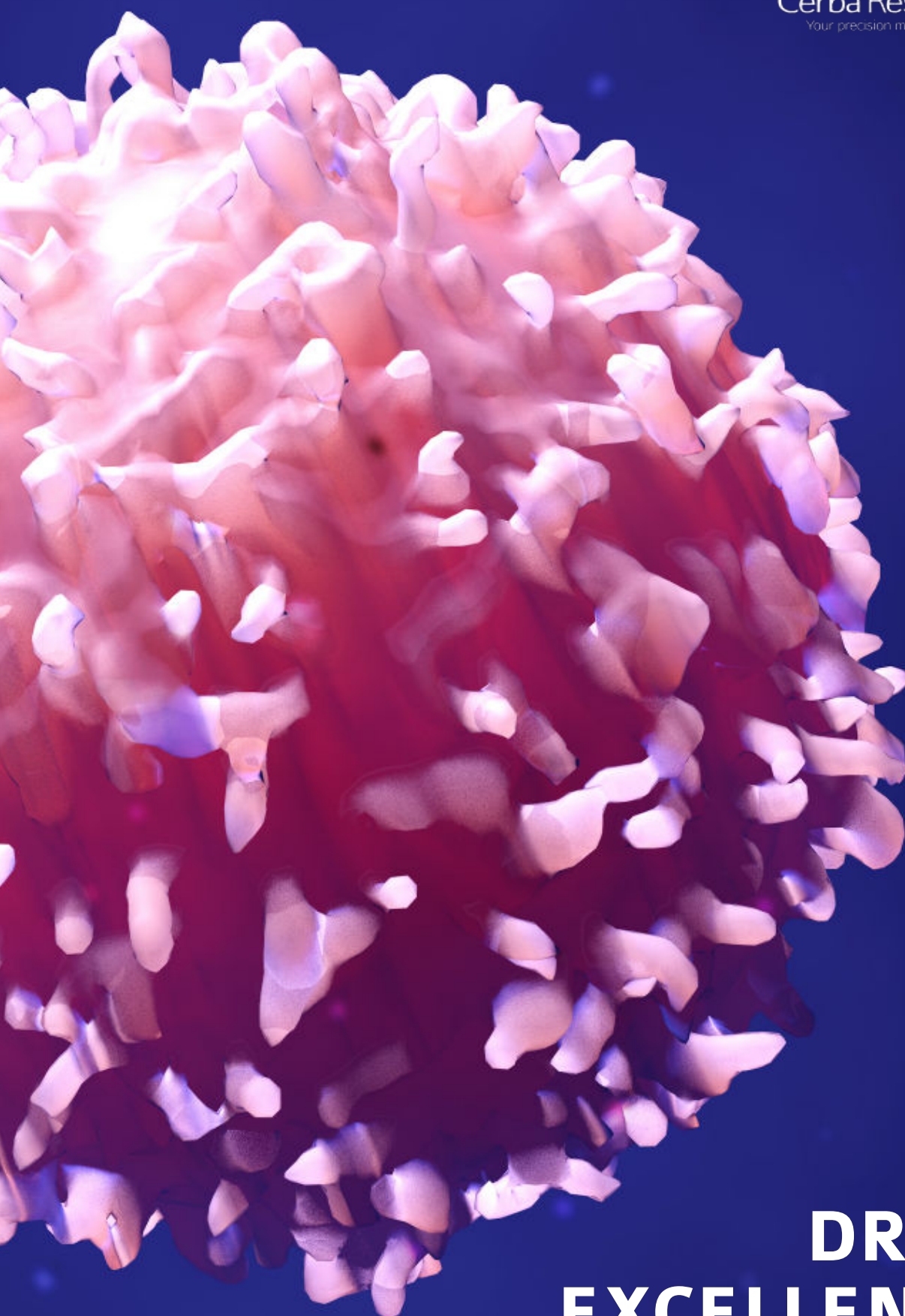


Cerba Research
Your precision medicine partner



**DRIVING
EXCELLENCE IN
IMMUNO-ONCOLOGY**

CERBA RESEARCH, YOUR PARTNER IN IMMUNO-ONCOLOGY STUDIES

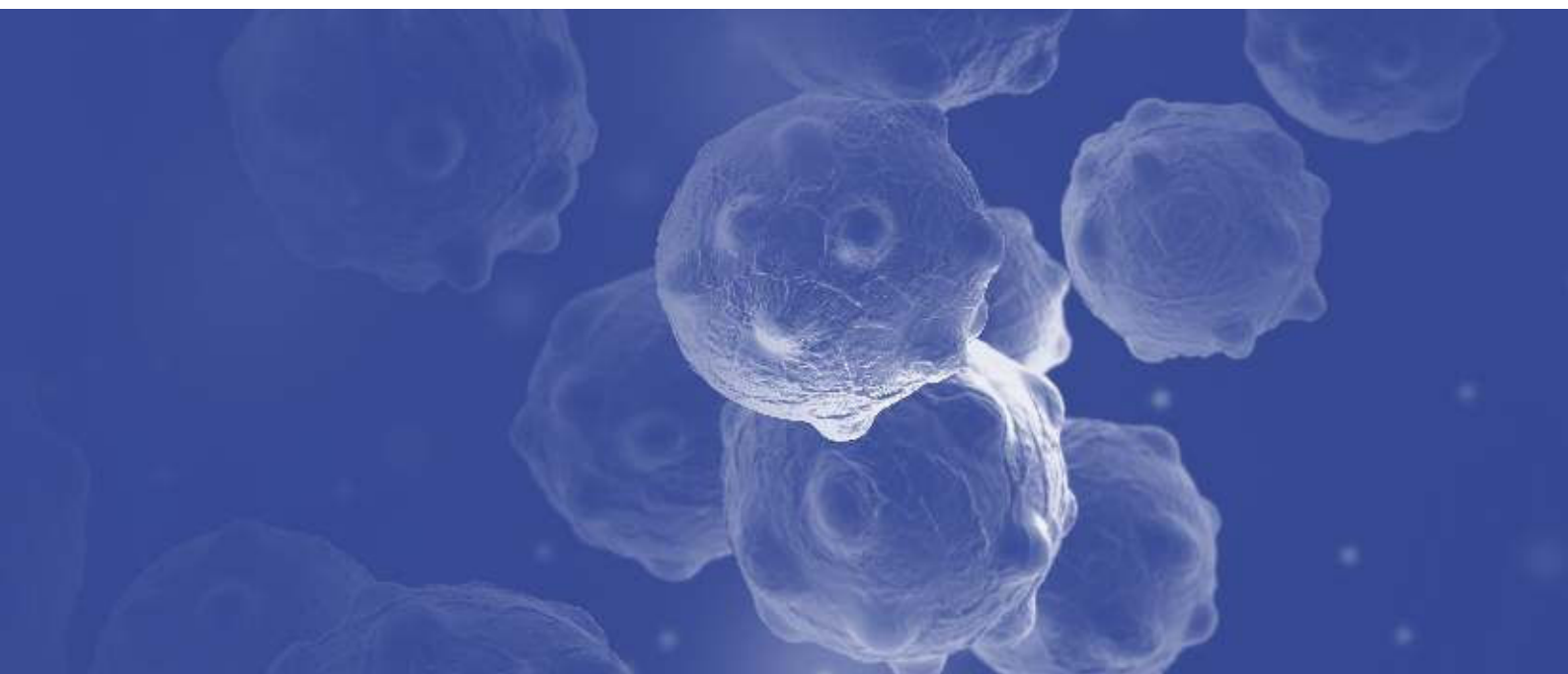
Immuno-oncology (IO) refers to cancer treatments that utilise immune regulation. This very promising therapeutic approach is particularly interesting for cancers that have high resistance to cytotoxic drugs. IO exploits the possibility that the immune system can recognise and respond to tumor-associated antigens. Research is ongoing with a range of therapeutic modalities, including vaccines, recombinant cytokines, monoclonal antibodies, bispecific antibodies, and autologous and allogeneic T cells and NK cells.

Regardless of the IO treatment, efficient and successful trials depend on accurate methodologies that reveal the responses of the tumor cells and the immune system. It is also essential to investigate what the genome of the patient and the tumor can say about the best treatment approach and prognosis.

Cerba Research's global central laboratory has the comprehensive expertise and technology to reveal the impact of the full range of IO approaches. With **more than 50% of our clinical trials focused on oncology**, our clinical and technology experts have gained extensive first-hand experience in:

- **Genetic profiling** based on cell, tissue, and body fluid samples, including liquid biopsies, with methods such as quantitative real-time and digital PCR, microarrays, and next-generation sequencing
- **Circulating biomarker detection** and identification, with methods such as ELISA and various single and multiplex automated immunoassays
- Cell work, including custom-made **flow cytometry panels** for characterizing general immune responses and assessing the efficacy of antibody- and CAR-T cell-based therapies, cell enrichment, and PBMC preparation
- **Tissue work**, including tissue prep, staining, IHC, and multiplex IHC for assessing in situ immune cell infiltrates, digital pathology, and ISH

As IO-focused projects are highly complex and sometimes exploratory, we often work closely together with our clients' scientists to develop custom-made solutions. We are happy to advise you on how we can provide such bespoke support for your projects.



