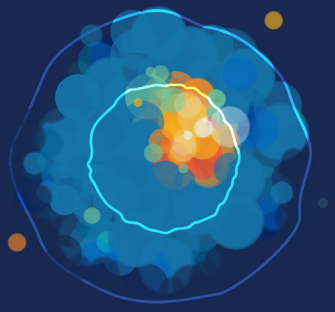

Article:

CAPABILITIES OF MEDPACE LABORATORIES TO SUPPORT CELL AND GENE THERAPY STUDIES

Pipelines for cell and gene therapies have expanded significantly in recent years, with many therapies already approved for clinical use worldwide. There are currently more than 4,200 cell and gene therapies in development, ranging from pre-clinical through pre-registration, including over 2,100 gene therapies (including genetically modified cell therapies such as CAR-T cell therapies) accounting for 50% of gene and cell therapies and over 880 non-genetically modified cell therapies accounting for 21% of cell and gene therapies *(Source: Citeline, April 2026)*.

Cell and gene therapies can be classified into several categories:

I. **Adoptive Cell Therapies:** A form of cellular immunotherapy that harnesses the body's immune system to fight diseases by isolating, modifying, expanding, and reinfusing immune cells into the patient to enhance their cancer-fighting capabilities
II. **Regenerative Cell Therapies:** A medical approach that uses stem cells and other cell-based therapies to repair, replace, or regenerate damaged tissues and organs with the goal of restoring normal function
III. **Expression Modulation Therapies:** Therapies that modulate expression (e.g., oligonucleotides, typically small interfering RNA introduced to modulate expression of a protein product to treat disease conditions)
IV. **Gene Replacement:** Viral (e.g., AAV or LV) or nonviral (e.g., LNPs or naked DNA/RNA) vectors introduce and transfect host cells, enabling the cells to produce a desired protein product that's either missing or nonfunctioning in a disease state
V. **Gene Editing:** Viral or nonviral vectors introduce an endonuclease to edit a faulty genomic DNA sequence to permanently correct a gene and downstream protein to address a disease state

Medpace's four wholly owned central laboratories offer full-service support to six continents for Phase I-IV studies. Medpace Reference Laboratories (MRL) has extensive experience supporting clinical trials ranging from small, early Phase studies to large, global, and complex programs. Our global laboratory facilities, standardized testing platforms, comprehensive test menu, and stellar project management teams allow Medpace to set up fully customized projects for our clients.

Combined with Medpace's Clinical Research Organization (CRO) expertise, Medpace provides a fully integrated solution for cell and gene therapy clinical development needs. **Table 1** summarizes the assays currently offered at Medpace laboratories.

ASSAY/TEST	RATIONALE
CAR-T PERSISTENCE/KINETICS - Cellular kinetics, transgene detection, expansion dynamics	
CAR+ T cell frequency (%CAR of CD3+)	Quantify circulating T cell over time
qPCR - transgene copy number	Measurement of CAR T persistence
CAR mRNA expression	Measure expression of the CAR mRNA transcripts
dPCR - transgene quantitation	Measurement of CAR T persistence
CAR T expansion kinetics (Cmax/Tmax/AUC)	Predict treatment efficacy and risk of toxicity
CYTOKINE KINETICS/CRS MONITORING/ICANS - Cytokine and inflammatory cascade profiling	
V-Plex Pro-Inflammatory panel	Proinflammatory Cytokine profiling
S-Plex Pro-Inflammatory panel	Ultra-sensitive Proinflammatory Cytokine profiling
Chemokine panel	Chemokine profiling
Cytokine panel	Cytokine profiling
Quanterix panel	Neurotoxicity Monitoring
IMMUNOGENICITY - Anti-CAR T cell responses	
T-cell ICS to CAR peptides	Cellular immunogenicity to CAR construct
CAR ADA	Cellular immunogenicity to CAR construct
SAFETY/ORGAN TOXICTY	
Complete Blood Count (CBC) with differential	Safety Monitoring
Chemistry panels	Safety Monitoring
NephroCheck	Safety Monitoring
PHARMACODYNAMICS/ IMMUNE RECONSTITUTION/B-CELL APLASIA	
B cell recovery panel (CD19/CD20/...)	Monitor B cell reconstitution
TBNK assay	Monitor T, B and NK reconstitution
26-color phenotyping panel	Monitor broad immune phenotype
BCR and TCR repertoire analysis	Track CAR-T cell expansion
T cell memory subsets (Tcm/Tem, etc.)	Characterize CAR T and T cell compartment
T cell exhaustion/activation (PD-1/TIM-3/LAG-3)	Characterize CAR T fitness
MRD analysis	Monitor disease progression
CAR T fitness expression analysis	Evaluate CAR T fitness
ctDNA	Monitor disease progression after CAR-T treatment
BIODISTRIBUTION/INSERTIONAL SAFETY	
Recombinant viral vector biodistribution	Ensure vector is localized to the desired immune cells
Recombinant viral vector shedding	Potential environmental release and transmission risks
RCR using GalV gene	Infectious Replication-Competent Retrovirus
RCL using VSV-G	Infectious Replication-Competent Lentivirus
Vector copy number	Quantification of vector copy number
On target/off target integration analysis	Ensure no off-target effect
Viral integration site (VIS)	Determine where the virus is integrated in the genome
CRISPR gRNA binding site	Ensure the guide RNA binding site is not mutated

