Singulex®

CUSTOMER INSIGHT

Accelerating Drug Development and Clinical Validation through Ultrasensitive Immunoassay Technology

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>
> *- Ole Vesterqvist, Senior Director of Clinical Laboratory Science at Covance, Inc.*

INTRODUCTION

Drug development is a lengthy and expensive process that includes numerous verification stages. One pivotal stage involves validating candidate biomarkers for their predictiveness toward clinical outcomes. Having the right technology, one that is able to provide robust and sensitive measurements of the target in clinically relevant specimens, may help to accelerate informative go/no-go decisions, potentially shaving years from the development timeline and millions from investment.

That is exactly what researchers at Wyeth Pharmaceuticals (acquired by Pfizer Inc. in 2009) understood when they turned to Singulex over other immunoassay technologies. Singulex's ultrasensitive Erenna® Immunoassay System allowed researchers at Wyeth to quantify for the first time a low-abundance efficacy marker in response to asthma therapeutics in development, providing insight that allowed continuation of a critical clinical program.

CHALLENGE

In 2007, Wyeth researchers focused their sights on a therapeutic target for asthma. Interleukin 13 (IL-13), a Th2 cytokine shown to be an important mediator of airway inflammation contributing to asthma lesions, emerged as a likely biomarker for their study.

However, researchers were unable to draw any conclusion of the effects of their therapy. The enzyme-linked immunosorbent assay (ELISA), that had been developed internally using a proprietary antibody, was not sensitive enough to detect the low concentrations of IL-13 in humans. In order to measure robustly the effects of targeted therapy, Wyeth researchers needed a more sensitive technology that would provide detection of IL-13.

SOLUTION

Wyeth turned to Singulex's Erenna Immunoassay System. The Erenna Immunoassay System couples microparticle-based immunoassays with proprietary single-molecule counting technology, offering unparalleled assay sensitivity capable of quantifying both baseline and elevated biomarker concentrations in healthy and disease subjects.

For some at Wyeth, Singulex's technology claims seemed almost unbelievable.

"I didn't believe them. As a scientist you never believe in anything until you see the final results," said Ole Vesterqvist, who then served as Senior Director of the Biomarker Lab and Biomarker Outsourcing in Clinical Translational Medicine at Wyeth Research.

Vesterqvist and his skeptical team of Wyeth researchers required Singulex to perform a test: a blind study on 40 to 50 samples using the Erenna System.

"When I saw the results of their analysis, I had never been so surprised," said Vesterqvist. "The results clearly showed that this assay was far more sensitive than any ELISA assay I had seen."

With evidence in hand, Wyeth chose to employ Singulex's technology to measure IL-13 in their asthma therapeutic.

RESULTS

The proprietary microparticle-based Erenna IL-13 Human Immunoassay Kit, developed for researchers

at Wyeth, had a lower limit of quantification of 0.07 pg/mL and a sensitivity improvement of 140-fold over the previous analytical method[1]. Results demonstrated that the Erenna technology has the capabilities to provide microparticle-based immunoassays that are far more sensitive than regular ELISA methods.

The Erenna assay also enabled baseline measurements in a clinical study population with 98-100 percent quantifiability (n=182 from 3 cohorts). All 99th percent cut-off values for healthy and asthmatic subjects at baseline were less than 1 pg/mL, previously immeasurable by other methods. A subsequent pharmacokinetics/pharmacodynamics (PK/PD) study was able to distinguish between placebo and biologics treated serum IL-13 levels by utilizing the Erenna assay[2].

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According to Vesterqvist, results made possible by the collaboration with Singulex and the ultrasensitivity of their Erenna immunoassays were critical to the clinical program. Researchers could establish the impact on serum IL-13 when a drug was administered. During a Phase I trial, it is crucial that researchers are able to follow a drug's effect on a target using methods with high sensitivity, like the Erenna Technology.

"Without the Singulex instrument, we would never have been able to characterize the effects of the drug on concentrations of IL-13 in humans. In clinical development and translational medicine, this is huge," said Vesterqvist.

Vesterqvist was also impressed by Singulex's willingness to openly discuss the research team's needs and work to make sure they were met.

"I trusted every decision that was made and appreciated their willingness to work with us one-on-one. I find Singulex to be a company that I personally trust very much."

THE FUTURE

Vesterqvist is now Senior Director of Clinical Laboratory Science at Covance Inc.; a biopharmaceutical development services Contract Research Organization (CRO). Through the positive collaboration with Singulex, Vesterqvist lobbied Covance to also adopt the Erenna platform for their Central Laboratory operation. Since implementing the system they have validated three ultrasensitivity assays and continue to see a high demand for more.

"The Erenna system has become a very important technology for our central lab when pharmaceutical companies come to us requiring high sensitivity measurements," said Vesterqvist.

Vesterqvist attributes this demand to the increased interest by pharma to translate personalized medicine from the bench to bedside. Gone are the days of single dosing for an overall patient population. The ability to characterize therapeutic effects and the duration of such effects on a target enables drug developers to better understand dosage, which in turn provides them the information needed to start planning for pivotal Phase II and III studies.

"Singulex's assay technology and other high-sensitivity technologies make it possible for translational medicine to be successful. Without it, we never would have been able to draw any conclusions about IL-13 in our study," said Vesterqvist. "If we can continue to conduct research using this approach, personalized medicine will change the way clinical studies are conducted."

Equipped with novel detection technology, scientific expertise and business professionalism, Singulex has proven to be the go-to source for ultrasensitive assay development and may very well be a game changer in the future of personalized medicine.

References

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2. Gauvreau GM et al. Effects of interleukin-13 blockade on allergen- induced airway responses in mild atopic asthma. Am J Respir Crit Care Med. 2011;183(8):1007-14.

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