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Epidermal growth factor receptor

Organism: Homo sapiens (Human) | **Gene names:** EGFR, ERBB, ERBB1, HER1

Entry: P00533

Mass: 134.277 Da

Transmembrane: 1

Subcellular location: Cell membrane {ECO:0000269|PubMed:17182860, ECO:0000269|PubMed:20462955, ECO:0000269|PubMed:23589287, ECO:0000269|PubMed:27153536, ECO:0000269|PubMed:2790960}, Single-pass type I membrane protein {ECO:0000269|PubMed:27153536}. Endoplasmic reticulum membrane {ECO:0000269|PubMed:27153536}, Single-pass type I membrane protein. Golgi apparatus membrane, Single-pass type I membrane protein. Nucleus membrane, Single-pass type I membrane protein. Endosome {ECO:0000269|PubMed:17182860, ECO:0000269|PubMed:27153536}. Endosome membrane. Nucleus {ECO:0000269|PubMed:17115032, ECO:0000269|PubMed:17909029, ECO:0000269|PubMed:20551055, ECO:0000269|PubMed:20674546}. Note=In response to EGF, translocated from the cell membrane to the nucleus via Golgi and ER (PubMed:20674546, PubMed:17909029). Endocytosed upon activation by

ligand (PubMed:2790960, PubMed:17182860, PubMed:27153536, PubMed:17909029). Colocalized with GPER1 in the nucleus of estrogen agonist-induced cancer-associated fibroblasts (CAF) (PubMed:20551055). {ECO:0000269|PubMed:17182860, ECO:0000269|PubMed:17909029, ECO:0000269|PubMed:20674546, ECO:0000269|PubMed:27153536, ECO:0000269|PubMed:2790960}., [Isoform 2]: Secreted.

Cofactor: -

Extinction coefficient: 0.96

Isoelectric Point: 6.26

PubMed ID: 6328312, 7654368, 8918811, 9103388, 11161793, 6326261, 6330563, 6093780, 3329716, 1988448, 2991899, 6324343, 3138233, 15340161, 2985580, 16543144, 9556602, 6325948, 3039909, 2790960, 2543678, 7679104, 8650580, 9852145, 10523301, 8144591, 7657591, 8962717, 9419975, 9488479, 10228163, 10026169, 10731668, 11602604, 12731890, 12873986, 15282549, 10805725, 11116146, 11483589, 15590694, 15611079, 16083266, 16140940, 17081983, 17115032, 16420529, 17909029, 17671655, 17182860, 17334392, 18602463, 19172738, 18220336, 18691976, 18669648, 19413330, 19836242, 19509291, 19159218, 19369195, 19749156, 19718021, 20674546, 20551055, 20462955, 20068231, 21269460, 21487020, 21258366, 21516087, 21518868, 22298428, 22179831, 23418353, 23186163, 24275569, 25187647, 23589287, 25311788, 23912460, 25922362, 27153536, 26988023, 28479384, 30352854, 12297049, 12297050, 12620237, 15374980, 15837620, 15840573, 17349580, 18046415, 18227510, 19563760, 19560417, 20471394, 20837704, 22888118, 15623594, 15118125, 16533793, 16205628, 16672372, 17344846, 24691054

Family: -

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Function:

Receptor tyrosine kinase binding ligands of the EGF family and activating several signaling cascades to convert extracellular cues into appropriate cellular responses (PubMed:2790960, PubMed:10805725, PubMed:27153536). Known ligands include EGF, TGFA/TGF-alpha, AREG, epigen/EPGN, BTC/betacellulin, epiregulin/EREG and HBEGF/heparin-binding EGF (PubMed:2790960, PubMed:7679104, PubMed:8144591, PubMed:9419975, PubMed:15611079, PubMed:12297049, PubMed:27153536, PubMed:20837704, PubMed:17909029). Ligand binding triggers receptor homo- and/or heterodimerization and autophosphorylation on key cytoplasmic residues. The phosphorylated receptor recruits adapter proteins like GRB2 which in turn activates complex downstream signaling cascades. Activates at least 4 major downstream signaling cascades including the RAS-RAF-MEK-ERK, PI3 kinase-AKT, PLCgamma-PKC and STATs modules (PubMed:27153536). May also activate the NF-kappa-B signaling cascade (PubMed:11116146). Also directly phosphorylates other proteins like RGS16, activating its GTPase activity and probably coupling the EGF receptor signaling to the G protein-coupled receptor signaling (PubMed:11602604). Also phosphorylates MUC1 and increases its interaction with SRC and CTNNB1/beta-catenin (PubMed:11483589). Positively regulates cell migration via interaction with CCDC88A/GIV which retains EGFR at the cell membrane following ligand stimulation, promoting EGFR signaling which triggers cell migration (PubMed:20462955). Plays a role in enhancing learning and memory performance (By similarity). {ECO:0000250|UniProtKB:Q01279, ECO:0000269|PubMed:10805725, ECO:0000269|PubMed:11116146, ECO:0000269|PubMed:11483589, ECO:0000269|PubMed:11602604, ECO:0000269|PubMed:12297049, ECO:0000269|PubMed:12297050, ECO:0000269|PubMed:12620237, ECO:0000269|PubMed:12873986, ECO:0000269|PubMed:15374980, ECO:0000269|PubMed:15590694, ECO:0000269|PubMed:15611079, ECO:0000269|PubMed:17115032, ECO:0000269|PubMed:17909029, ECO:0000269|PubMed:19560417, ECO:0000269|PubMed:20462955, ECO:0000269|PubMed:20837704, ECO:0000269|PubMed:21258366, ECO:0000269|PubMed:27153536, ECO:0000269|PubMed:2790960, ECO:0000269|PubMed:7679104, ECO:0000269|PubMed:8144591, ECO:0000269|PubMed:9419975}.; Isoform 2 may act as an antagonist of EGF action.; (Microbial infection) Acts as a receptor for hepatitis C virus (HCV) in hepatocytes and facilitates its cell entry. Mediates HCV entry by promoting the formation of the CD81-CLDN1 receptor complexes that are essential for HCV entry and by enhancing membrane fusion of cells expressing HCV envelope glycoproteins. {ECO:0000269|PubMed:21516087}.

