Synexa Large Molecule Bioanalysis Services

Synexa Life Sciences is a global provider of biomarker and bioanalytical services, specialising in the development, validation and delivery of a wide range of complex and custom-designed assays. Synexa's bioanalysis experience is extensive; for over 20 years we've supported customers across all clinical research phases, with studies focused on therapeutic large molecules including monoclonal antibodies, bispecifics and peptides.

Through in-depth knowledge and application of the various regulations, Synexa develops and validates all assays for clinical sample analysis to the highest standards established by the FDA, EMA and the latest whitepapers. With dedicated project management, scientific, quality assurance and sample logistics teams, the journey of a sample from syringe to lab bench to data release is seamless and controlled.

Our Expertise

Using the latest technical platforms, Synexa develops robust, specific and sensitive assays, specialing in:

- Pharmacokinetics
- Immunogenicity:
  - Binding antibody
  - Neutralising antibody: ligand-binding and cellular
- Pharmacodynamic markers

Analytical Platforms

- MSD electrochemiluminescence
- ELISA
- AlphaLISA
- Delfia
- Luminescence
- Fluorescence/FRET
- Gyrolab

Assay validation approach

All assays are validated according to strict parameters and the latest guidelines, providing customers the upmost trust in their data. Although subject to minor modification depending on the context of use, key parameters for assay validation include:

Pharmacokinetics
- Precision and accuracy
- Selectivity (matrix effect)
- Specificity (co-medication and target interference)
- Dilution linearity and hook effect
- Parallelism
- Stability (baseline, freeze/thaw, on-bench and long term)

Immunogenicity
- Precision and accuracy
- Selectivity (matrix effect)
- Sensitivity and low positive control level
- Assay cut-point
- Drug tolerance
- Stability (baseline, freeze/thaw, on-bench)
- Hook effect and titration
- Target interference

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Case Studies/Data

Functional cell-based neutralising antibody assays

Regulatory guidelines recommend that bioanalytical assays be representative of the potential environment in the patient. Ligand-binding approaches can be more cost effective but in the case of bispecific antibodies may lead to the detection of functionally irrelevant antibodies. Neutralising antibodies (nAb) specifically block the function of the drug.

An example applying this principle is shown in Figure 1. The therapeutic was a bispecific antibody therapy which targeted CD3, for T-cell activation, and HER2 (oncology target). Synexa developed pharmacokinetic and binding anti-drug antibody assays, and additionally, a functionally relevant assay to detect neutralising antibodies.

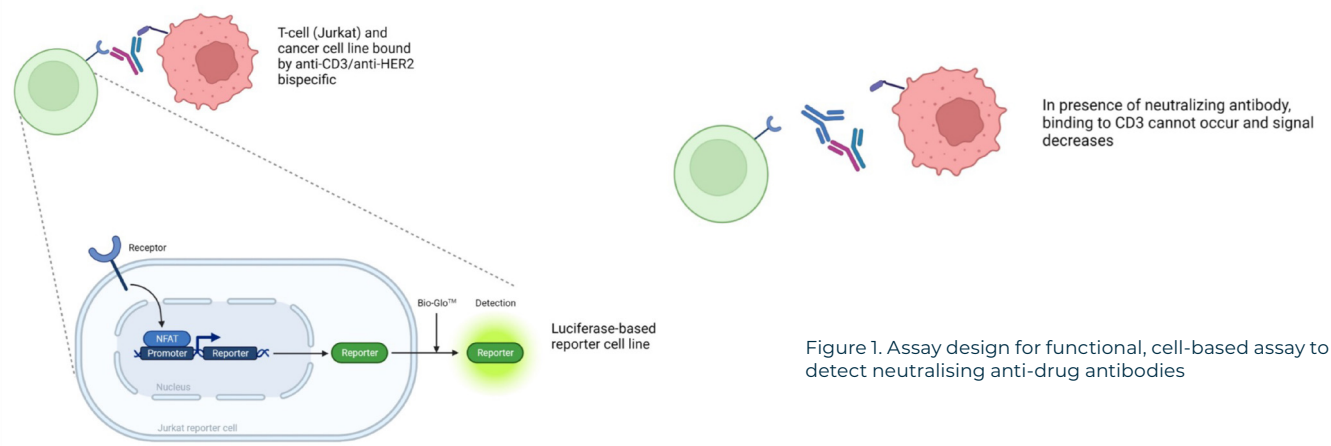

Figure 1. Assay design for functional, cell-based assay to detect neutralising anti-drug antibodies

Addressing sample pre-treatment requirements

Assay interference is a significant issue for bioanalytical assays. Assay interference may be caused by:

- Heterophile antibodies
- Rheumatoid factors
- Bind to Ab Fc regions
- Circulating drug
- Soluble receptors
- Multimeric targets

Synexa has addressed this through a number of tailored strategies including:

- Assay saturation assay (as shown in Figure 2 for a anti-GDF-15 drug)
- Biotin-drug extraction and acid dissociation (BEAD)
- Precipitation and acid (PandA) dissociation

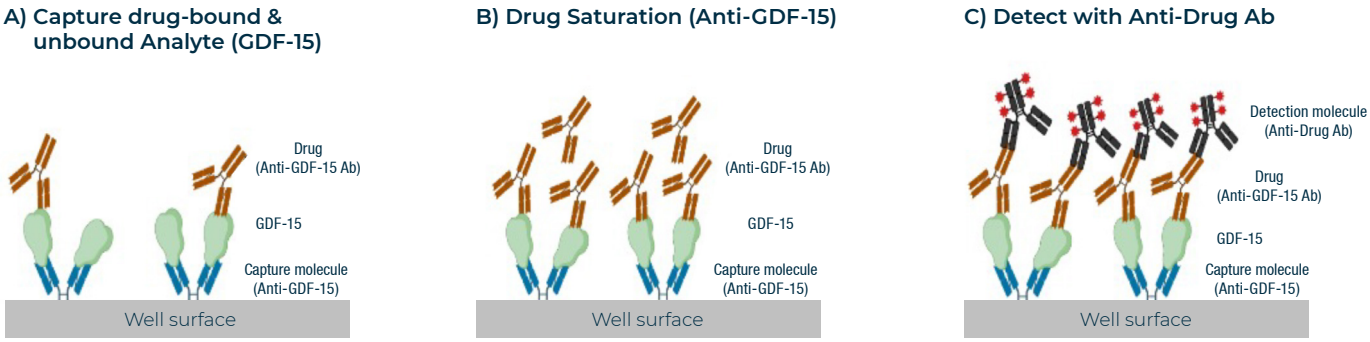

Figure 2. Pre-treatment assay saturation strategy example for anti-GDF-15 drug.

For more information **contactus@synexagroup.com** to see if we can find a solution to your bioanalytical challenges.

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