Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

GPER (G protein-coupled estrogen receptor 1)

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Identity

Other names: GPR30; CEPR; CMKRL2; DRY12; FEG-1; GPCR-Br; LERGU; LERGU2; LyGPR; mER

HGNC (Hugo): GPER

Location: 7p22.3

DNA/RNA

Note

GPR30 is an estrogen-responsive GPCR (7-transmembrane G protein-coupled receptor).

Description

The open reading frame of GPR30 is encoded by a single exon (1125 bp) located at chromosome 7p22.3.

Transcription

GPR30 mRNA is about 3.0 kb in human with an 1125 bp open reading frame.

Protein

Description

The gene encodes a 7-transmembrane G protein-coupled receptor (GPCR) of 375 amino acids.

Expression

GPR30 is widely express throughout the body.

Localisation

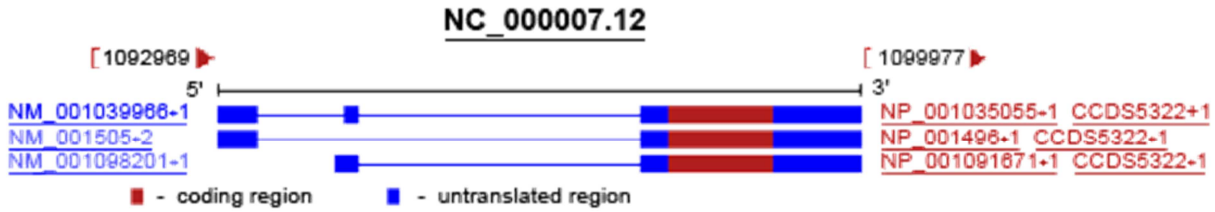
Predominantly in the Endoplasmic Reticulum.

Function

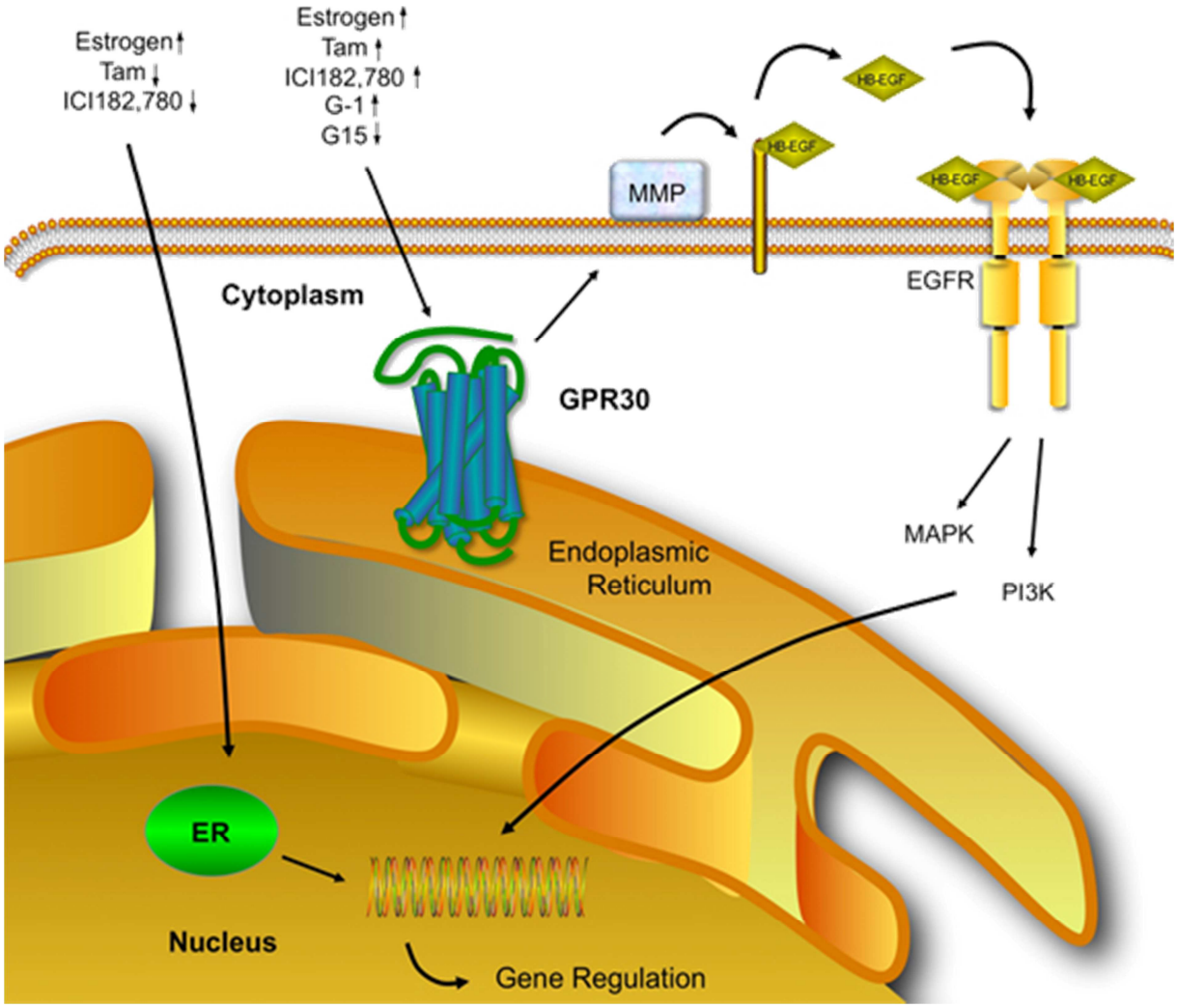
Rapid and transcriptional responses to estrogen.

