



## Product Information

### MONOCLONAL ANTI-HEREGULIN CLONE 7D5

Purified Mouse Immunoglobulin

Product Number **H 6286**

#### Product Description

Monoclonal Anti-Heregulin (HRG) (mouse IgG2a isotype) is derived from the hybridoma produced by the fusion mouse myeloma NSO cells with splenocytes from BALB/c mice immunized with the recombinant extracellular domain of rat HRG/NDF protein coupled to keyhole limpet hemocyanin (KLH). The antibody is purified by Protein A/Protein G chromatography.

Anti-HRG recognizes the 44 kDa human, rat and mouse HRG/NDF glycoprotein. This highly specific antibody is directed against the extracellular domain of HRG/NDF. It does not crossreact with EGF and reacts with both  $\alpha$  and  $\beta$  isoforms, suggesting that its epitope is outside the EGF domain. It does not inhibit the binding of HRG to the ErbB receptors. The antibody may be used in immunoblotting, immunohistochemistry with frozen or formalin-fixed, paraffin-embedded tissue sections, and in immunoprecipitation studies.

Heregulin, also known as glial growth factor-2 (GGF2), *neu* Differentiation Factor (NDF) or neuregulin (NRG1), is a 44 kDa glycoprotein that interacts with the NEU/ERBB2 receptor tyrosine kinase to increase its phosphorylation on tyrosine residues. NRG1 is a member of a family of structurally related glycoproteins that includes NRG2, NRG3, and NRG4. Alternative splicing of at least 15 exons generates a minimum of 14 NRG1 isoforms.<sup>1</sup>

Neuregulins are a family of growth and differentiation factors related to epidermal growth factor (EGF). Through interaction with their receptors, the ErbB proteins, neuregulins induce the growth and differentiation of epithelial, neuronal, glial, and other types of cells. In particular, the neuregulin-ErbB signaling pathways play crucial roles in regulating the proliferation and differentiation of Schwann cells and oligodendrocytes, the myelin-forming cells in the peripheral nervous system.<sup>2</sup> Neuregulins and their receptors are essential for neuronal development. The CRD-NRG-1-mediated signaling is necessary for coordinating nerve, target, and Schwann cell interactions in the normal maintenance of peripheral synapses, and ultimately in the survival of CRD-NRG-1-expressing neurons.<sup>3,4</sup>

Mice homozygous for disruptions of all NRG1 isoforms, all Ig-NRG1 isoforms, and all cytoplasmic tail-containing isoforms die at embryonic day 10.5 from cardiac defects. In particular, these mice die before significant expression of CRD-NRG1 isoforms, which predominate after midgestation.

Mice with experimental autoimmune encephalomyelitis treated with rhGGF2 during both the acute and relapsing phases showed delay in the disease signs, decreased severity, and statistically significant reductions in relapse rate. rhGGF2-treated groups displayed central nervous system lesions with more remyelination than in controls. These beneficial effects of rhGGF2 treatment on the clinical, pathologic, and molecular manifestations of autoimmune demyelination, associated with increased expression of a T helper 2 cytokine may represent a novel approach to the treatment of multiple sclerosis.<sup>5,6</sup>

#### Reagent

Monoclonal Anti-Heregulin is supplied as a solution in phosphate buffered saline, pH 7.4, with 0.08% sodium azide as a preservative.

#### Precautions and Disclaimer

Due to the sodium azide content, a material safety data sheet (MSDS) for this product has been sent to the attention of the safety officer of your institution. Consult the MSDS for information regarding hazards and safe handling practices.

#### Storage/Stability

Store at  $-20^{\circ}\text{C}$ . Upon initial thawing freeze the solution in working aliquots for extended storage. Avoid repeated freezing and thawing to prevent denaturing the antibody. Do not store in a frost-free freezer. The antibody is stable for at least 12 months when stored appropriately. Working dilutions should be discarded if not used within 12 hours.

#### Product Profile

A recommended working dilution of 1:20 to 1:40 is determined the immunohistochemistry on formalin-fixed, paraffin-embedded human prostate carcinoma tissue sections.

The recommended working concentration for immunoblotting is 1 to 5 µg/ml and for immunoprecipitation is 2 µg/mg of protein lysate. Note: In order to obtain best results using different techniques and preparations we recommend determining optimal working concentration by titration.

#### References

1. Beerli, R. R., et al., *Neu* Differentiation Factor activation of Erb-3 and Erb-4 is cell-specific and displays a differential requirement for ErbB-2. *Mol. Cell. Biol.*, **15**, 6496-6505 (1995).
2. Burden, S. and Yarden, I., Neuregulins and their receptors: a versatile signaling module in organogenesis and oncogenesis. *Neuron*, **18**, 847-855, (1997).
3. Carraway, K. L., et al., Neuregulin-2, a new ligand of ErbB3/ErbB4-receptor tyrosine kinases. *Nature*, **387**, 512-516 (1997).
4. Huang, Y. Z., et al., Regulation of neuregulin signaling by PSD-95 interacting with ErbB4 at CNS synapses. *Neuron*, **26**, 443-455 (2000).
5. Wolpowitz, D., et al., Cysteine-rich domain isoforms of the neuregulin-1 gene are required for maintenance of peripheral synapses. *Neuron*, **25**, 79-91 (2000).
6. Cannella, B., et al., The neuregulin, glial growth factor 2, diminishes autoimmune demyelination and enhances remyelination in a chronic relapsing model for multiple sclerosis. *Proc. Nat. Acad. Sci. USA*, **95**, 10100-10105 (1998).

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