CONCEPT LIFE SCIENCES
a spectris company

ANTIBODY DRUG CONJUGATE SERVICES

Antibody drug conjugates (ADCs) are attracting a significant amount of attention as they have the potential to revolutionise cancer treatment. Chemical ligation of cytotoxic agents to monoclonal antibodies allows the selective delivery of cytotoxins to tumour cells thereby potentially mitigating some of the damaging side-effects of cancer chemotherapy. There are currently a number of FDA-approved ADCs and numerous others at varying stages of development. Concept Life Sciences has expertise in all aspects of ADC synthesis and characterisation to help expedite your ADC projects from discovery to the clinic.

ADC SYNTHESIS

Concept Life Sciences have successfully delivered complex linker and cytotoxic warhead projects for our clients underpinned by our synthetic organic chemistry expertise. As an example, we have developed an optimised process for the large-scale preparation of the crucial MC-Val-Cit-PAB-OH linker in enantiopure fashion (figure 1). Our specialist SOLO Containment® flexible film isolator allows us to safely handle a suite of typical OEB5 level cytotoxins employed in ADC research. ADCs with drug-antibody ratios (DAR) of 1 – 6 have successfully been prepared by utilising cutting-edge bioconjugation technology. In addition, our sister company Malvern Panalytical supply us with their world-leading analytical instrumentation including the OMNISEC and Xetasizer Ultra for assessment of ADC aggregation profiles.

ADC STRUCTURAL CHARACTERISATION

One of the critical parameters in ADC development is the calculation of DAR. Concept Life Sciences scientists have fully developed protocols allowing the calculation of DAR by mass spectrometry and via ADC digestion followed by subsequent UV-visible absorption (subunit analysis) (Figure 2). This second method allows glycoform profiling which is a critical quality attribute when manufacturing antibody containing APIs. Furthermore, our peptide mapping expertise allows us to analyse chemical and post-translational modifications of the antibody and pinpoint drug binding sites. We also have procedures to measure the *in vitro* metabolic stability of ADCs which can vary with linker, antibody, drug binding site and bioconjugation method.

Continued overleaf...

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Figure 1. Example of ADC synthesised by Concept Life Sciences.

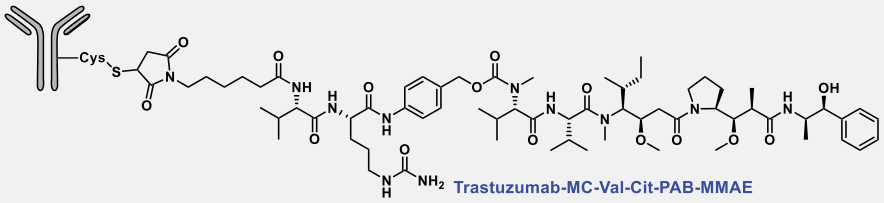
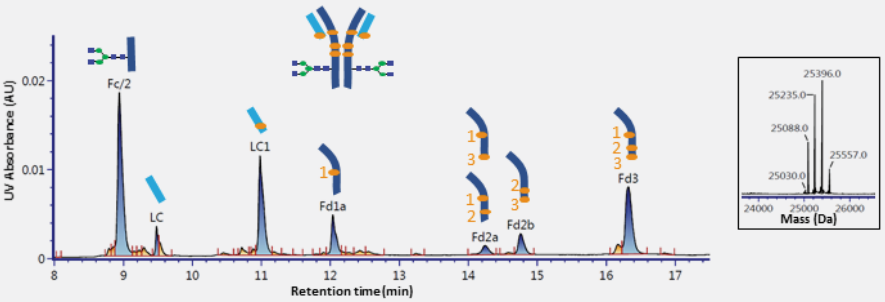


Figure 2 Left. Subunit analysis chromatogram of ADC following IdeS-mediated digestion and DTT-mediated reduction, orange dots refer to drug binding sites; Right. Deconvoluted mass chromatogram of Fc/2 fragment.



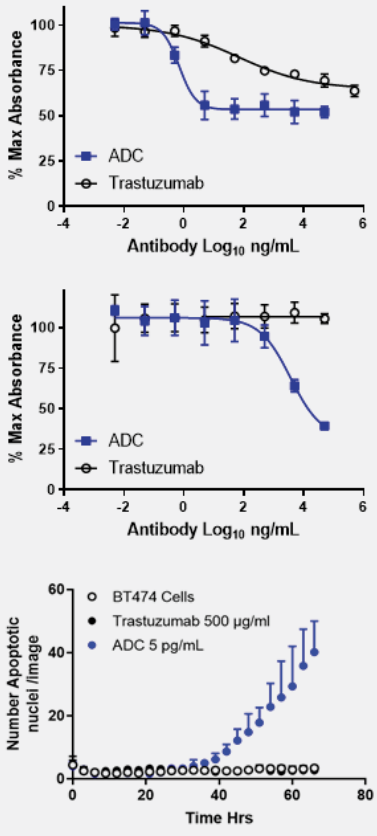
ADC BIOLOGICAL CHARACTERISATION

Concept Life Sciences has the capacity to monitor the effect of antibodies and ADCs against target antigen-expressing and non-target antigen-expressing cell lines to study ADC specificity on cell metabolism by an MTT assay and their time dependent effect on apoptosis using an IncuCyte® (Figure 3). We have successfully shown that treatment of Trastuzumab-based ADCs on highly expressing human epidermal growth factor receptor 2 (HER2) cells results in reduced cellular metabolic activity and apoptosis at lower concentrations than against non-expressing HER2 cells. Indeed, the IncuCyte® allows for time lapse imaging of cells in culture and automated image analysis without disturbing the culture well, to assess changes during an experimental period from simple cell growth and death, to biological processes of migration and phagocytosis to name a few, many of which have traditionally been done with end point readouts.

SUPPORTING YOUR ADC PROJECTS

Concept Life Sciences has the knowledge, skills and capacity to offer a range of solutions to help our clients expedite the progression of their ADC projects. Our alliance with our sister company Malvern Panalytical allows us to support ADC projects with analytical expertise and advanced analytical instrumentation. Our team of experienced scientists, with depth and breadth of knowledge and expertise, share your passion for delivering science.

Figure 3 Top. BT474 (HER2+++) MTT absorbance after exposure to Trastuzumab-MC-Val-Cit-PAB-MMAE; Middle. MDA-MB-231 (HER2---) MTT absorbance after exposure to Trastuzumab-MC-Val-Cit-PAB-MMAE; Bottom BT474 caspase 3/7 positive cells over time after exposure to Trastuzumab-MC-Val-Cit-PAB-MMAE. NB MTT absorbance is proportional to a cell population's metabolic activity; Caspase 3/7 activity is a measurement of apoptosis.



AS YOUR DEDICATED PARTNER AND COLLEAGUE, WE ARE HERE TO HELP YOU ACHIEVE YOUR GOALS

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