More Tools for Speedy Antibody-Drug Conjugate Discovery

αOIgG-CL-MMAF

Anti-Rabbit IgG (H+L)-MMAF Antibody with Cleavable Linker

Catalog Number **AO-112-AF**

DESCRIPTION

αOIgG-CL-MMAF is anti-rabbit IgG (H+L) specific antibody conjugated to monomethyl auristatin F (MMAF) with a cleavable linker. The antibody portion is a polyclonal antibody which is specific to rabbit IgGs. Monomethyl auristatin F (MMAF) is a cytotoxic small molecule which inhibits cell division by blocking the polymerization of tubulin. The cleavable linker connecting MMAF to the antibody is stable in extracellular fluid, but is cleaved by cathepsin in endosome once the conjugate has entered a cell via endocytosis.

APPLICATIONS

Antibody-drug conjugates (ADCs), which have become a new targeted therapy against cancer, consist of an antibody linked to a cytotoxic drug. The ADCs bind selectively to the target cancer cells via the monoclonal antibody portion. Internalization of the ADCs releases the drug to do its damage. Prior to testing the function of ADCs in cell-based assays, each monoclonal antibody is typically conjugated directly with a cytotoxic drug. This step is time consuming and expensive, requiring milligram quantities of purified antibody, separate conjugation of each antibody, and further isolation of the ADC from the unconjugated drug. Using secondary antibody-drug conjugates (2°ADC) in a cell-based cytotoxic assay is a quick and economical alternative to pre-screening monoclonal antibodies as ADC candidates against tumor cells. Instead of conjugating the monoclonal antibody with a cytotoxic drug, the naked monoclonal antibody is added directly to the cells in the presence of the 2°ADC. Internalization of the monoclonal antibody/2°ADC complex can achieve a similar effect of targeted drug release within the cells as the monoclonal antibody-drug conjugate. Furthermore, the 2°ADC can also be applied to screen protein ligands for receptor-mediated cell targeting.

αOIgG-CL-MMAF is a 2°ADC for pre-screening rabbit monoclonal IgGs to determine their cytotoxicity as MMAF bioconjugates. When applied in combination with tumor specific rabbit monoclonal antibodies, **αOIgG-CL-MMAF** can help determine the cytotoxic potential for these antibodies against target cell lines.

EXAMPLE DATA

It has been demonstrated that Herceptin-DM1 conjugates (T-DM1) displayed potent killing activity against Her2-overexpressing tumor cells but not normal Her2 expression or Her2 negative cells. Here cytotoxicity of a rabbit anti-human Her2 (αHER2) mAb was tested in four breast cancer tumor cell lines expressing different amount of Her2 marker. SKBR3 is a Her2 overexpressing cell line, MCF7 has normal Her2 expression, and MDA-MB468 is Her2 negative. The rabbit αHER2 mAb has no effect on the viability of the cells (Fig A), or does the unconjugated anti-rabbit IgG antibody (αOIgG). However, in the presence of 1:1 ratio of αHER2 mAb/**αOIgG-CL-MMAF**, the αHER2 mAb displays potent cytotoxicity against Her2-overexpressing SKBR3 and HCC1954 cells, while shows no significant killing of MCF7 or MDA-MB468 cells (Fig B). The 2°ADC **αOIgG-CL-MMAF** alone has minimal toxicity towards these cells (Fig C).

Fig A. Cytotoxic Profile of Rabbit αHER2 mAb Alone

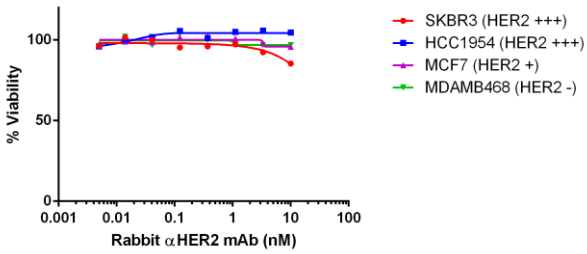


Fig B. Cytotoxic Profile of Rabbit αHER2 mAb in the Presence of 1:1 Ratio of αOIgG-CL-MMAF

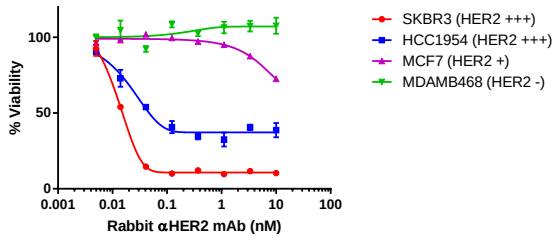
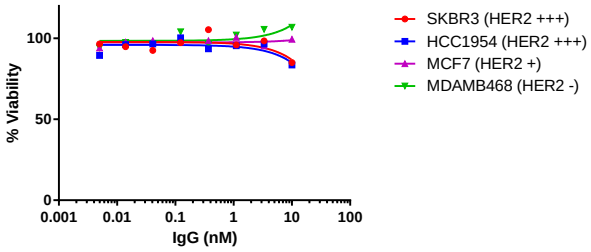


Fig C. Cytotoxic Profile of αOIgG-CL-MMAF Alone



STORAGE

Store in -20°C or -70°C manual defrosted freezer. Avoid repeated freeze-thaw cycle.