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Data from experiment(s): Hek293 membrane pellets

DIBMA 10	0.409802	DIBMA 12	0.480192
DIBMA Glycerol	0.280256	DIBMA Glucosamine	0.419304
Amphipol 17	0.709978	Amphipol 18	0.638817
AASTY 6-45	0.170599	AASTY 11-45	0.270076
AASTY 6-50	0.248669	AASTY 11-50	0.213488
AASTY 6- 55	0.40638	AASTY 11- 55	0.358815
SMALP 502-E	0.598447	SMALP 140-I	0.653115
SMALP 300	0.781966	SMALP 200	0.725718
SMALP 140	NaN	DDM	0.8522
DM	0.915323	LMNG	0.896809
Fos-12	0.927113	Digitonin-A	0.547749
RIPA	0.867901		

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

DIBMA 10	NaN	DIBMA 12	NaN
DIBMA Glycerol	0.446126401	DIBMA Glucosamine	No data
Amphipol 17	0.795875072	Amphipol 18	0.727205992
AASTY 6-45	No data	AASTY 11-45	0.550313652
AASTY 6-50	0.781077445	AASTY 11-50	No data
AASTY 6- 55	0.439399719	AASTY 11- 55	No data
SMALP 502-E	0.397106797	SMALP 140-I	No data
SMALP 300	0.571338415	SMALP 200	0.312169403
SMALP 140	No data	DDM	1
DM	No data	LMNG	0.887826383
Fos-12	No data	Digitonin-A	0.439438641
RIPA	No data		

Involvement in disease:

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:15118125, ECO:0000269|PubMed:16533793, ECO:0000269|PubMed:16672372}. Note=The gene represented in this entry is involved in disease pathogenesis.; Inflammatory skin and bowel disease, neonatal, 2 (NISBD2) [MIM:616069]: A disorder characterized by inflammatory features with neonatal onset, involving the skin, hair, and gut. The skin lesions involve perioral and perianal erythema, psoriasiform erythroderma, with flares of erythema, scaling, and widespread pustules. Gastrointestinal symptoms include malabsorptive diarrhea that is exacerbated by intercurrent gastrointestinal infections. The hair is short or broken, and the eyelashes and eyebrows are wiry and disorganized. {ECO:0000269|PubMed:24691054}. Note=The disease is caused by variants affecting the gene represented in this entry.

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Binding site:

2

Tissue specificity:

Ubiquitously expressed. Isoform 2 is also expressed in ovarian cancers. {ECO:0000269|PubMed:17671655}.

3D (X-ray crystallography):

Model (4); X-ray crystallography (221); NMR spectroscopy (6)

Pharmaceutical use:

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AS sequence:

MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLKTIQEV
AGYVLIALNTVERIPLENLQIIRGNMYYENSYALAVLSNYDANKTGLKELPMRNLQEILHGAVRFSNNPALCNVESIQWRDIVSSD
FLSNMSMDFQNHLGSCQKCDPSCPNGSCWGAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGCTGPRESDCLVCRK
FRDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYVVTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRK
VCNGIGIGEFKDSLSINATNIKHFKNCTSISGDLHILPVAFRGDSFTHTPPLDPQELDILKTVKEITGFLLIQAWPENRTDLHAFENL
EIIRGRTKQHGQFSLAVVSLNITSLGLRSLKEISDGDVIISGNKNLCYANTINWKKLFGTSGQKTKIISNRGENSCKATGQVCHALCS
PEGCWGPEPRDCVSCRNVSRGRECVDKCNLLEGEPREFVENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTC
PAGVMGENNTLVWKYADAGHVCHLCHPNCTYGCTGPGLEGCPTNGPKIPSIATGMVGALLLLLVVALGIGLFMRRRHIVRKRTL
RRLLQERELVEPLTPSGEAPNQALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREATSPKANKEILDEAYVMA
SVDNPHVCRLLGICLTSTVQLITQLMPFGCLLDYVREHKDNIGSQYLLNWCVQIAKGMNYLEDRRLVHRDLAARNVLVKTPQHV
KITDFGLAKLLGAEEKEYHAEGGKVPIKWMALESILHRIYTHQSDVWSYGVTVWELMTFGSKPYDGIPASEISSILEKGERLPQPPI
CTIDVYMIMVKCWMIDADSRPKFRELIIEFSKMARDPQRYLVIQGDERMHLPSPTDSNFYRALMDEEDMDDVVDADEYLIPQQ
GFFSSPSTSRTPLLSSLSATSNNSTVACIDRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKRPAGSVQN
PVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKG
STAENAEYLRVAPQSSEFIGA

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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)