Trastuzumab

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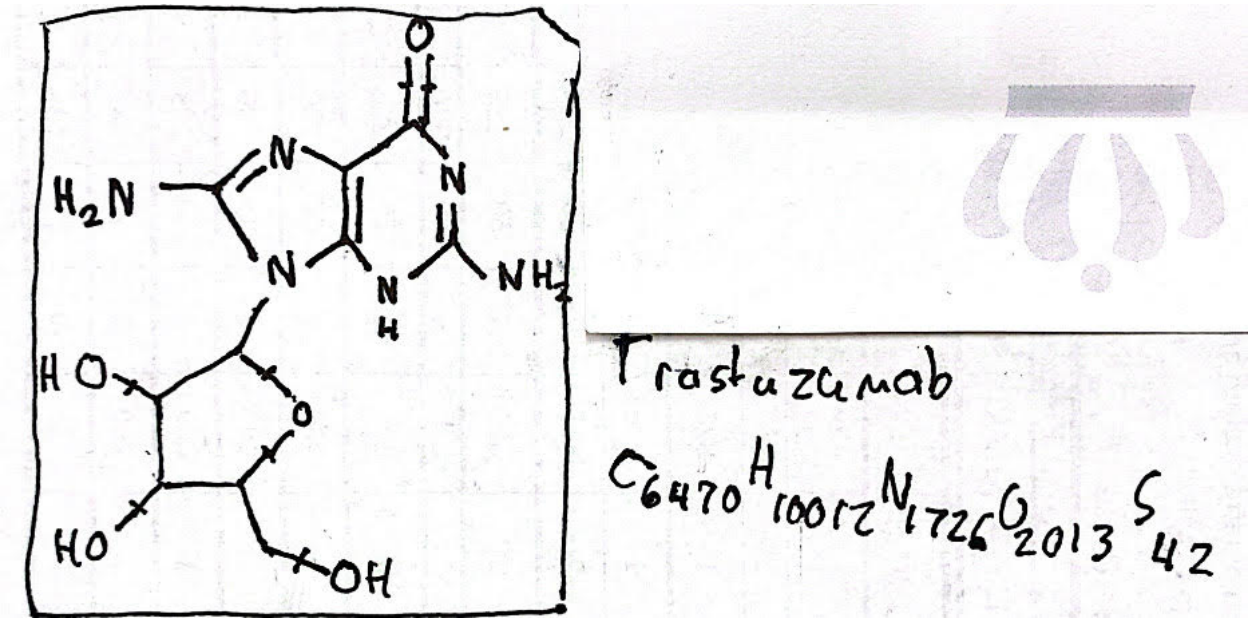
Monoclonal antibodies are immune system proteins produced in a laboratory environment. They can be utilized as targeted cancer therapies or as immunotherapies marking cancer cells for the immune system to recognize and destroy(1). Trastuzumab, brand name Herceptin, is a monoclonal antibody utilized in the treatment of both breast and stomach cancer. Trastuzumab is an IgG1 antibody that has undergone the process of humanization, targeting the human epidermal growth factor receptor 2 (HER2) (2).

Human epidermal growth factor receptor 2 (HER2) is a transmembrane glycoprotein receptor in the epidermal growth factor family(EGRF). Changes in the signaling of HER2, particularly overexpression and amplification, are connected to the growth and proliferation of stomach and breast cancers. Activating mutations to HER2 are connected with the alliteration of tumorigenesis and metastasis(3). The suggested rate of breast cancer patients who have HER2 mutations is 1.6% (4). Another suggested rate for HER2 overexpression in cases of breast cancer is 20-30%(5) (6). primarily binds with itself or other EGFR family proteins, these pairings activate growth signals that drive the processes of cellular division, survival, and migration. Since the HER2 pathways discovery multiple therapies have been developed including Trastuzumab (Herceptin), Pertuzumab (Perjeta), Ado-trastuzumab emtansine (Kadcyla), Trastuzumab deruxtecan (T-DXd), Neratinib that block HER2 signaling(3).

Trastuzumab particularly binds the extracellular domain of the HER2 protein, inhibiting homodimerization, thus blocking HER2 signaling(3)(7). Antibody-dependent cell-mediated cytotoxicity (ADCC), an immune host surveillance mechanism targeting tumors, is thought to be an additional way that Trastuzumab works against HER2 positive cancers(8). First described by

Schechter et al. in 1984 the neu gene discovered in rat neuro/glioblastomas its product protein HER2 was first described by Coussens et al in 1985(9)(10). Trastuzumab, the first drug targeting HER2, was developed by Genentech and approved for sale in the US in 1998(11) (12). Trastuzumab is typically administered in the form of an intravenous infusion with an initial loading dose of 8 mg/kg and a maintenance dose of 2-6 mg/kg every 3 weeks(7). Trastuzumab is known to induce cardiomyopathy, leading to the increase in reactive oxygen species in Cardiomyocytes, as a side effect(13).

Trastuzumab Structure:



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