

# Contract Immune Monitoring and Research

**E**stablishing new bioanalytical laboratory assays requires a major investment of effort and capital. Would you like to save both time and money? Let CTL's team of experts handle the details for you.

Cellular Technology Limited (CTL) has been providing contract research services to government agencies, major pharmaceutical companies, biotechnology companies, and academic institutions for over 15 years. In 2007, CTL was chosen to serve as an ELISPOT reference laboratory by the Immune Tolerance Network and the Sabin Vaccine Institute's Cancer Vaccine Consortium. In addition, CTL has been awarded multiple IDIQ contracts by the U.S. National Institutes of Health (NIH) for the development and validation of human and animal models for infectious diseases and biodefense applications.

Thanks to its in-house expertise, CTL can conduct all assays in a GLP-compliant manner. We can validate the test methods, accommodate FDA requirements, or develop assays to evaluate specimens for scientific interest. CTL specializes in high-throughput assays from specimen processing to data acquisition, analysis, and quality control. We can offer a four to five week turnaround time period for processing, testing, and analysis of data from 1,000 specimens.

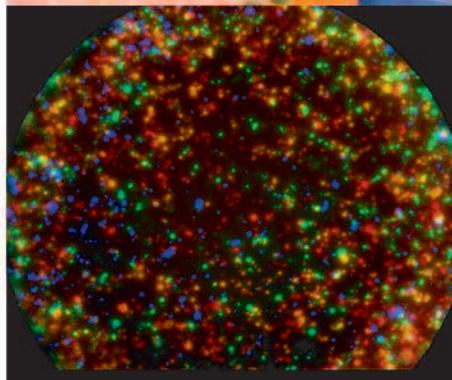
## Specimen Processing

CTL provides laboratory services for processing and cryopreserving both pre-clinical and clinical specimens. Our scientific team has a wealth of experience in processing whole blood to obtain peripheral blood mononuclear cells, (PBMC) or separate cell populations (CD4, CD8, NK cells, monocytes, and others). We also have experience in the processing of solid organs (e.g., spleens, lymph nodes) to obtain lymphocytes.

From any given blood sample, we can isolate the PBMC, discard any unwanted cell types, extract the serum for use in ELISA tests, and then cryopreserve the remaining PBMC. Our revolutionary method for cryopreservation enables us to freeze cells with excellent recovery and viability rates and without loss of functionality, as tested in antigen-specific ELISPOT assays. This technology enables researchers to collect samples from multiple time points and evaluate them within the same assay, thus allowing subjects to serve as their own controls.

At the customer's request, CTL can

provide shipping instructions, boxes, media, data loggers, and additional materials for shipping specimens. CTL can serve as central PBMC processing site to streamline the blood processing and separation of PBMCs in multi-center clinical trials. CTL can also train customers in whole blood collection, proper PBMC processing, freezing and shipping procedures, as well as verify cell recovery and viability processed by each site through a series of quality control (QC) experiments. In this manner, the customer is assured that the optimal recovery and viability rates of the frozen cells are achieved by the process before a single patient is enrolled.



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## Contracted ELISPOT Testing for Immune Monitoring and Biomarker Screening in Preclinical Studies and Clinical Trials

Are you using the appropriate readout system for evaluating your test subject response?

