

IGF2R

Identity

Other names **M6P/IGF2R**
Hugo **IGF2R**
Location 6q25-q27

DNA/RNA

Note no known splice variants
Description 138376 bp
Transcription 9090 bp mRNA
Pseudogene None known

Protein

Description 2491 aa
Expression Subject to parental genomic imprinting in some viviparous mammals. Preferential transcription of maternally-derived allele in some mammals with the exception of primates and close relatives. Humans harbor a parentally imprinted differentially methylated CpG island, but human IGF2R transcripts are not preferentially maternally derived.
Function M6P/IGF2R translates to a protein whose diverse functions include lysosomal enzyme trafficking, fetal organogenesis, tumor suppression, and cytotoxic T-cell induced apoptosis. The M6P- and IGF2-binding sites are distinct within the protein, and are thought to have evolved independently, partly explaining the gamut of functions attributable to a single protein: the ancestral M6PR dates back at least 450 million years, and appears to have been a suitable platform for acquiring an IGF2 binding function in ancestral mammals roughly 150 to 200 million years ago; as with M6P-tagged molecules, bound IGF2 is targeted to lysosomes, where IGF2 is degraded. To the extent that the tumor suppressor role of M6P/IGF2R relies on IGF2 binding, the M6P/IGF2R is a very young tumor suppressor.
Homology CD-MPR

Mutations

Note Include genetic and epigenetic derangements.
Epigenetics Beyond biochemical and DNA sequence properties, M6P/IGF2R epigenetic traits have been described. In humans, there is a differentially methylated region (DMR) in intron 2 of the gene which is preferentially methylated on the maternally inherited copy of the gene; in addition, the human M6P/IGF2R resides in an asynchronously replicating genomic region, such that the gene allele inherited from the mother replicates first.
Despite these parentally pre-programmed epigenetic behaviors, human M6P/IGF2R transcription appears to be equivalent between both parentally-inherited alleles. Thus, human M6P/IGF2R alleles are

encoded with information about parental origin, but this information is evidently uncoupled from transcriptional ramifications. This uncoupling is particularly intriguing in light of mouse genetic manipulations which causally link an imprinted M6p/igf2r DMR to imprinted transcription. Thus, the human M6P/IGF2R provides a rare example of uncoupling of stable gene imprinting --evidenced by somatically heritable parent-specific DNA methylation-- from stable imprinted transcription. Interestingly, the marsupial M6P/IGF2R homologue manifests parentally imprinted maternal transcription in the absence of imprinted differential methylation.

M6P/IGF2R, thus, is remarkably divergent across animal species with respect to both biochemical and epigenetic properties. Within the imprinted family of genes, M6P/IGF2R manifests a distinctive uncoupling of imprinted methylation from imprinted transcription, which frustrates efforts to establish the precise role of DNA methylation in the imprinting process. M6P/IGF2R is somewhat of a devil's advocate and a reminder that genes don't always read the journals.

Germinal Epigenetic alterations associated with fetal developmental abnormalities.
Somatic PCR-platform IGF2R LOH, microsatellite instability, and point mutations described in tumors.
 Somatic mutations of M6P/IGF2R DNA sequence have been identified in human [colon](#), [liver](#), [lung](#), [breast](#) and [ovarian](#) cancers, suggestive of Knudson-type two-hit oncogenetics at first glance; however, M6P/IGF2R loss of heterozygosity (LOH) is reported to precede point mutation of the remaining allele in the hepatocellular carcinoma model, in distinction from RB and other genes following the two-hit principle of Knudson. Statistically significant differences in M6P/IGF2R allelic variants have been identified between Japanese and American populations, but any functional significance has not been ascribed.

Implicated in

Entity Development, immunity, tumorigenesis.

External links

| | |
|-----------------------------|---|
| | Nomenclature |
| Hugo | IGF2R |
| GDB | IGF2R |
| Entrez_Gene | IGF2R_3482 insulin-like growth factor 2 receptor |
| | Cards |
| Atlas | IGF2RID380 |
| GeneCards | IGF2R |
| Ensembl | IGF2R |
| CancerGene | IGF2R |
| Genatlas | IGF2R |
| GeneLynx | IGF2R |
| eGenome | IGF2R |
| euGene | 3482 |
| | Genomic and cartography |
| GoldenPath | IGF2R - chr6:160360542-160497992 + 6q25.3 (hg17-May_2004) |

[Ensembl](#) [IGF2R - 6q25.3 \[CytoView\]](#)
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[OMIM](#) [Disease map \[OMIM\]](#)
[HomoloGene](#) [IGF2R](#)

Gene and transcription

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[AceView](#) [IGF2R AceView - NCBI](#)
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Protein : pattern, domain, 3D structure

[SwissProt](#) [P11717](#) [SRS] [P11717](#) [EXPASY] [P11717](#) [INTERPRO]
[Prosit](#) [PS00023 FIBRONECTIN_2](#) [SRS] [PS00023 FIBRONECTIN_2](#) [Expasy]
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[Prodom](#) [PD000995 FN_Type_II](#) [INRA-Toulouse]
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Polymorphism : SNP, mutations, diseases

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General knowledge

[Family Browser](#) [IGF2R](#) [UCSC Family Browser]
[SOURCE](#) [NM_000876](#)
[SMD](#) [Hs.487062](#)
[SAGE](#) [Hs.487062](#)
[Amigo](#) [function|insulin-like growth factor receptor activity](#)
[Amigo](#) [component|integral to plasma membrane](#)
[Amigo](#) [component|lysosome](#)
[Amigo](#) [function|receptor activity](#)

[Amigo](#) [process|receptor mediated endocytosis](#)
[Amigo](#) [process|signal transduction](#)
[Amigo](#) [process|transport](#)
[Amigo](#) [function|transporter activity](#)
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Other databases

Probes

[Probe](#) [IGF2R Related clones \(RZPD - Berlin\)](#)

PubMed

[PubMed](#) [25 Pubmed reference\(s\) in LocusLink](#)

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Medline [22697205](#)

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