***Table 1**: A summary of tests available at Medpace laboratories to support cell and gene therapy studies*

CENTRAL LABORATORY CAPABILITIES FOR CELL AND GENE THERAPY

Molecular testing plays a critical role in advancing the development of safer and more effective cell and gene therapies, helping accelerate the time-to-patient. Medpace's central laboratories offer a comprehensive off-the-shelf biomarker test menu designed to accelerate clinical trial timelines with validated, ready-to-use assays in our US, Belgium, and Singapore laboratories to support cell and gene therapy studies.

Medpace's central laboratories also closely collaborate with Sponsors to develop new biomarker assays when they are not readily available.

- **Gene therapy:** The Medpace molecular laboratory offers an array of tests to support studies that utilize delivery systems including adeno-associated viruses (AAVs), lentiviruses (LVs), or nonviral delivery mechanisms, such as lipid nanoparticles (LNPs) or naked DNA/RNA. These tests include vector and transgene detection/quantitation by qPCR or digital PCR, viral shedding in multiple sample types by qPCR or digital PCR, and viral integration sites.
- **Lipid nanoparticles-messenger RNA drug products:** Medpace molecular laboratories can use RT-qPCR for the quantification of the LNP-mRNA drug products.
- **Gene editing:** Medpace's central laboratories have Sanger and next-generation sequencing (NGS) capabilities to support on-target/off-target integration analysis, CRISPR guide for RNA binding site sequencing, and long-term monitoring of insertional mutagenesis.
- **CAR-T cell therapy:** Medpace molecular laboratories support CAR-T biodistribution (Vector Copy Number) in blood and PBMCs using both qPCR and digital PCR. RCL (Recombination-Competent Lentivirus) through quantification of the envelope gene vesicular stomatitis virus G glycoprotein (VSV-G), and RCR (Recombination-competent Retrovirus) through quantification of GAL-V gene (Gibbon Ape Leukemia Virus) by qPCR.

MEDPACE FLOW CYTOMETRY CAPABILITIES

Medpace's central laboratories also offer an experienced flow cytometry team overseen by PhD-level scientists with more than 50 years of combined team experience designing, analyzing, and interpreting multicolor flow cytometry assays. In addition to the in-house validated, ready-to-use panels (e.g., TBNK, T-Cell, B Cell, NK Cell, Dendritic Cell, Monocyte, Stem/Progenitor Panel, and PNH), our flow team also offers study-specific fully customized panels using conventional or high-parameter spectral flow cytometry. Whether a study requires the development of a custom panel or the transfer of a method, the Medpace flow team has the experience to quickly validate and implement flow cytometry testing. Medpace has harmonized global flow cytometry capabilities at the US, Belgium, and Singapore laboratories.

Our flow cytometry platform provides comprehensive biomarker and immunophenotyping solutions to support cell and gene therapy studies from discovery through late-stage clinical development. We develop and validate fit-for-purpose assays that enable robust enumeration and characterization of therapeutic cell products, assessment of pharmacodynamic responses, and longitudinal immune monitoring in clinical trials.

Our expertise includes high-parameter multiparametric flow cytometry for the enumeration, evaluation of cell identity, purity, viability, memory differentiation, activation status, exhaustion phenotype, proliferation, and functional activity across a wide range of therapeutic modalities, including CAR-T, TCR-T, CAR-NK, Treg, stem cell, and gene-edited cell therapies.

Representative Flow Cytometry Panels:

- Custom CAR-T enumeration and immunophenotyping panel to assess CAR+ T cells (CD3, CAR, CD4, CD8) with the other major cell subsets (CD19, CD14, CD56) + WBC marker CD45 and Live/Dead dye and to identify the activation status of the CAR+ T cells and include late activation markers (HLADR, ICOS, CD137).
- Custom CAR-T enumeration and immunophenotyping panel to assess the frequency of CAR expressing T cells and T-cell phenotypic markers (CD4, CD8, CD3, CCR7, CD45RO, CD45RA, and CD95) on starting material (apheresis samples), drug product samples (with CAR expression), and on samples from subjects infused with the drug product (exploratory).

