

# ErbB family

**Overview:** ErbB family receptors (ENSM00410000138465, provisional nomenclature) are cell-surface receptors, which, when activated by members of the epidermal growth factor (EGF) family, activate a transmembrane tyrosine kinase activity (E.C. 2.7.1.112), leading to the stimulation of multiple signal transduction pathways (see Yarden and Sliwkowski, 2001). ErbB2 (also known as HER-2 or NEU, ENSG00000141736) appears to act as an essential partner for the other members of the family without itself being activated by a cognate ligand (Graus-Porta *et al.*, 1997).

Ligands of the ErbB family of receptors are peptides including EGF (ENSG00000138798), amphiregulin (also known as colorectal cell-derived growth factor, ENSG00000109321), betacellulin (ENSG00000174808), epigen (ENSG00000182585), epiregulin (ENSG00000124882), heparin-binding EGF-like growth factor (HB-EGF or diphtheria toxin receptor, ENSG00000113070), neuregulins (NRG-1, also known as Neu differentiation factor, acetylcholine receptor-inducing activity, heregulin or glial growth factor, ENSG00000157168; NRG-2, ENSG00000158458; NRG-3, ENSG00000185737 and NRG-4, ENSG00000169752) and transforming growth factor- $\alpha$  (TGF $\alpha$ , ENSG00000163235). These ligands appear to be generated by proteolytic cleavage of cell-surface peptides.

Nomenclature	ErbB1	ErbB3	ErbB4
Other names	EGF, HER1	HER3	HER4
Ensembl ID	ENSG00000146648	ENSG00000065361	ENSG00000178568
Agonist activity	EGF, amphiregulin, betacellulin, epigen, epiregulin, HB-EGF, TGF $\alpha$	NRG-1, NRG-2	Betacellulin, epiregulin, HB-EGF, NRG-1, NRG-2, NRG-3, NRG-4
Probes	[ <sup>125</sup> I]-EGF	–	–

The extracellular domain of ErbB2 can be targeted by the antibodies trastuzumab and pertuzumab to inhibit ErbB family action. The intracellular ATP-binding site of the tyrosine kinase domain can be inhibited by GW583340 (7.9–8.0, Gaul *et al.*, 2003), gefitinib, erlotinib and tyrphostins AG879 and AG1478.

**Abbreviations:** **Erlotinib**, *N*-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine, also known as OSI774; **gefitinib**, *N*-(3-chloro-4-fluoro-phenyl)-7-methoxy-6-(3-morpholin-4-ylpropoxy)quinazolin-4-amine, also known as ZD1839; **GW583340**, *N*-(3-chloro-4-[[3-fluorophenyl]methoxy]phenyl)-6-(2-[[2-([methylsulfonyl]ethyl)amino]methyl]-4-thiazolyl)-4-quinazolinamine dihydrochloride; **tyrphostin AG1478**, *N*-(3-chlorophenyl)-6,7-dimethoxyquinazolin-4-amine hydrochloride; **tyrphostin AG879**,  $\alpha$ -cyano-(3,5-di-*t*-butyl-4-hydroxy)thiocinnamide

## Further Reading

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## References

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