SONY

CGX10 Cell Isolation System

Sony Biotechnology Inc.


POWER
STOP
CGX10 CELL ISOLATION SYSTEM

Cell Isolation You Can Count On

The CGX10 Cell Isolation System is the only fully closed cell isolation system for GMP compliant cell production and cell sorting applications. The innovative system design provides superior cell isolation along with ease of operation, with unparalleled flexibility that enables a smooth transition from process development to cell production.

Progress in the area of cell and gene therapies has accelerated significantly in recent times. Flow cytometry based cell sorting has been used to sort cells by desired phenotype based on the presence of one or more biomarkers. Sorted cells have been expanded ex vivo and reinfused into patients as cell-based therapies. The ability to use multiple biomarkers is important. It enables identification and isolation of specific immune cells possessing the desired phenotype. Multi-marker based cell isolation not only delivers a higher purity of isolated cells, but also enables selection to eliminate non-target cells, or therapeutically ineffective cells, for example, over-differentiated T cells.

However, the use of traditional flow cytometers has been limited to research laboratories and preclinical and early phase studies. The complex design of conventional flow cytometers and their usability issues make them poorly suited to a cell production environment that is GMP compliant. Certain conventional flow cytometers have also been known to shear or cause electrically-induced stress or damage to sorted cells.

The CGX10 Cell Isolation System has been developed with the goal of enabling multi-marker selection to isolate target cells while ensuring high cell viability. The system delivers a user experience that is suited to the GMP compliant cell production environment, and transcends the complexity and subjectivity of conventional sorter platforms.

The CGX10 is designed to fit your GMP environment with its compact design, intuitive touch screen user interface, ease of operation, and sterile single-use consumables which ensure operation as a fully closed system.

Next Generation Cell Therapy Enablement

Closed System

The CGX10 Cell Isolation System is the only fully closed, cell isolation system that addresses GMP-compliant cell production and cell isolation needs. The innovative system design provides superior cell isolation along with ease of operation and unparalleled flexibility, which enables a smooth transition from process development to cell production.

GMP Ready

The tubing kits are sterilized using the Ethylene Oxide Gas (EOG) sterilization process to fit into a controlled environment. The sterilization and closed mode operation of the tubing kit protect cells from the external environment and lower the risk of contamination. All consumables which may come in contact with cells are manufactured and tested in ISO 13485 standard compliant facilities.

Moreover, certification is available for each lot of consumables to support work in a compliant facility.

Simple Operation

On-screen prompts guide users on how to isolate cells of interest. The software automates appropriate instrument setup without requiring beads, reducing the risk of contamination. A dedicated operator mode is available for routine operation in a GMP environment backed by 21 CFR Part 11 compliance tools. Touch screen operation eliminates the need for a keyboard and mouse, reducing space required.

High Cell Viability

Sony's novel microfluidics based cell isolation technology isolates cells, minimizing stress to the cells due to absence of mechanical valves and droplet based methods. This technology maintains cell viability and helps maintain function.

Additionally, independent temperature control of the sample and sort output reservoirs (from 4°C to 34°C) provides the environment needed for your cells (Figure 1).

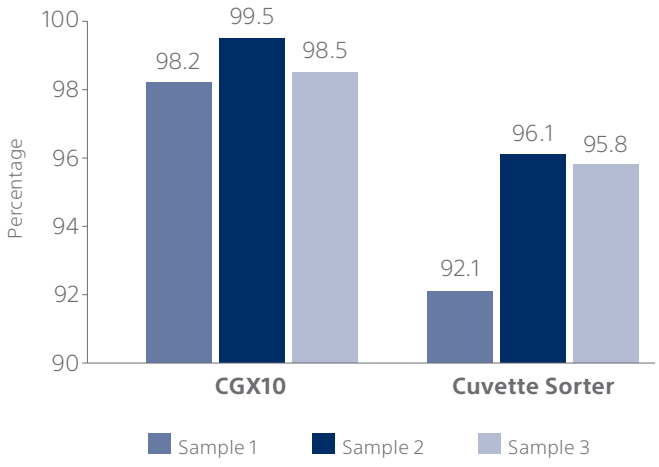


Figure 1: Comparison of cell viability obtained when using a conventional cuvette based sorter and the CGX10 Cell Isolation System

Three samples were used to sort target cells using the two types of systems. The viability of sorted cells was calculated and compared side by side. Data indicates that cells isolated using the CGX10 consistently showed higher viability than those sorted using the conventional cuvette based sorter in all three cases.

