CHANGE

Generic Gene Name

GPRC6A

Synonyms

GPCR; bA86F4.3

String

9606.ENSP00000309493 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000309493)

Sequence Similarities

Belongs to the G-protein coupled receptor 3 family.

GO - Molecular Function

UniProtKB Homo sapiens

Q5T6X5 (http://www.uniprot.org/uniprot/Q5T6X5)

GenebankID or UniProtKB

()

GO:0004930 : G protein-coupled receptor activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0004930)

GO - Biological Process

GO:0007186 : G protein-coupled receptor signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0007186)
GO:0019722 : calcium-mediated signaling
(https://www.ebi.ac.uk/QuickGO/term/GO:0019722)
GO:0043200 : response to amino acid
(https://www.ebi.ac.uk/QuickGO/term/GO:0043200)

GO - Cellular Component

GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0005887 : integral component of plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0005887)
GO:0009986 : cell surface (https://www.ebi.ac.uk/QuickGO/term/GO:0009986)

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title)

Aberration Type

Deletion (https://www.gephebase.org/search-criteria?/and+Aberration Type=^Deletion^#gephebase-summary-title)

Deletion Size

1-9 bp

Molecular Details of the Mutation

KGRKLP>KGRK-Y in the third intracellular loop (ICL3) with surface expression and function greatly reduced

Experimental Evidence

Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Candidate Gene^#gephebase-summary-title)

Main Reference

Genetic Variations in the Human G Protein-coupled Receptor Class C, Group 6, Member A (GPRC6A) Control Cell Surface Expression and Function. (2017)
(https://pubmed.ncbi.nlm.nih.gov/27986810)

Authors

JÃ¸rgensen S; Have CT; Underwood CR; Johansen LD; Wellendorph P; Gjesing AP; JÃ¸rgensen CV; Quan S; Rui G; Inoue A; Linneberg A; Grarup N; Jun W; Pedersen O; Hansen T; BrÃ¤uner-Osborne H

Abstract

GPRC6A is a G protein-coupled receptor activated by l-amino acids, which, based on analyses of knock-out mice, has been suggested to have physiological functions in metabolism and testicular function. The human ortholog is, however, mostly retained intracellularly in contrast to the cell surface-expressed murine and goldfish orthologs. The latter orthologs are G-coupled and lead to intracellular accumulation of inositol phosphates and calcium release. In the present study we cloned the bonobo chimpanzee GPRC6A receptor, which is 99% identical to the human receptor, and show that it is cell surface-expressed and functional. By analyses of chimeric human/mouse and human/bonobo receptors, bonobo receptor mutants, and the single nucleotide polymorphism database at NCBI, we identify an insertion/deletion variation in the third intracellular loop responsible for the intracellular retention and lack of function of the human ortholog. Genetic analyses of the 1000 genome database and the Inter99 cohort of 6,000 Danes establish the distribution of genotypes among ethnic groups, showing that the cell surface-expressed and functional variant is much more prevalent in the African population than in European and Asian populations and that this variant is partly linked with a stop codon early in the receptor sequence (rs6907580, amino acid position 57). In conclusion, our data solve a more than decade-old question of why the cloned human GPRC6A receptor is not cell surface-expressed and functional and provide a genetic framework to study human phenotypic traits in large genome sequencing projects linked with physiological measurement and biomarkers.

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Additional References

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

3 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^GPRC6A^/and+Taxon ID=^9606^/or+Gene Gephebase=^GPRC6A^/and+Taxon ID=^9606^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS