More Tools for Speedy Antibody-Drug Conjugate Discovery

αMFc-CL-PBD

Anti-Mouse IgG Fc-PBD Antibody with Cleavable Linker

Catalog Number **AM-106-PB**

DESCRIPTION

αMFc-CL-PBD is anti-mouse IgG Fc specific antibody conjugated to pyrrolobenzodiazepine (PBD) with a cleavable linker. The antibody portion is a polyclonal antibody which is specific to the Fc region of mouse IgGs. PBD, a derivative of actinomycetes, is a cytotoxic small molecule which causes cell death by selectively alkylating DNA and inhibiting replication. The cleavable linker connecting PBD 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.

αMFc-CL-PBD is a 2°ADC for pre-screening antibodies with a mouse IgG Fc moiety or recombinant mouse IgG Fc fusion proteins to determine their cytotoxicity as PBD bioconjugates. When applied in combination with tumor specific monoclonal antibodies or recombinant Fc fusion proteins, **αMFc-CL-PBD** can help determine the cytotoxic potential for these antibodies or proteins 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 [1]. Here cytotoxicity of a high affinity mouse anti-human Her2 (αHER2) mAb was tested in four breast cancer tumor cell lines expressing different amount of Her2 marker. SKBR3 and HCC1954 are Her2 overexpressing cell lines, MCF7 has normal Her2 expression, and MDA-MB468 is Her2 negative. *In vitro* the growth of SKBR3 is slightly stimulated by the αHER2 mAb, while HCC1954, MCF7 and MDA-MB468 are not affected by the unconjugated αHER2 mAb (data not shown). The unconjugated anti-mouse IgG Fc antibody (αMFc) does not change the apparent effect of the αHER2 mAb against these cell lines (Fig A). In contrast, in the presence of 1:1 ratio of **αMFc-CL-PBD**, the αHER2 mAb displays potent cytotoxicity against Her2-overexpressing SKBR3, but not HCC1954, MCF7 or MDAMB468 cells (Fig B).

Fig A. Cytotoxic Profile of Mouse αHER2 mAb in the Presence of Unconjugated αMFc Secondary IgG

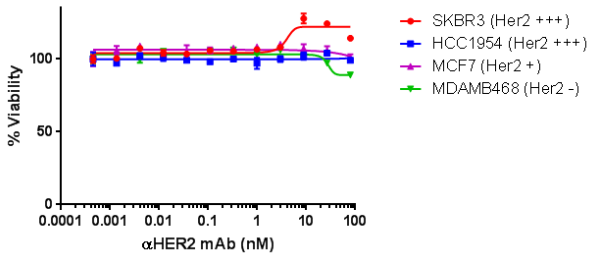
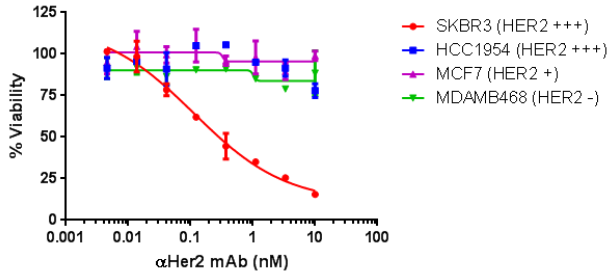


Fig B. Cytotoxic Profile of Mouse αHer2 in the Presence of 1:1 Ratio of αMFc-CL-PBD



STORAGE

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