CD Creative Diagnostics®

# Tools for ADCs PK Analysis

## - Efficient Anti-ADCs Payload Antibodies

Antibody-drug conjugates (ADCs) are emerging as powerful cancer treatments that combine antibody-mediated tumor targeting with the potent cytotoxic activity of toxins, allowing sensitive discrimination between healthy and diseased tissue. The mAb recognizes antigens overexpressed on the surface of tumor cells, and the cytotoxic payload is responsible for the execution of tumor cell killing. The investigation of pharmacokinetics (PK) of ADCs is vitally significant in both preclinical and clinical studies. Notably, there may be differences in the PK profiles of ADCs between animal models and human studies. The selection of appropriate antibody reagents is expected to reduce the interference caused by such differences.

## ADCs PK Analysis

Due to the structural heterogeneity of ADCs and the dynamic variation of the drug-to-antibody ratio (DAR) *in vivo*, the biological analysis of ADCs is challenging. PK is the material basis for interpreting drug efficacy and safety, and its importance is unquestionable. Analytes commonly used to characterize the PK characteristics of ADC drugs include total antibodies, conjugated antibodies, and binding/free small molecule drugs. ELISA is an important method for ADC PK research, and anti-loading antibodies are one of the tools.

## Validation Data of Antibodies to ADC Payload

- **SN-38**

Irinotecan (CPT-11), a camptothecin derivative belonging to the topoisomerase I inhibitor class, is a prodrug of SN-38 that is readily converted to its active metabolite (SN-38) primarily in the liver. The approval and clinical success of Sacituzumab govitecan showed the potential of the unconventional payload, SN-38.
The Anti-SN38 mAb (CABT-L3115) developed by Creative Diagnostics has demonstrated excellent stability as shown in the table below:

| Temperature | Duration | Pass or Not |
|---|---|---|
| 37°C | 14 Days | Pass |
| 4°C | 1 year | Pass |
| -20°C | 2 years | Pass |

Table.1 Stability test of Anti-SN38 Mab.

**Coating:** SN38-Ag

**Sample**: Mouse Anti-SN38 monoclonal antibody, clone 20G22B0E7 (CABT-L3115).

**Detection**: Rabbit Anti-Mouse IgG-HRP

## • MMAE

Monomethyl auristatin E (MMAE) is a potent anti-cancer microtubule-targeting agent (MTA) used as a payload in three approved MMAE-containing ADCs and several ADCs in clinical development to treat different types of cancers.

The Anti-MMAE mAb (CABT-B8992) developed by Creative Diagnostics has good affinity, as shown below:

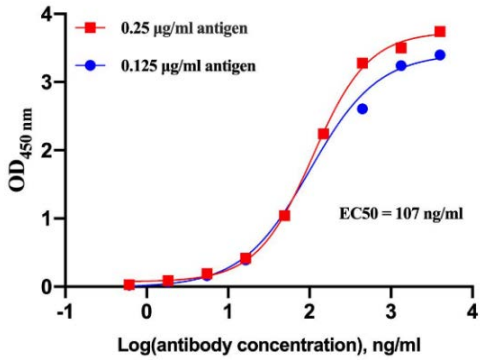


Fig.2 Anti-MMAE Mab Affinity Curves.

**Coating**: MMAE [BSA] (DAG603S)

**Sample**: Anti-MMAE monoclonal antibody, clone 3F3 (CABT-B8992)

**Detection**: Rabbit anti-Mouse IgG-HRP

**$EC_{50}$** =107 ng/ml

## • DM1

DM1 is a synthetic derivative of the tubulin-binding agent maytansine that was developed to overcome systemic toxicity associated with maytansine and to enhance tumor-specific delivery. Antibody-DM1 conjugates showed promising results in preclinical and clinical evaluations.

Creative Diagnostics has developed the Anti-DM1/4 pAb (CABT-L3104) with good antigen binding ability as shown below:

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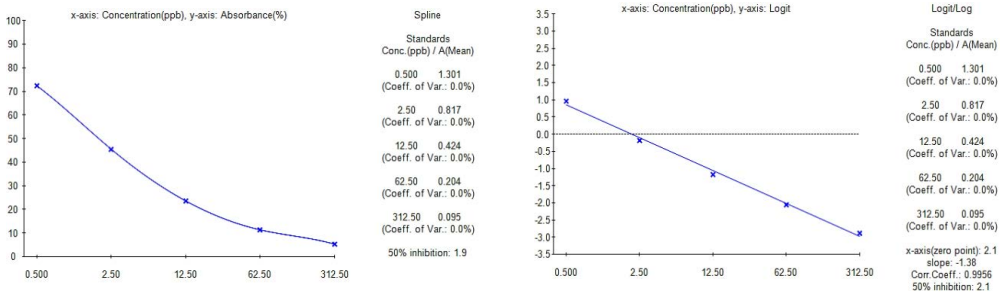


Fig.3 ELISA binding of Anti-DM1/4 Pab with DM1-SMCC.

