Humanized Anti-Her2/neu (Herceptin/ trastuzumab) Assay Kits

HER2 (Human Epidermal Growth Factor Receptor 2) also known as Neu, ErbB-2, CD340 (cluster of differentiation 340) or p185 is a protein that in humans is encoded by the ERBB2 gene. Neu is so named because it was derived from a rodent glioblastoma cell line, a type of neural tumor. HER2 is named because it has a similar structure to human epidermal growth factor receptor, or HER1. HER2 is a member of the epidermal growth factor receptor (EGFR/ErbB) family. Amplification or over-expression of this gene has been shown to play an important role in the pathogenesis and progression of certain aggressive types of breast cancer and in recent years it has evolved to become an important biomarker and target of therapy for the disease.

The ErbB family is composed of four plasma membrane-bound receptor tyrosine kinases. All four contain an extracellular ligand binding domain, a transmembrane domain, and an intracellular domain that can interact with a multitude of signaling molecules. Unlike the other family members, HER2 is considered to be an orphan receptor as it has no known ligand. HER2 can heterodimerise with any of the other three receptors. Dimerisation results in the autophosphorylation of tyrosine residues within the cytoplasmic domain of the receptors and initiates a variety of signaling pathways. Signaling through the ErbB family of receptors promotes cell proliferation and opposes apoptosis, and therefore must be tightly regulated to prevent uncontrolled cell growth from occurring.

Amplification or over-expression of the ERBB2 gene occurs in approximately 30% of breast cancers. It is strongly associated with increased disease recurrence and a worse prognosis. Over-expression is also known to occur in ovarian, stomach, and aggressive forms of uterine cancer, such as uterine serous endometrial carcinoma. The extracellular domain of HER2 can be shed from the surface of tumour cells and enter the circulation. HER2 testing is performed in breast cancer patients to assess prognosis and to determine suitability for Herceptin therapy. It is important that Herceptin is restricted to HER2-positive individuals as it is expensive and has been associated with cardiac toxicity. Measurement of serum HER2 by ELISA offers a far less invasive method of determining HER2 status than a biopsy and consequently has been extensively investigated.

HER2 is the target of the monoclonal antibody trastuzumab (**Herceptin**). Trastuzumab is effective only in cancers where HER2 is over-expressed.

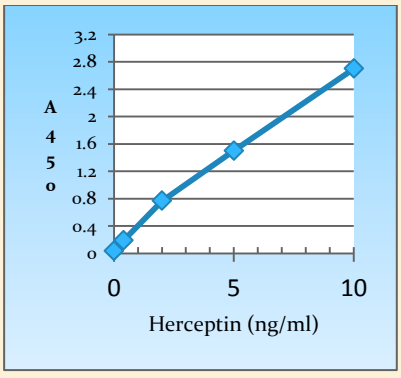
Herceptin is fully humanized mab (IgG1 kappa) produced in CHO cell culture. It binds to the domain IV of the extracellular segment of the HER2/neu receptor. Trastuzumab is recommended in 3+-Her2 (~2 million her2 per cell) positive breast tumors. Testing is performed on biopsy and immunohistochemistry. Trastuzumab has had a "major impact in the treatment of HER2-positive metastatic breast cancer". The combination of Trastuzumab with chemotherapy has been shown to increase both survival and response rate, in comparison to Trastuzumab alone. Herceptin costs about $100,000 for a full treatment. Another monoclonal antibody, **Pertuzumab (2c4 or Omnitrag)**, which inhibits dimerization of HER2 and HER3 receptors, is in advanced clinical trials.

Other approaches such as DNA-based vaccines against Her2 using either the full length expression of her2 (pE2A) or extracellular domain or intracellular domains (pE2TM, pSec2, p185 or MVA-BN-Her2) are being used to produce antibodies to Her2. Similarly, Her 2 peptide-derived vaccine (E75, GP2, AE37 peptide or multiple peptides) are being tested to induce antibodies to Her2.

Like many humanized antibodies, Herceptin can antibodies or human anti-human antibodies (**HAHA**) (1 patient in 903). However, this is highly dependent upon the sensitivity of the assay. ADI has developed new ELISA kits that measures **"Free Hercpetin"** in patients treated with Herceptin. ADI has also developed ELISA kits to detect antibodies to Herceptin (**Human Anti- Hercpetin Antibodies**) in patients receiving long-term treatments. These kits will allow to research better ways to monitor herceptin treatment. Additional ELISA kits are available to monitor the increase other autoimmune diseases (ANA, anti-dsDNA IgGs, tuberculosis). ADI also have variety of antibodies to human, mouse, and rat herceptin and Her2 peptides for vaccine studies.

