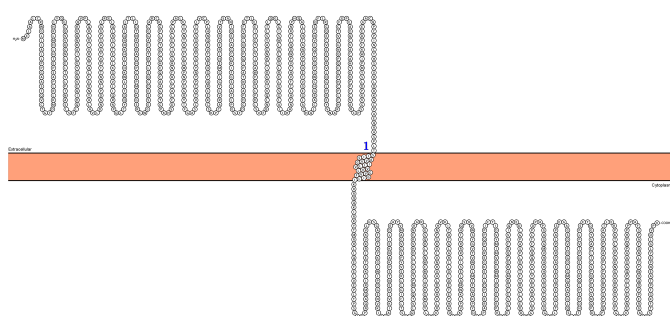


Receptor tyrosine-protein kinase erbB-2

Organism: Homo sapiens (Human) | **Gene names:** ERBB2, HER2, MLN19, NEU, NGL



Entry: P04626

Mass: 137.91 Da

Transmembrane: 1

Subcellular location: [Isoform 1]: Cell membrane

{ECO:0000269|PubMed:31138794}, Single-pass type I

membrane protein. Early endosome

{ECO:0000269|PubMed:31138794}. Cytoplasm,

perinuclear region. Nucleus. Note=Translocation to the

nucleus requires endocytosis, probably endosomal

sorting and is mediated by importin beta-1/KPNB1. Also

detected in VPS35-positive endosome-to-TGN

retrograde vesicles (PubMed:31138794).

{ECO:0000269|PubMed:31138794}., [Isoform 2]:

Cytoplasm. Nucleus., [Isoform 3]: Cytoplasm. Nucleus.

Cofactor: -

Extinction coefficient: 1.003

Isoelectric Point: 5.58

PubMed ID: 3003577, 2999974, 15489334, 3039351, 24722188, 2995967, 2992089, 8104414, 10358079, 10805725, 12939402, 15380516, 15210733, 15156151, 16314522, 17081983, 16794579, 16978839, 17554007, 18691976, 18669648, 18719096, 19372587, 20010870, 20937854, 20068231, 21097718, 21555369, 21190959, 21406692, 23186163, 24275569, 26517842, 27134172, 31138794, 10593938, 12444095, 12975581, 12610629, 15093539, 19299620, 20696930, 21454582, 8095488, 15457249, 17344846

Family: -

Function:

Protein tyrosine kinase that is part of several cell surface receptor complexes, but that apparently needs a coreceptor for ligand binding. Essential component of a neuregulin-receptor complex, although neuregulins do not interact with it alone. GP30 is a potential ligand for this receptor. Regulates outgrowth and stabilization of peripheral microtubules (MTs). Upon ERBB2 activation, the MEMO1-RHOA-DIAPH1 signaling pathway elicits the phosphorylation and thus the inhibition of GSK3B at cell membrane. This prevents the phosphorylation of APC and CLASP2, allowing its association with the cell membrane. In turn, membrane-bound APC allows the localization of MACF1 to the cell membrane, which is required for microtubule capture and stabilization. {ECO:0000305}.; In the nucleus is involved in transcriptional regulation. Associates with the 5'-TCAAATTC-3' sequence in the PTGS2/COX-2 promoter and activates its transcription. Implicated in transcriptional activation of CDKN1A; the function involves STAT3 and SRC. Involved in the transcription of rRNA genes by RNA Pol I and enhances protein synthesis and cell growth. {ECO:0000269|PubMed:10358079, ECO:0000269|PubMed:15380516, ECO:0000269|PubMed:21555369}.

Data from experiment(s): Hek293 membrane pellets

DIBMA 10	NaN	DIBMA 12	0.0813207
DIBMA Glycerol	NaN	DIBMA Glucosamine	NaN
Amphipol 17	0.839449	Amphipol 18	0.234736
AASTY 6-45	NaN	AASTY 11-45	NaN
AASTY 6-50	0.00379232	AASTY 11-50	NaN
AASTY 6- 55	NaN	AASTY 11- 55	0.349486
SMALP 502-E	0.325499	SMALP 140-I	NaN
SMALP 300	0.751661	SMALP 200	0.546779
SMALP 140	NaN	DDM	0.553319
DM	0.856722	LMNG	0.829871
Fos-12	0.683587	Digitonin-A	0.443571
RIPA	0.721261		

Data from experiment(s): Hek293 membrane pellets 1 %

DIBMA 10	NaN	DIBMA 12	NaN
DIBMA Glycerol	0.256836265	DIBMA Glucosamine	No data
Amphipol 17	0.853725731	Amphipol 18	0.831465781
AASTY 6-45	No data	AASTY 11-45	0.584431171
AASTY 6-50	0.82886523	AASTY 11-50	No data
AASTY 6- 55	0.384484321	AASTY 11- 55	No data
SMALP 502-E	0.662823379	SMALP 140-I	No data
SMALP 300	0.6483109	SMALP 200	0.438631266
SMALP 140	No data	DDM	0.992251873
DM	No data	LMNG	0.908049345
Fos-12	No data	Digitonin-A	0.538111508
RIPA	No data		

Involvement in disease:

Glioma (GLM) [MIM:137800]: Gliomas are benign or malignant central nervous system neoplasms derived from glial cells. They comprise astrocytomas and glioblastoma multiforme that are derived from astrocytes, oligodendrogliomas derived from oligodendrocytes and ependymomas derived from ependymocytes.

{ECO:0000269|PubMed:15457249}. Note=The gene represented in this entry is involved in disease pathogenesis.;

Ovarian cancer (OC) [MIM:167000]: The term ovarian cancer defines malignancies originating from ovarian tissue.