Our laboratory supports analysis of whole blood, PBMCs, fresh and cryopreserved samples, using standardized and harmonized workflows. Assays are developed and validated according to Good Laboratory Practice/Good Clinical Practice (GLP/GCP) principles with rigorous instrument qualification, reagent control, and quality assurance processes to ensure reproducibility and regulatory readiness.

Combined with experienced scientific consultation, customized panel design, and advanced data analysis, our flow cytometry capabilities provide high-quality biomarker data to support product characterization, mechanism-of-action studies, dose optimization, pharmacodynamic assessments, and clinical decision-making throughout the cell and gene therapy development lifecycle.

MEDPACE BIOANALYTICAL LABORATORY CAPABILITIES

Cell and gene therapy studies also benefit from the services provided by the Medpace Bioanalytical Laboratory (MBL).

The MBL team has proven experience in a broad range of small and large molecule bioanalytical (e.g., toxicokinetic and pharmacokinetic) and biomarker support. The team has extensive expertise in developing sensitive methods for LC-MS/MS – qualifying methods for multiple-analytes, metabolites, prodrugs, and light- and temperature-sensitive compounds, as well as bioanalytical analysis of emerging modalities, including oligonucleotides (e.g., siRNA and ASO), Antibody-Drug Conjugates (ADC), and encapsulated drugs by Lipid Nanoparticles (LNPs). The MBL team can also support the analysis of large molecule biomarkers not covered in the Medpace central laboratory test directory using ELISA/Electrochemiluminescence (ECL) methods.

For cell and gene therapies, MBL can support anti-vector and anti-transgene antibodies (ADA) testing as well as neutralizing anti-transgene antibodies (NAbs) following GLP/CGP principles. MBL has capabilities for developing and validating immunogenicity methods. The team has extensive experience examining ADA responses targeting the viral gene therapy delivery vector as well as the protein product expressed as a result of successful viral integration. Meso Scale Discovery ECL-based and traditional ELISA methods are used in this type of analysis. A three-tiered analysis strategy is employed where samples are first screened for potential antibody responses, potential positive samples are then confirmed for a specific ADA response and, lastly, titrated to quantitate a relative strength of antibody response.

MBL has a wide range of experience in the field of NAb assays using validated plate and cell-based methods to support GLP/GCP studies. Plate-based methods are usually reserved for determining when neutralizing antibody targets are circulating in the bloodstream. Cell-based methods are used when the neutralizing antibody is expected to block drug-cell interaction or impair a cell signaling function. One general cell-based NAb category is methods developed for specific cellular functions, such as measuring drug uptake and subsequent reduction by a neutralizing antibody. Another general category of NAb assay utilizes a cell line modified with reporter construct. In the presence of drug, the reporter gene is activated; a neutralizing antibody in combination with drug prevents the reporter from functioning. Using a combined ADA and NAb analysis strategy can provide insight as to which component of a drug therapy may be immunogenic, and if an ADA response is present, whether the antibodies generated have the ability to neutralize drug function.

SUMMARY

Medpace's central and bioanalytical laboratories, with their teams of scientific experts, collaborate closely with Sponsors to develop unique solutions for various cell and gene therapy programs. We are well versed in the development, optimization, and validation of complex assays to deliver premier services to support Sponsors' testing needs. Our globally harmonized laboratories utilize standardized platforms, validated workflows, and state-of-the-art instrumentation to deliver consistent, high-quality results across global studies.

ABOUT THE AUTHOR

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Dr. El Mustapha Bahassi is a Research Scientist with over 20 years of clinical and research laboratory experience. He is experienced in biomarker development and well-versed in various molecular biology techniques such as DNA cloning, PCR, protein purification, mass spectrometry, flow cytometry, mouse modeling, mammalian/bacterial cell culturing and cell-free DNA/circulating tumor cells manipulation. He received his PhD in molecular biology and biotechnology from the University of Brussels in Belgium. He then joined the University of Texas Southwestern Medical Center in Dallas as a postdoctoral fellow in molecular oncology. Following his training at UT Southwestern, Dr. Bahassi moved to the department of cancer biology at the University of Cincinnati and later became a faculty member in the division of hematology/oncology. As an independent faculty, Dr. Bahassi developed a translational line of research where he worked closely with clinical oncologists to develop new companion diagnostics using cutting-edge genomic technologies.