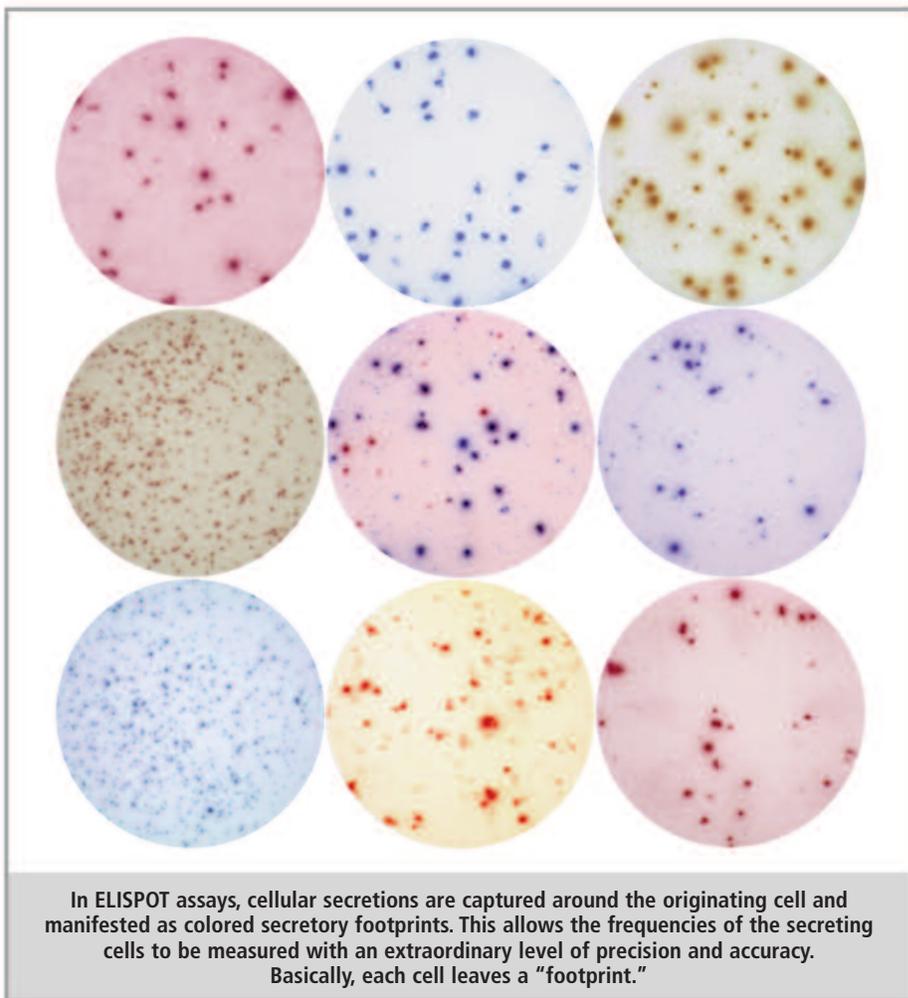
CTL has years of experience in contracted research. Many pharmaceutical and biotechnology companies have entrusted CTL with evaluating cell-mediated immunity (CMI) to their vaccines, drugs, and biologic products using the ELISPOT technique.

CTL's greatest strength lies in its high-throughput T cell monitoring capabilities and world-class ELISPOT (Enzyme-Linked ImmunoSpot® Assay) expertise.

The ELISPOT technique allows researchers to generate secretory footprints in the form of colored spots within a 96-well plate. These images are then scanned, counted, and readily evaluated for statistical significance. The ELISPOT method can be used to determine whether a patient population responds positively or negatively to a vaccine, drug, or biologic product, and in addition, measure the extent of each person's immune response.

This method opens the door for a variety of tests, such as:

- Testing T cell mediated immunity at a single-cell level for preclinical and clinical specimens
- Antigen determinant mapping with overlapping peptides
- Measurement of cytotoxic T cell responses
- Measurement of B cell responses
- The ability to run multiple assays using a limited number of cells (e.g. perform two sequential ELISPOT assays using the same cells, or perform an ELISPOT assay, harvest cells and use them in flow cytometry)



**In ELISPOT assays, cellular secretions are captured around the originating cell and manifested as colored secretory footprints. This allows the frequencies of the secreting cells to be measured with an extraordinary level of precision and accuracy. Basically, each cell leaves a "footprint."**

The ability to measure cell mediated immunity to antigens using ELISPOT is vital when measurement of the *ex vivo* low frequency T cell responses is required. The T cell readout at a single-cell resolution using the ELISPOT technique is necessary to achieve this goal.

CTL has developed, optimized, qualified, and validated test methods for its clients in various test systems including, but not limited to, human, monkey, mouse, rat, rabbit, and pig. This has provided CTL a wealth of expertise encompassing a wide range of assay types (ELISPOT, ELISA, multiplex bead arrays, and FACS) in a nonregulated and regulated environment. We have a GLP-compliant high-

throughput laboratory capable of processing 150 samples per day and up to 450 samples per week. This allows us to significantly speed up the development process for vaccines entering the clinical testing phase and their subsequent immune monitoring. Our team of highly-trained scientists will gladly assist in all phases of your study.

