

Trastuzumab

Cat. No.:	HY-P9907
CAS No.:	180288-69-1
Molecular Formula:	C ₆₄₇₀ H ₁₀₀₁₂ N ₁₇₂₆ O ₂₀₁₃ S ₄₂
Molecular Weight:	145531.5
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description	Trastuzumab is a humanized monoclonal antibody for patients with invasive breast cancers that overexpress HER2. Trastuzumab has the potential for HER2 Positive Metastatic Breast Cancer and HER2 Positive Gastric Cancer research.
IC₅₀ & Target	HER2
In Vitro	<p>Treatment of HER2-overexpressing breast cancer cell lines with Trastuzumab results in induction of p27KIP1 and the Rb-related protein, p130, which in turn significantly reduces the number of cells undergoing S-phase. A number of other phenotypic changes are observed in vitro as a consequence of Trastuzumab binding to HER2-overexpressing cells. Interaction of Trastuzumab with the human immune system via its human immunoglobulin G1 Fc domain may potentiate its antitumor activities. In vitro studies demonstrate that Trastuzumab is very effective in mediating antibody-dependent cell-mediated cytotoxicity against HER2-overexpressing tumor targets^[1]. Trastuzumab consists of two antigen-specific sites that bind to the juxtamembrane portion of the extracellular domain of the HER2 receptor and that prevent the activation of its intracellular tyrosine kinase. Trastuzumab recruits immune effector cells that are responsible for antibody-dependent cytotoxicity^[2]. The presence of Trastuzumab IgG significantly increases killing of all breast cancer cell lines. The ADCC activity of PBMCs evoked by Trastuzumab is equally strong against Trastuzumab-sensitive (SKBR-3) or Trastuzumab-resistant (JIMT-1) breast cancer cells, with dose-dependent cell death reaching 50–60% killing at an effector/target ratio of 60:1^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>Trastuzumab treatment of mouse xenograft models results in marked suppression of tumor growth. When given in combination with standard cytotoxic chemotherapeutic agents, Trastuzumab treatment generally results in statistically superior antitumor efficacy compared with either agent given alone^[1]. Trastuzumab causes a significant growth inhibition of the outgrowth of macroscopic JIMT-1 xenograft tumors in both nude and SCID mice^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Cell Assay^[3]	The effects of Trastuzumab and Trastuzumab-F(ab') ₂ on the growth of JIMT-1, SKBR-3, and BT-474 cells are evaluated using the AlamarBlue method. Exponentially growing cells are harvested and plated in single wells of a 96-well flat-bottomed tissue culture plate at defined densities, ranging from 4,500-8,000 cells per well depending on the cell line. After overnight culture, the regular medium is exchanged to medium containing 0, 1, 10, or 100 µg/mL Trastuzumab or Trastuzumab-F(ab')
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2. Cell viability is tested after 72 h of treatment. Fluorescence is detected at an excitation of 544 nm, and emission is detected at 590 nm^[3].

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Animal Administration ^[3]

Trastuzumab and Trastuzumab-F(ab')₂ are given at a dose of 5 and 25 µg/g, respectively, by weekly i.p. injection. The five times greater amount of administered F(ab')₂ is chosen based on the different half-lives of IgG and F(ab')₂. Control mice are treated with weekly i.p. injection of 100 µL physiologic saline (saline). Animals are euthanized by CO₂ inhalation^[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2020 Sep 14;5(1):200.
- Nat Commun. 2020 Feb 26;11(1):1049.
- Cancer Lett. 2020 Apr 10;475:53-64.
- Elife. 2019 Jun 7;8:e46983.
- J Exp Clin Cancer Res. 2019 May 22;38(1):214.

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REFERENCES

[1]. Sliwkowski MX, et al. Nonclinical studies addressing the mechanism of action of trastuzumab. Semin Oncol. 1999 Aug;26(4 Suppl 12):60-70.

[2]. Hudis CA, et al. Trastuzumab--mechanism of action and use in clinical practice. N Engl J Med. 2007 Jul 5;357(1):39-51.

[3]. Barok M, et al. Trastuzumab causes antibody-dependent cellular cytotoxicity-mediated growth inhibition of submacroscopic JIMT-1 breast cancer xenografts despite intrinsic drug resistance. Mol Cancer Ther. 2007 Jul;6(7):2065-72.

Caution: Product has not been fully validated for medical applications. For research use only.

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