Herceptin/Trasuzumab ELISA Kit for human, 96 tests #200-510-HLG

This kit measures Active Herceptin (Her2-binding) in human or animal samples (buffers, serum or plasma). It is a sandwich ELISA in which only active or non-liganded Herceptin from the sample is captured on the plate and then detected by antibody specific for Herceptin. No interference from endogenous IgGs from animal or human serum or plasma due to the proprietary design of the ELISA kit. For in vitro research use only.



ELISA Kit Features

- Active Herceptin/Trasuzumab binding, pre-coated, stabilized, ready-to-use 96-well strip plate, suitable for multiple runs over 6-12 months.
- Herceptin standards (0-10 ng/ml).
- Sample size 100 ul (serum or plasma diluted ~1:100 or more).
- 105 minutes, 3 incubation steps at room temp
- Sensitivity ~0.2 ng/ml; Good Recovery and Assay Precision.
- Contains all necessary reagents. Shelf life ~6 months.
- Sample values are calculated from the standard curve.

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List of Herceptin Related reagents and ELISAs available from ADI.

Catalog#	Product Description
200-510-HLG	Herceptin/Trasuzumab ELISA Kit for human, 96 tests
200-520-HAG	Human Anti-Herceptin/Trasuzumab Antibody (HAHA) ELISA Kit 96 tests
200-530-HER	Her2/neu/Erbb2/CD340 protein ELISA kit, 96 tests
HER21-R-10	Recombinant (HEK) **human** Her2/Erbb2/Neu (1-652)-**hIgG-Fc** fusion protein
HER22-R-5	Recombinant (sf9) **human** Her2/Erbb2/Neu (676-1255)-**GST** fusion protein
HER23-R-10	Recombinant (HEK) **human** Her2/Erbb2/Neu (1-652)-**his tag** fusion protein
HER24-R-10	Recombinant (HEK) **mouse** Her2/Erbb2/Neu (1-653)-his tag fusion protein
HER25-R-10	Recombinant (HEK) **mouse** Her2/Erbb2/Neu (1-653)-hIgG1-Fc fusion protein
HER26-R-10	Recombinant (HEK) **rat** Her2/Erbb2/Neu (4-656)-his tag fusion protein
HER27-R-10	Recombinant (HEK) rat Her2/Erbb2/Neu (4-656)-his tag fusion protein
HER28-R-10	Recombinant (HEK) rat Her2/Erbb2/Neu (4-656)-hIgG1-Fc fusion protein
HER29-R-10	Recombinant (HEK) monkey/rhesus Her2/Erbb2/Neu (1-652)-his tag fusion protein
HER30-R-10	Recombinant (HEK) monkey/rhesus Her2/Erbb2/Neu (1-652)-hIgG1-Fc fusion protein
HER31-M	Rabbit mono anti-human Her2/Erbb2/Neu (1-652) protein IgG
HER32-A	Anti-human Her2/Erbb2/Neu (1-652) protein IgG
HER33-M	Mouse mono anti-monkey/rhesus Her2/Erbb2/Neu (1-652) protein IgG
HER34-A	Anti-monkey/rhesus Her2/Erbb2/Neu (1-652) protein IgG

Catalog#	***ProdDescription***
#HER2-369-P	*HER2 peptide, (369 – 377), E 75 vaccine candidate*
#HER2-597-P	*HER2 peptide, cyclic, (597-626, disulphide bond) vaccine candidate*
HER2-654-P	*HER2 peptide, (654 – 662), GP2 vaccine candidate*
#HER2-776-P	*HER2 peptide, (776 – 790 fused with LRMK), GP2 vaccine candidate*
HER2-563-P	*HER2 peptide, cyclic, (563-598,); vaccine candidate*
#HER2-585-P	*HER2 peptide, cyclic, (585-598,); vaccine candidate*
HER2-613-P	*HER2 peptide, cyclic, (613-626,); vaccine candidate*

ADI is also offering custom testing of animal or human samples for herceptin or antibodies to herceptin, and her2 measurements.

Rev. 120914

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