### CTL offers an extensive range of ELISPOT assays, including:

- IFN- $\gamma$
- IL-1 $\beta$
- IL-2
- IL-3
- IL-4
- IL-5
- IL-6
- IL-8
- IL-10
- IL-12 p70
- IL-13
- IL-15
- IL-17
- TNF- $\alpha$
- GM-CSF
- perforin, and Granzyme B ELISPOT assays

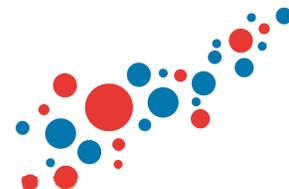
Other ELISPOT test systems available including testing of B cells, NK cells, dendritic cells, or any other single-cell solutions.

**QA**

CTL's GLP Laboratory complies with CLIA and with FDA regulations (21 CFR Part 58 and 21 CFR Part 11). CTL is a member of the Society of Quality Assurance (SQA) and the Regulatory Affairs Professionals Society (RAPS).

**RA**





## ELISA, Multiplex, and Flow Cytometry Testing

CTL's ELISPOT assay expertise is complemented by its ELISA testing, cytokine bead array (CBA), and flow cytometry services (FACS). ELISA testing can be used to extract additional information on the production of antibodies or other cytokines from the same sample—that is, without requiring the use of additional blood draws. Similarly, flow cytometry can be used to determine which cell population is prevalent in the monitored response. It is also an invaluable tool when T cell responses are excessively large, i.e., too numerous to count using the ELISPOT method. All of these assays can be used in conjunction with the ELISPOT assay.

The supernatant can be collected for example from ELISPOT plates and used in other test systems such as ELISA assays and cytokine bead arrays. Together, these technologies can provide a more comprehensive view of the subject's immune response.

CTL also offers standardized ELISA protocols for multiple species. In addition, CTL's GLP laboratory has diversified its service portfolio to include cytokine bead arrays, intracellular cytokine staining, surface marker staining via flow cytometry, and other assay types.

**CTL's advanced protocol for cryopreserving PBMC specimens produces recovery rates of more than 80%, viability rates exceeding 90%, and 100% functionality for humans and most animal species.**



**CTL offers high-throughput immune monitoring and biomarker analysis, as well as research & development services customized to suit your needs. Some areas of focus include:**

- Vaccine Development
- Infectious Diseases
- Tumor Immunity
- Immune Toxicity
- Immunogenicity Testings
- Epitope Discovery
- Autoimmunity
- Allergies
- Transplantation

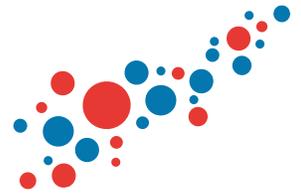


## Specimen Management

CTL's specimen management department is solely dedicated to monitoring preclinical and clinical samples from receipt to disposition. Our thorough quality control measures ensure proper specimen handling and accurate data management. The movement of every specimen is tracked meticulously until CTL receives disposition instructions from the sponsor/client.

CTL is a member of the International Society for Biological and Environmental Repositories (ISBER), the leading international forum that addresses the technical, legal, ethical, and managerial issues relevant to repositories of biological and environmental specimens.

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## Assay Standardization

Cell-based assays have a reputation for variability when performed in different laboratories. This is because minor variations in the procedures used can create significant differences in the experimental outcome. Because of this, CTL has made a concerted effort to standardize ELISPOT assays.

CTL's highly-trained research team has identified the parameters that can impact the results, such as cell preparation, membrane selection, reagent concentra-

tions, cryopreservation techniques, thawing, cell counting, and more.

CTL is the premier provider of comprehensive standardization packages for ELISPOT assays. This includes the following:

- Serum-free media solutions
- Cryopreservation reagents
- Standardized antigens (e.g., CEF peptide pools)
- Cryopreserved PBMC (both characterized and uncharacterized for HLA types and with established antigen reactivity)

- ELISPOT reference sample QC sets
- Whole blood processing kits
- Whole blood shipping materials
- Scanning services for ELISPOT plates

Also included are training sessions for blood processing, ELISPOT assays, and whole blood shipping procedures. Further information can be found on the CTL website and in CTL literature (available upon request).



For further information, call us at **+1 216-791-5084**, or email to **info@immunospot.com**. You may also visit us at **www.immunospot.com**.

# CTL

With over 15 years of experience, Cellular Technology Limited leads the field of biomedical image analysis. More than 1600 customers worldwide have selected CTL readers and software solutions to meet their requirements, including the "who's who" of academia, government agencies, major pharmaceutical companies, and biotechnology companies.

## Cellular Technology Limited

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