Successful Cell-Based ADA Collaboration in mRNA Gene Replacement Therapy - Reducing Time and Variability

Client: US-based Biotech company

Therapeutic Area: Respiratory

Therapeutic: mRNA-based Gene Replacement

Services:
Cell bank preparation
Method development and validation services
Analytical testing services
Reporting services
Data management services
Storage and archive services

Number of Patients: 300

Number of Samples: 246

TAT: 3 business days

PROJECT AT A GLANCE

A client presented Eurofins Bioanalytical Services with a project to determine the feasibility of using a cell-based method to detect ADAs. Due to the transmembrane nature of their therapeutic and an inability to isolate the protein and preserve its structure, cells engineered to express the full length target protein were utilized.

Initially, the client recommended a 5-day continuous culture in-cell ELISA. The client offered to collaborate by conducting development activities in parallel with Eurofins Scientists to accelerate delivery under their aggressive timeline.

The requirement was to detect the presence of ADAs that bind to the RNA-encoded end-product utilizing a cell-based strategy. Analysis needs would include samples at clinical study termination as well as those of any in-study subjects with suspected immunogenicity.

Sample Analysis at the

RIGHT TIME & RIGHT PLACE

to satisfy data delivery requirements

CASE STUDY

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CHALLENGES

- The initial continuous culture method was reduced from a 5-day to 3-day process but assay performance remained suboptimal with unacceptable variability in data.
- The assay labor was intensive; and had an EPA risk factor, as there was a need to eliminate the use of formaldehyde.
- Continuous cell culture method required ongoing resource support and would be subject to greater variability due to repetitive subculture and modest environmental changes
- Timeline constraints
- Despite evaluating multiple detection strategies and assay conditions, the background noise remained elevated due to non-specific serum binding which was variable from individual-to-individual. A change in assay design was required.

SOLUTIONS

- In collaboration with the client, the approach transitioned from an in-cell ELISA to a cellular lysate-based strategy
  - Eliminated the need for continuous cell culture and utilized single large-scale batch preparations of cellular lysates to reduce variability by significantly removing the background noise in the assay.
  - Reduced overall assay method from 3-day from 1-day process which provided higher throughput per analyst thereby increasing the efficiency of the analysis and reducing the turnaround time for sample analysis data
  - Delivered improved assay sensitivity (360 ng/ml) for a cell-based method and exceeded regulatory expectations of 1-5 micrograms/ml (original cell culture method sensitivity was >10 micrograms/ml)
- Significantly reduced variability between individuals in non-specific background signal
- Tested each sample in both cells induced to express the target protein and in non- induced cells
- Utilized the ratio of the resulting raw responses (induced /non-induced) as the assay outcome.
- Method successfully validated per validation plan and industry guidelines.[1]

1. Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products. April 2016. https://www.fda.gov/downloads/Drugs/Guidances/UCM192750.pdf

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Over 15 years of industry-leading global **Scientific Expertise** supporting the widest breadth of Biologics' clinical trials with PK/TK, ADA, Nab and Biomarker assays and sample analyses.

Versatile Performance and Project Management Excellence to adapt to a client's specific needs. Clinical or preclinical, regulated or non-regulated, assay development, qualification or validation; we custom design our support to match the client's program.

State-of-the art laboratory facilities in Oxford, UK and St. Louis, USA providing **Global Reach and Capacity** to address clients' needs while simultaneously offering regionally-based solutions.

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