Although many histologic types of ovarian tumors have been described, epithelial ovarian carcinoma is the most common form. Ovarian cancers are often asymptomatic and the recognized signs and symptoms, even of late-stage disease, are vague. Consequently, most patients are diagnosed with advanced disease.

{ECO:0000269|PubMed:15457249, ECO:0000269|PubMed:17344846}. Note=The gene represented in this entry is involved in disease pathogenesis.;

Lung cancer (LNCr) [MIM:211980]: A common malignancy affecting tissues of the lung. The most common form of lung cancer is non-small cell lung cancer (NSCLC) that can be divided into 3 major histologic subtypes: squamous cell carcinoma, adenocarcinoma, and large cell lung cancer. NSCLC is often diagnosed at an advanced stage and has a poor prognosis. {ECO:0000269|PubMed:15457249}. Note=The gene represented in this entry is involved in disease pathogenesis.;

Gastric cancer (GASC) [MIM:613659]: A malignant disease which starts in the stomach, can spread to the esophagus or the small intestine, and can extend through the stomach wall to nearby lymph nodes and organs. It also can metastasize to other parts of the body. The term gastric cancer or gastric carcinoma refers to adenocarcinoma of the stomach that accounts for most of all gastric malignant tumors. Two main histologic types are recognized, diffuse type and intestinal type carcinomas. Diffuse tumors are poorly differentiated infiltrating lesions, resulting in thickening of the stomach. In contrast, intestinal tumors are usually exophytic, often ulcerating, and associated with intestinal metaplasia of the stomach, most often observed in sporadic disease. {ECO:0000269|PubMed:15457249, ECO:0000269|PubMed:17344846}.

Note=The protein represented in this entry is involved in disease pathogenesis.;

Note=Chromosomal aberrations involving ERBB2 may be a cause gastric cancer. Deletions within 17q12 region producing fusion transcripts with CDK12, leading to CDK12-ERBB2 fusion leading to truncated CDK12 protein not in-frame with ERBB2.

{ECO:0000269|PubMed:21097718}.

Binding site:

1

Tissue specificity:

Expressed in a variety of tumor tissues including primary breast tumors and tumors from small bowel, esophagus, kidney and mouth. {ECO:0000269|PubMed:15380516}.

3D (X-ray crystallography):

Model (1); X-ray crystallography (27); NMR spectroscopy (6); Electron microscopy (1)

Pharmaceutical use:

-

AS sequence:

MELAALCRWG LLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMRLHLYQGCQVVQGNLELTYLPTNASLSFLQDIQEVQGYV
LIAHNQVRQVPLQRLRIVRG TQLFEDNYALAVLDNGDPLNNTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWK
DIFHKNNQLALTIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLTRTV CAGGCARCKGPLPTDCCHEQCAAGCTGPKHSDCL
ACLHFNHSGICELHCPALVTYNTDTFESMPNPEG RYTFGASCVTACPYNYLSTDVGSCTLVCP LHNQEVTAE DGTQRCEKCSKP
CARVCYGLGMEHLREVRAVTSANIQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSL PDL
VFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLALIH HNTHLCFVHTVPWDQLFRNPHQALLHTANRPEDECVGE
GLACHQLCARGHCWGPPTQCVNCSQFLRGQECVEECRVLQGLPREYVNARHCLPCHPECQPQNGSVTCFGPEADQCVACAH
YKDPFFCVARCPSGVKPDL SYMPIWKFPDEEGACQPCINCTHSCVDLDDKGCPAEQRASPLTSIISAVVGILLVWV LGVVFILIK
RRQQKIRKYTMRRLLQETELVEPLTPSGAMPNQAQMRILKETELRKVKVLGSGAFGT VYKGIWIPDGENVKIPVAIKVLRENTSP
KANKEILDEAYVMAGVGSPYVSRLLGICLTSTVQLVTQLMPYGCLLDHVREN RGRLGSDLLNWCMQIAKGMSYLEDVRLVHR
DLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMAL ESILRRRFTHQSDVWSYGVTVWELMTFGAKPYDGIPA
REIPDLLEKGERLPQPPICTIDVYMIMVKCWMIDSECRPRFREL VSEFSRMARDPQRFVVIQNE DLGPASPLDSTFYRSLLEDDD
MGDLVDAEEYLVPQQGFFCPDPAPGAGGMVHHRHRSSTRSGGDLTLGLEPSEEEAPRSPLAPSEGAGSDVFDGDLGMGAA
KGLQSLPTHDPSP LQRYSEDPTVPLPSETDGYVAPLTCSPQPEYVNQPDVRPQPPSPREGPLPAARPAGATLERPKTLSPGKN
GVVKDVF AFGGA VENPEYLT PQGGAAPQPHPPPAFSPAFDNLYYWDQDPPERGAPPSTFKGTPTAENPEYLG LDVPV

Creditnotes:

The protein visualizations are generated with the help of Protter:

Omasits, U., Ahrens, C.H., MÃ¼ller, S., Wollscheid, B. "Protter: interactive protein feature visualization and integration with experimental proteomic data". *Bioinformatics*. 2014 Mar 15; **30**(6):884-6. doi: 10.1093/bioinformatics/btt607.

IP and extinction coefficients are gathered from Protparam by ExPASy:

Gasteiger, E., Hoogland, C., Gattiker, A., Duvaud, S., Wilkins, M.R., Appel, R.D., Bairoch, A. "Protein Identification and Analysis Tools on the ExPASy Server". (In) *John M. Walker (ed): The Proteomics Protocols Handbook*, Humana Press (2005). pp. 571-607

The basic knowledge is found on UniProt:

The UniProt Consortium. "UniProt: the universal protein knowledgebase in 2021". *Nucleic Acids Res.* **49**:D1 (2021)