CASE STUDY

Creating Neutralizing Antibody Assays for the Identification of Antibodies Against Adeno-Associated Virus for Gene Therapy

STUDY BACKGROUND

TYPE OF STUDY

Development and qualification of a cell-based neutralizing antibody assay for serotype 9 of adeno-associated virus (AAV9) for gene therapy

REGULATORY PARAMETERS

Non-regulated assay development and qualification and regulated assay validation and sample analysis in both USA and Europe

OBJECTIVE

Rapidly detect pre-existing antibodies with a high level of accuracy using different read-outs

The adeno-associated virus (AAV) is one of the most used viral vectors for gene therapy work today because it can be engineered for very specific functionality across a wide range of clinical applications. While to date AAV has been shown to have an excellent safety profile, there can be a high prevalence of neutralizing antibodies (NAbs) against some AAV serotypes; in these cases the NAbs may impair the efficacy of the AAV transduction in patients.

CHALLENGE

BioAgilytix's customer—a biopharmaceutical company focused on developing therapies for rare genetic diseases—required rapid development of a cell-based assay to measure the prevalence of pre-existing antibodies against the AAV9 serotype in patients for its gene therapy clinical trial.

This specific strain of AAV was known to transduce most cell lines poorly and therefore required a method that could increase transduction efficiency. There was also a concern for matrix interference, both potentiating and inhibitory.

BioAgilytix

SOLUTION

Leveraging its USA and European teams' deep expertise in cell-based and neutralizing antibody assays, particularly for gene therapy vectors, BioAgilytix was able to create the optimal assay conditions for the challenging AAV9 serotype and effectively determine the prevalence of pre-existing antibodies against the vector, detecting immunoglobulin of any isotype.

The team utilized a specialized host cell line and unique culture conditions to enhance virus transduction and thereby better distinguish between NAb positive and NAb negative samples, and its cell imaging plater reader to deliver luminescent reporter gene readouts.

BioAgilytix was able to facilitate rapid turnaround of these results using assay-ready cells, effectively meeting the customer's stringent timeline requirements.

OUTCOME

BioAgilytix was able to proficiently perform statistical analysis for cut point determination with high prevalence of pre-existing antibodies, and method qualification has been completed. Preclinical and clinical studies are currently running in BioAgilytix's laboratories in both Europe and USA using the customized cellular NAb assay, and the customer's project remains on time and on track for next steps.

While in this particular case the developed assay was used to measure NAbs against the AAV9 serotype, the same method can be applied to many gene therapy-related studies.

Learn more about our services for large molecule bioanalysis at **www.bioagilytix.com.**

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