**Coating**: BSA-DM1-SMCC (1 mg/mL, 1:10,000).

**Sample**: Rabbit Anti-DM1/4 polyclonal antibody (CABT-L3104) (1:80,000).

**Detection**: Goat Anti-Rabbit IgG HRP (1:2,000)

$IC_{50}$=1.9 ppb.

## Product List

The anti-payload antibody developed by Creative Diagnostics has been fully validated for good sensitivity and stability, and can be used for quantitative analysis of ADC.

| Cat. No | Product Name | Host | Payload Category |
|---|---|---|---|
| CABT-L3115 | Anti-SN38 Mab | Mouse | DNA Topoisomerase I Inhibitor |
| CABT-L3114 | Anti-SN38 Pab | Rabbit | DNA Topoisomerase I Inhibitor |
| CABT-B8992 | Anti-MMAE Mab | Mouse | Tubulin Inhibitor |
| CABT-L3104 | Anti-DM1/4 Pab | Rabbit | Tubulin Inhibitor |


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# CREATIVE DIAGNOSTICS

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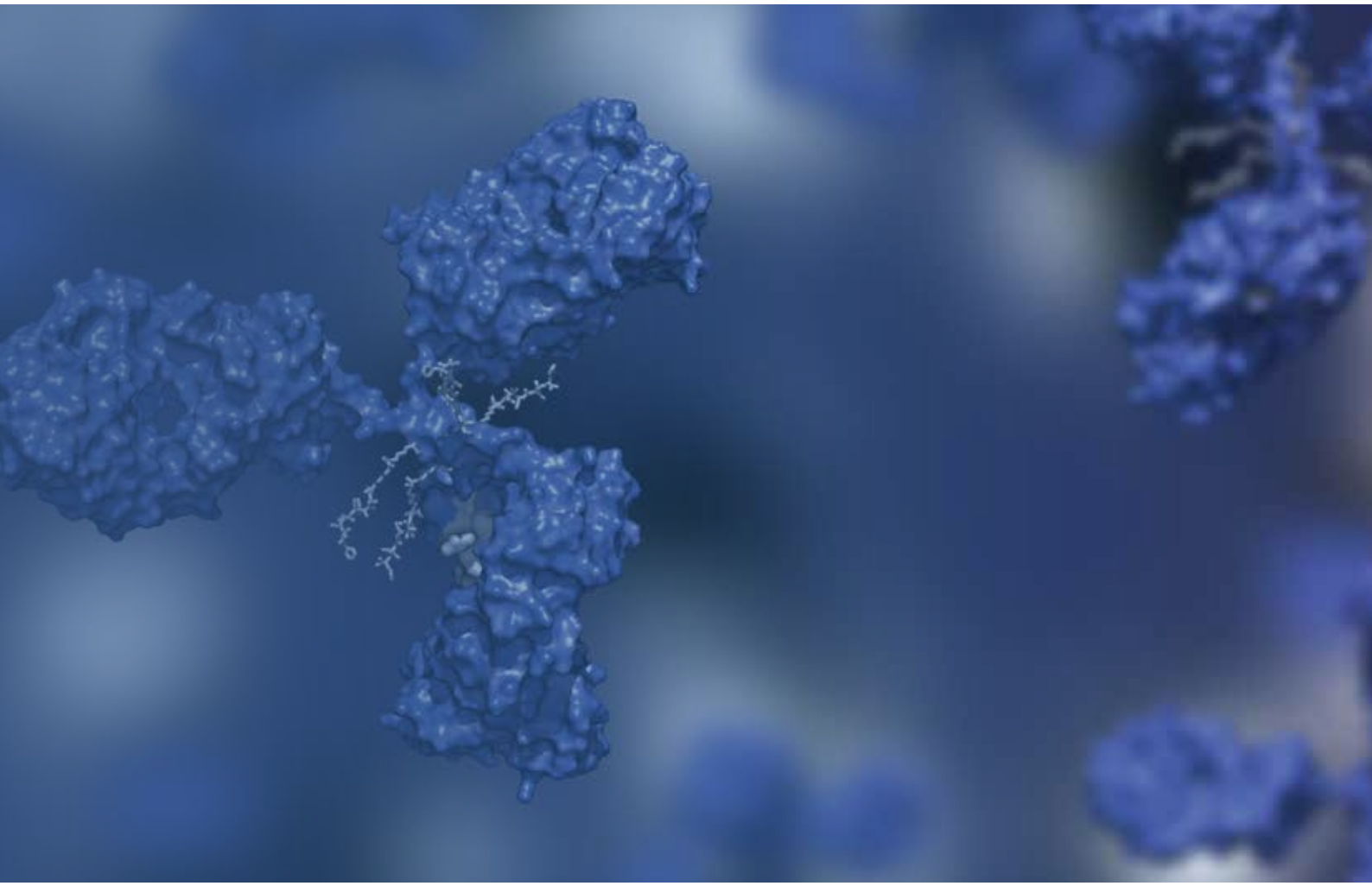


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