



The Epidermal Growth Factor (EGF) Family

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GroPep: The respected name for Insulin-like Growth Factor-related reagents is now a trusted name for the EGF Family.

The Epidermal Growth Factor (EGF) Ligand Family:

At least 11 different polypeptide ligands from distinct genes can bind to the extracellular domain of the EGF Receptor. These molecules collectively comprise the EGF family and are:

- Epidermal Growth factor (EGF)
- Transforming Growth Factor α (TGF- α)
- Amphiregulin (AR)
- Heparin Binding-EGF (HB-EGF)
- Epiregulin (EPR)
- Betacellulin (BTC)
- Neuregulins 1 - 4 (NRG 1-4)
- Terato Carcinoma Derived Growth Factor (Cripto 1).

Each member contains at least one characteristic EGF-like domain, defined by 6 cysteine residues that generate 3 peptide loops through the formation of disulphide bonds. Less homology exists outside the essential cysteines and several glycine residues required for the EGF-like fold.

EGF family members are synthesized as transmembrane precursors and the soluble cytokine may be released by proteolytic cleavage.

EGF Receptors:

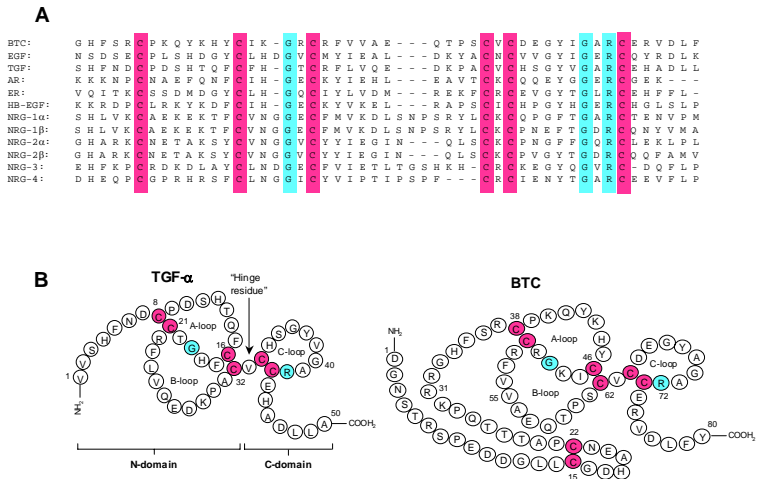
The Epidermal Growth Factor Receptors are homodimers or heterodimers made up of a family of four highly homologous transmembrane glycoproteins comprising ErbB-1 (also known as EGF-R), ErbB-2, ErbB-3 and ErbB-4. The receptors all have an extracellular ligand binding domain, a single hydrophobic membrane-spanning domain and a cytoplasmic tyrosine kinase domain that is responsible for signal transduction through Type 1 receptor tyrosine kinase activity. Ligand binding to any of the EGF receptors results in receptor dimerization and autophosphorylation followed by phosphorylation of a number of cellular substrates leading to a range of biological effects including cell division and proliferation.

Interactions between Ligands and Receptors:

A snapshot of recent highlights in this area include:

- Over expression of the EGF receptors is highly correlated with aggressive growth of certain tumors, including breast and pancreatic tumors (Salomon, *et al*, 1995; Neimeyer *et al*, 1999 and Woodburn, 1999).
- Ten possible receptor dimeric complexes exist, but those containing ErbB-2, and especially the ErbB-2/ErbB-3 heterodimers, are more stable and their signalling more potent.
- ErbB-2 acts as the preferred heterodimeric partner for the other three ErbB receptors.
- Different members of the EGF ligand family bind to the different receptors with varying specificity and affinities.
- EGF and TGF- α bind primarily to ErbB-1 and have low binding affinity for ErbB-3 and ErbB-4. However, this affinity can be enhanced by the presence of ErbB-2 in the receptor heterodimer.
- Only BTC and EGF (with significantly lower affinity) can induce cell growth and differentiation in the absence of ErbB-1.
- Only BTC stimulates insulin secretion in pancreatic β cells.
- Cripto 1 fails to bind to any of the known ErbB receptors but can indirectly induce tyrosine phosphorylation of the ErbB-4 receptor. A functional ErbB-4 receptor is believed to be required for the full biological activity of Cripto 1.

These examples illustrate that to understand the role of the EGF family in biological systems it is important to take into account the three layers of complexity at the ligand, receptor and signal transduction levels.



A. Amino acid sequence alignment of the conserved EGF motif of the EGF-family of peptide ligands. Conserved cysteine residues are indicated by pink boxes. Other conserved residues are indicated by blue boxes.

B. Representation of the secondary structure of TGF- α and BTC. (adapted from Dunbar, A. J. and Goddard, C. (2000) *Int. J. Biochem. Cell Biol.*, **32**, 805-815)

Useful References:

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- Jorissen, R. N., *et al.* (2000) Characterization of a comparative model of the extracellular domain of the epidermal growth factor receptor. *Protein Sci.*, **9**, 310-324.
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The GroPep EGF Family Product Range:

For specifications on any of these reagents, click on the product title below.

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Betacellulin, recombinant bovine

Code: ARU020 20 μ g US\$160 Code: ARU100 100 μ g US\$260

EGF, recombinant mouse (Receptor Grade)

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EGF, recombinant porcine (Receptor Grade)

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Code: AWM005 5 mg US\$1075 Code: AWM010 10 mg US\$1790
Code: AWM050 50 mg US\$5365

TGF- α , recombinant human (Receptor Grade)

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Growth Factors for Cell Growth studies and Cell Culture:

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Code: VM010 10 mg US\$1075
Code: VM020 20 mg US\$1790

LongTMEGF (Media Grade)

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Code: NM005 5 mg US\$715
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Anti-Rat Betacellulin, Rabbit antiserum

Code: PAAQ1 100 μ l US\$220

Anti-human EGF, Rabbit antiserum (also recognises porcine EGF)

Characterized for RIA and suitable for immunohistochemistry

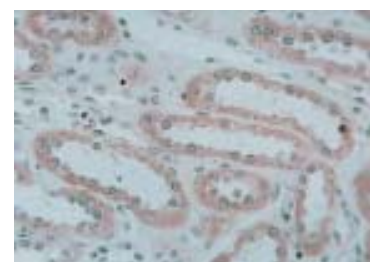
Code: PAD1 5 μ l US\$110

Code: 5PAD1 25 μ l US\$220

Anti-human TGF- α , Rabbit antiserum

Characterized for EIA

Code: PAL1 100 μ l US\$220



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