INTERPRETING GENE EXPRESSION

Gene expression can tell a detailed story about the biological response to a drug or cancer, but it requires a range of techniques to understand it. Cerba Research goes beyond the basic quantitative RT-PCR and PCR to offer the full range of powerful modern methods for reading and interpreting gene expression. Dozens of genes with a described impact on myeloid malignancies and solid tumors can be assayed with both our **off-the-shelf sequencing panels and whole exome and genome (WES/WGS) next-generation sequencing (NGS) solutions**.

Copy number variation (CNV) and rare events can be detected with highly sensitive digital PCR assays. Our sequencing methods enable the determination of tumor mutation burden (TMB), identification of neoantigens, quantification of CAR-T cells, and the discovery of new RNA/WDNA biomarker signatures.

From whole exome sequencing to targeted MSI status determination and miRNA sequencing, our experts can develop and validate new assays and skilfully interpret the results. Cerba Research will deliver the answers hidden in your samples.

Cerba Research uses **state-of-the-art platforms for genome work** to ensure reliable and reproducible results from each sample:

- Illumina® MiSeqDX®, NextSeq® 500, HiSeq® 1500, and NovaSeq® 6000 for sequencing
- Bio-Rad® CFX384™ for real-time PCR
- Bio-Rad® QX100™ for digital PCR
- Affymetrix® Cytoscan® HD for SNP detection
- Bio-Rad® qPCR Chip panel for verification of tumor microenvironment

Case study

Phase I/II of a novel type of antibody targeting CD70 to determine the biological range of solid tumors and hematological malignancies

Cerba Research's solution:

Developed and validated a quantitative RT-PCR assay to accurately measure CD70 levels in liquid biopsy samples (whole blood)

REVEALING CIRCULATING BIOMARKER PROFILES

Circulating biomarkers have justified the attention paid to them since their discovery, rewarding scientists with diagnostic and prognostic insights into diseases. A range of biomarkers have proved useful in IO, **from the well-established to the exploratory**: familiar hematology parameters, like absolute lymphocyte counts; biochemical parameters, such as β 2-microglobulin and LDH; and cytokines and chemokines, which still have considerable potential to reveal.

Cerba Research offers a full range of methods for identifying, assessing, and monitoring circulating biomarkers, including techniques ideal for delivering reliable results across the length of demanding long-term studies. For new **exploratory biomarkers**, our expert scientific team has developed a **fast, fit-for-purpose, and reliable pre-validation protocol** that gauges which solution is best suited to the needs of the study. We then bring this to full validation to ensure the best support for your R&D programs and clinical trials.

To unlock their full potential as inclusion/exclusion and monitoring tools, our experts have applied this development approach to create a range of **off-the shelf biomarker assays**, each running on the most suitable instrument:

- MSD® S600 Meso Scale Discoveries
- ELISA platform
- Magpix Luminex
- Quanterix Simoa HD1
- Ella Protein Simple System
- LC-MS/MS

Example

Assay type: V-PLEX immunoassays on the MSD® S600 have:

- High dynamic range for measurement across the spectrum from healthy to sick
- High sensitivity and lot-to-lot consistency

Our clinical trial-ready system:

- Allows for high-throughput, single-well multiplexing with low sample volume
- Offers comprehensive panels of chemokines, cytokines, and pro-inflammatory and angiogenesis markers
- Has been validated on human serum and plasma
- Has established sensitivities and stabilities

INVESTIGATING IMMUNE CELL SUBPOPULATIONS

Flow cytometry (FCM) enables **fast and complex phenotyping** without compromising on sensitivity. It reports characteristics of cell subpopulations with high sensitivity, even with frequencies as low as 1:10,000. Results can be given as percentages, absolute cell counts, or the number of molecules per cell.

Through its global and harmonized network of expert laboratories, and with more than 25 years of experience with FCM analyses, Cerba Research can apply this **versatile technology** in a range of ways to support your IO studies. We have developed immunophenotyping panels for both **peripheral blood and bone marrow aspirates**, which are suitable for patient follow-up and for assessing recovery and remission in clinical trials targeting leukemia, lymphoma, and myeloma.

