More Tools for Speedy Antibody-Drug Conjugate Discovery

αHFab-NC-DM1

Anti-human IgG Fab-DM1 Antibody with Non-cleavable Linker

Catalog Number **AH-123-D1**

DESCRIPTION

αHFab-NC-DM1 is anti-human IgG Fab specific antibody conjugated to maytansinoid DM1 with a non-cleavable linker. The antibody portion is a polyclonal antibody (full length IgG) which is specific to the Fab region of human IgGs. DM1 is a cytotoxic small molecule which inhibits cell division by blocking the polymerization of tubulin. The non-cleavable linker connecting DM1 to the antibody is relatively stable in extracellular fluid, but can be cleaved upon entering cells.

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.

αHFab-NC-DM1 is a 2°ADC for pre-screening antibodies with a human Fab moiety to determine their cytoxocity as DM1 bioconjugates. **αHFab-NC-DM1** alone displays no obvious toxicity against multiple cell lines at 1 μg/ml (6.6 nM) or lower concentration. When applied in combination with tumor specific monoclonal antibodies, **αHFab-NC-DM1** can help determine the cytotoxic potential for these antibodies or proteins against target cell lines.

EXAMPLE DATA

It has been demonstrated that Herceptin antibody-drug conjugate (T-DM1) displayed potent killing activity against Her2-overexpressing tumor cells but not normal Her2 expression or Her2 negative cells [1]. SKBR3 is a Her2 overexpressing cell line, MDA-MB468 is Her2 negative. In the presence of 2:1 ratio of Herceptin Fab/**αHFab-NC-DM1**, potent killings are observed for the Her2 overexpressing SKBR3 cells, while the Her2 negative MDAMB468 cells are not affected (Fig A). The 2°ADC **αHFab-NC-DM1** alone has minimal toxicity towards these cells (Fig B).

Fig A. Cytotoxic Profile of Herceptin Fab in the Presence of 2:1 Ratio of αHFab-NC-DM1

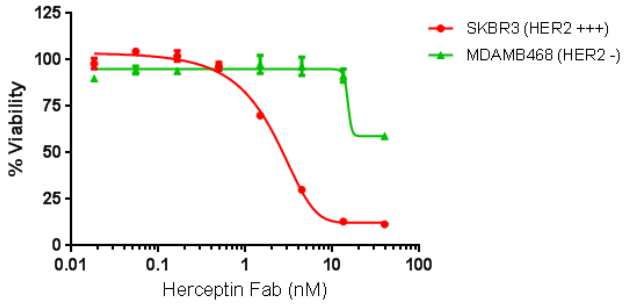
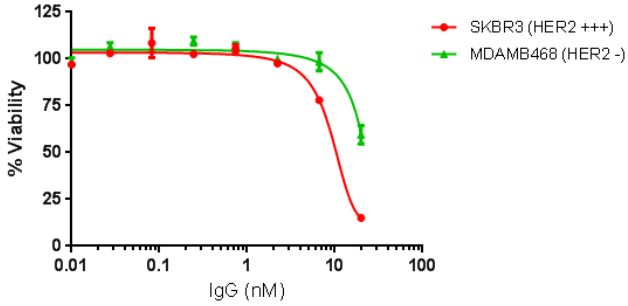


Fig B. Cytotoxic Profile of the αHFab-NC-DM1 Alone



Please Note: Optimal dilutions of **αHFab-NC-DM1** should be determined for each specific antibody or recombinant Fab fusion in each assay.

STORAGE

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

REFERENCE

1. Lewis Phillips GD, et al. Targeting Her2-positive breast cancer with trastuzumab-DM1, an antibody-cytotoxic drug conjugate. (2008), Cancer Res, **68(22)**, page 9280-90**.**