DISCOVERY CASE STUDY

In vitro toxicology assay development

In vitro assay development for respiratory inflammation

The challenge

A client requested development of a series of *in vitro* assays to measure *in vitro* biomarkers associated with disease-relevant adverse outcome pathways (AOPs) for use as a screening tool.

The solution

Following extensive literature searches and discussions with the client, we identified the key AOPs involved in the disease mechanism.

Our subject matter experts and skilled technical teams established robust methods for measurement of a series of biomarkers and endpoints that aligned with the disease relevant AOPs. The techniques and technologies used included organotypic culture, qPCR, ELISA, cell-based ELISA, TEER, CBF, MCC, viability assays and air-liquid-interface exposures.

The assays developed were biologically relevant and demonstrated overlap with the disease-relevant AOPs. They also included low or noninvasive measurables that could be incorporated into clinical studies.

AOP-196: Airway irritation and chemical sensitization

The challenge

A client requested development of *in vitro* assays to measure biomarkers associated with AOP-196 for use in screening environmental compounds for their potential to induce airway irritation in humans.

The solution

Our subject matter experts and skilled technical teams established robust methods for the measurement of the molecular initiating events in AOP-196 - activation of TRPV1 and TRPA1 ion channels. Using a human lung-derived cell line, presence of TRPV1 and TRPA1 was confirmed by flow cytometry. Known activators (capsaicin and allyl isothiocyanate) and inhibitors (CPZ and HC-030031) of TRPV1 and TRPA1 were subsequently used to confirm channel function using Ca2+ response as an indicator of activation.

Following development of the *in vitro* airway irritation assay, its suitability for screening airway irritants was confirmed using a known irritant and a non-irritant. The assays developed were biologically relevant, demonstrating not only overlap with the disease relevant AOPs, but also included low or non-invasive measurables that could be incorporated into clinical studies.

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Conclusion

Labcorp offers custom *in vitro* assays and New Approach Methodologies (NAMs) with flexible design options, and we work with you to determine which mechanistic and biological endpoints are most relevant. Our scientists are at the cutting edge of *in vitro* alternative method development and are frequently requested to participate in regulatory working groups and testing/validation programs.

Do you need a discovery partner who can implement flexible study designs to meet your needs?

Visit biopharma.labcorp.com/services/discovery/lead-optimization-non-glp-toxicology/in-vitro-toxicology.html to learn more.