In trials involving biopharmaceuticals, FCM is indispensable for immune monitoring and for accurate assessments of pharmacodynamics/receptor occupancy (PD/RO). We offer a range of panels identifying T cell phenotypes (naïve/memory, activation stages, T-helper subsets, and regulatory T cells), B cells, NK(T) cells, macrophages and monocytes, dendritic cells, neutrophils, basophils, and MDSCs.

Using **global standardization procedures and acceptance criteria** on 8- and 10-color state-of-the-art equipment, Cerba Research ensures consistency and reproducibility of results. As with our general testing, the sample workflow is fully integrated in our Clinical Trial Management System (CTMS), guaranteeing secure data transfer along the whole workflow, from test request to reporting.

Case study

First-in-human clinical safety and efficacy trial for CAR-T cell treatment for B-ALL

Cerba Research's solution:

Developed and validated pharmacokinetics FCM assay that utilises an anti-idiotypic antibody specific for the CAR-T cells used in the trial - monitors the immunophenotype, expansion and persistence of the CAR-T cells in the circulation of the patient.

Case study

Clinical efficacy trial for a monoclonal antibody targeting an epitope strongly expressed on leukaemic cells

Cerba Research's solution:

Developed and validated receptor occupancy qFCM assay with calibration beads running simultaneously with the clinical sample. It measures drug-to-target binding and yields strong pharmacodynamic data.

DELVING INTO TUMOR BIOMARKERS AND BEHAVIOR

Next-generation histo-cytopathology has opened up the possibilities for understanding tumor biology. In the context of IO, Cerba Research applies this approach to identify tumor biomarkers from patient biopsies and to characterize the tumor environment and its infiltration by immune cells, supporting:

- Patient stratification
- Inclusion/exclusion decisions
- Monitoring of immune response during treatment
- Correlation of target presence and disease evolution

To ensure comprehensive exploration of tumors, our experts have mastered a wide range of techniques relevant for successful application of next-generation histo-cytopathology, including (IHC), in situ hybridisation (ISH) and tissue microarrays. We use the relevant, world-class platform for each technique, including the Ventana® BenchMark® XT/Ultra, Leica® Bond III/RX, and Dako® Link 48, along with Leica® and Hamamatsu® digital imaging platforms. We also collaborate with our global network of experts and our clients' own scientists to ensure that trial results are characterized as needed.

Case study

Multiple myeloma trial focused on anti-CD138 antibody treatment

Cerba Research's solution:

Developed a comprehensive portfolio of IHC (CD138 staining) and FISH testing to evaluate complete response and very good partial response (CR+VGPR) rates - results useful for patient stratification.

Cerba Research also offers a **combined multiplex immunohistochemistry and digital pathology** approach that allows interactions between a target and various receptors and/or ligands to be assessed and ensures no operator bias effects during image analysis. This approach uses PerkinElmer's cutting-edge Vectra® Polaris™ Automated Quantitative Pathology Imaging System, allowing assessment of up to 8 markers on 1 slide.

Cerba Research can easily support the design and validation of protocols for new biomarkers, even for complex and multiplex stainings. Our typical time frame is just a few weeks. We are constantly expanding our portfolio to match the dynamic developments in IO research.

CERBA RESEARCH

A GLOBAL NETWORK OF EXPERTS

The expert network of Cerba Research's global central laboratory extends across five continents. We provide **custom-made solutions** to support the success of our clients' clinical trials. As a division of Cerba HealthCare, a European leader in clinical pathology, we're dedicated to improving the understanding of disease and quality of treatment.

At Cerba Research, we strongly believe in the added value of having experts anchored in real-life practice analysing your samples. All our affiliate laboratories have their routine activities, but also render and discuss results with community hospitals and physicians, ensuring the best possible interpretation of complex clinical and safety data.

Clinical trials are also unique opportunities to develop new tests and technologies that have yet to reach the clinic. Cerba Research has built a **seamless network of expert laboratories** specialized in key aspects of today's R&D challenges, such as circulating cell-free DNA detection, lncRNA sequencing, and multiplex IHC and scoring.

We ensure the successful coordination of communication and activities throughout our whole network of scientists, clinical experts, and physicians. They each have extensive academic and laboratory experience, as well as complementary backgrounds in pharmaceutical, biomedical, and biotechnological sciences. You can rely on us to discuss the details of even your most complex projects, translating your scientists' needs into concrete solutions.

Cerba Research is ready to make your IO studies a success.





CHANGE THE
SHAPE
OF YOUR CLINICAL
DEVELOPMENT



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