GPR30 is a 7-transmembrane G protein-coupled receptor (GPCR) that has been shown to be an estrogen responsive receptor, expressed predomin-antly in the endoplasmic reticulum. Signaling occurs via heterotrimeric G protein activation resulting in matrix-metalloproteinase activation, release of heparin-binding EGF and transactivation of EGFR with subsequent MAPK and Akt activation. Calcium mobilization has also been reported in multiple cell types including neurons. This protein plays a role in the rapid non-genomic signaling events often seen following stimulation with estrogen. Transcriptional activation has also been reported secondary to kinase activation. Actions of GPR30 can occur in parallel to those mediated by ERalpha and ERbeta in cells where multiple receptor are expressed, or in the absence of ERalpha and ERbeta. Note that GPR30 does not appear to mediate transcription via classical estrogen-response elements.

Diagram from Entrez Gene.



Alternate transcriptional splice variants (involving the 5' UTR region of the gene) have been characterized. Diagram from Entrez Gene.



Cellular activation by GPR30 and classical estrogen receptors (ERs). Receptor agonists and antagonists (indicated by upward and downward arrows, respectively) are shown for the indicated receptor (Tam, tamoxifen; G-1, GPR30-selective agonist; G15, GPR30-selective antagonist). Nuclear estrogen receptors classically mediate gene regulation although they can also mediate rapid signaling through kinases (not shown). GPR30 is found predominantly in the endoplasmic reticulum and mediates cell activation at least in part through the transactivation of EGFR leading to the stimulation of MAPK, PI3K and other rapid cellular processes, which can result in transcriptional activation.

Homology

High homology between species. Low homology to other GPCRs.

Mutations

Note

None

Implicated in

Cancer

Prognosis

Expression levels correlated with HER-2/neu, tumor size and the presence of metastatic disease in breast cancer. Expression correlated with survival and

high-risk disease in endometrial cancer. GPR30 mediates estrogen-dependent responses in breast, endometrial and ovarian cancer cell lines including proliferation and migration.

Other

Note

GPR30 has been implicated to play a role in estrogen-induced thymic atrophy, estrogen-media-ted amelioration of autoimmune encephalomyelitis, depression, pain, vascular function and oocyte maturation.

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