Transforming Drug Development in Cell and Gene Therapies

How to advance clinical trials with spectral flow cytometry.

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Pharmaceutical Technology sat down with Dr. Kevin Lang, Senior Research Scientist and Flow Cytometry lead at Thermo Fisher Scientific's, PPD™ Laboratory services bioanalytical lab to explore the cutting-edge world of spectral flow cytometry. As a recognized leader in immunophenotyping for clinical trials, Lang discusses how spectral flow cytometry is transforming drug development, particularly in cell and gene therapies like CAR-T. He also discusses his award-winning research, including his 2024 WRIB Poster Award-winning work, and his insights from presenting at AAPS PharmSci360 regarding CAR-T therapy. Whether you're developing immunotherapies, tracking immune responses, or optimizing cell therapy clinical trials, this paper dives into the benefits of spectral flow cytometry for pharmaceutical and biotech companies in need of complex immune monitoring data.

PHARMACEUTICAL TECHNOLOGY: What does your team do and why is flow cytometry so critical in clinical trials?

KEVIN LANG: At our bioanalytical lab, I lead the flow cytometry team where we design, validate, and analyze high parameter flow cytometry assays to support clinical trials. Our work spans from early phase to late phase III studies that ensure our pharmaceutical and biotech customers get the highest quality immunophenotyping data.

Flow cytometry is a powerful tool for clinical trials that allows us to track immune responses, measure drug efficiency, perform high dimensional phenotyping of immune cells, and monitor novel therapies, especially in the rapidly growing field of cell and gene therapy. Traditional cytometry has its limitations, but full-spectrum flow cytometry has completely transformed the analysis of complex immune populations.

PT: Can you explain what makes spectral flow cytometry superior to traditional flow cytometry?

LANG: Traditional flow cytometry relies on fixed detectors and compensation matrices. This limits the number of parameters we can measure at once. Spectral flow cytometry, on the other hand, captures the entire spectrum of fluorochromes. This in turn, allows for better resolution and more parameters that can be measured per sample. At times, you may exceed 30 markers, and there has been a recently released study with 50 markers in a single assay.[1]

Having deeper immune profiling and more reliable biomarker discoveries for pharmaceutical companies would be life changing. It would provide a better immune profile, more reliable discovery, and better data, all of which are crucial for regulatory submissions and clinical decision making. My team specializes in optimizing these high-dimensional assays to provide the most comprehensive immune monitoring available.

PT: Congratulations on winning the 2024 WRIB poster award. Can you tell us more about your background and what your research focused on?

LANG: Thank you very much. Winning the WRIB poster award was a huge honor. I was very grateful just to be involved and around so much research. Our research focused on developing and qualifying high-dimensional spectral flow cytometry assays for clinical trials. Thus, we created a 17-color and an 18-color panel specifically for T-cell analysis, targeting key activation and functional markers. We went on to show how we not only developed but validated this method for several different reportables.

One of the biggest challenges in spectral flow cytometry is panel design, so ensuring minimal spectral overlap while maximizing resolution. We developed innovative gating strategies and unmixing controls using our peripheral blood mononuclear cells (PBMC) and compensation beads to improve accuracy and reproducibility in our clinical samples. Our innovative strategies ensure accuracy and reproducibility. This work is critical for advancing precision medicine, particularly for immuno-oncology and cell therapy applications.

PT: You also presented at the AAPS PharmSci360 on CAR-T therapies. Can you talk about how flow cytometry supports these groundbreaking treatments?

LANG: CAR-T therapy has revolutionized cancer treatment and as a group, we are very honored to have had the ability to work with sponsors on some of these studies. CAR-Ts are amazing, but they require rigorous immune monitoring so we can ensure the safety and efficacy of the treatment.

In my AAPS PharmSci talk, I discussed how we go about developing and validating flow cytometry assays specifically for CAR-T studies and some of the intricacies of CAR-Ts that need to be addressed when developing these assays. Generally, we analyze CAR-T cell expansion, persistence, and exhaustion markers to understand how these engineered T-cells behave in patients. Spectral flow cytometry helps optimize CAR-T therapies for better outcomes and allows us to track these parameters with unparalleled precision. Henceforth, we can optimize these CAR-T therapies for better patient outcomes.

CAR-T therapies themselves have had some of the most amazing patient outcomes we have ever seen. In a few of these outcomes, they have actually cured cancer, and we do not use that term lightly.

The future is very bright for flow cytometry. It's all about higher dimensionality and automation.

PT: Why should pharmaceutical companies choose the PPD Laboratory services bioanalytical lab for their clinical flow cytometry needs?

LANG: The PPD bioanalytical lab offers unmatched expertise in flow cytometry. Our team has decades of experience while also leveraging the latest technology—specifically spectral flow—to provide high-quality data. So, what sets us apart? Well, we have regulatory expertise; we design and validate assays that will meet global regulatory standards. We use Cytek® Aurora Full-Spectrum cytometer to enable deeper immune profiling, and this is a little bit further than most conventional methods. Lastly, we have custom solutions no matter if they're for immune monitoring of cell and gene therapies or biomarker discovery. Our assays are tailored to meet each clinical trial's needs. By partnering with us, drug development and regulatory approval can be accelerated.

PT: In your expertise, what do you see as the future of flow cytometry in clinical trials?

LANG: The future is very bright for flow cytometry. It's all about higher dimensionality and automation. Right now, we're moving towards evermore complex immune profiling, which will probably necessitate the integration of artificial intelligence to streamline data analysis for clinical trials. Spectral flow cytometry will play a crucial role by allowing us to develop therapies that are tailored to the individual patient based on signatures within their immune system. At the PPD bioanalytical lab, we are going to ensure our clients stay ahead in drug development by being at the forefront of innovation.

References

1. Konecny, A. J., P. L. Mage, A. J. Tyznik, M. Prlic, F. Mair. 2024. OMIP-102: 50-color phenotyping of the human immune system with in-depth assessment of T cells and dendritic cells. Cytometry A 105: 430–436.