Data generated in collaboration with Mie University.

Innovative Microfluidics Based Cell Isolation Technology

The CGX10's novel microfluidics based cell isolation technology provides high speed, gentle, and robust sorting for cell manufacturing applications. The hydrodynamic sorting mechanism handles cells gently within the microfluidics without pressurizing cells being sorted. In addition, the independent temperature control function (4°C–34°C) helps keep cells viable. Well controlled cell positioning with laminar flow provides precise detection and higher purity (Figure 2, 3 and 4). The automatic clog detection and recovery function allow walkaway operations.

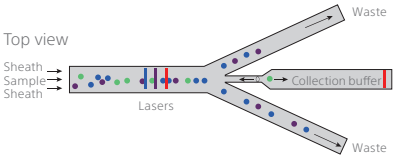
The system is equipped with four lasers (405 nm, 488 nm, 561 nm, 638 nm) and ten detection channels (two scatter and eight fluorescence) to provide flexible fluorochrome selection for various cell types such as naive T cells, memory T cells (Tscm, Tcm), regulatory T cells (Treg), induced pluripotent stem cells (iPSC). The mixed sorting ratio control feature expands capabilities for cell selection by allowing sorting of multiple target populations at fixed ratios.

The performance of the CGX10 Cell Isolation System was assessed to evaluate Sort Purity using cellular material and beads, where the starting materials were adjusted to contain (known) multiple levels of target populations. The sort purity performance of the CGX10 was systematically evaluated using both beads and PBMCs at varying sort target percentages.

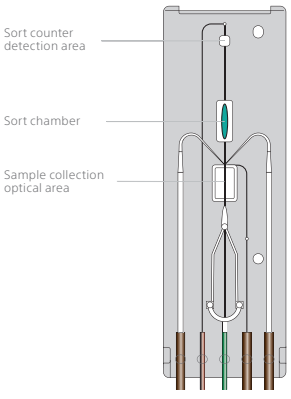
Mixtures of 5-µm (sort target) and 10-µm beads or CD3/CD28 activated and cultured PBMCs (stained with CD4 BV421 antibodies, sort target) were used. In all cases, the sort speed was approximately 15,000 events per second, while the sort target percentage was adjusted to approximately 5% (TGT 5%, for cells: 5%–10%) and 30% (TGT 30%, for cells: 20%–25%).

As a part of the cell sorting evaluation, viability before and after sorting was also evaluated using propidium iodide staining.

Hydrodynamic Sorting



Microfluidic Chamber



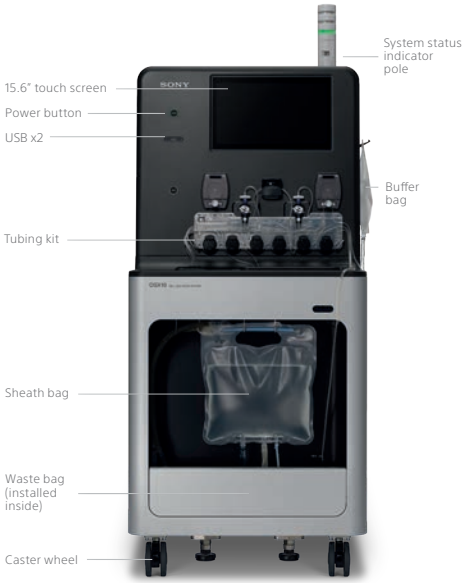
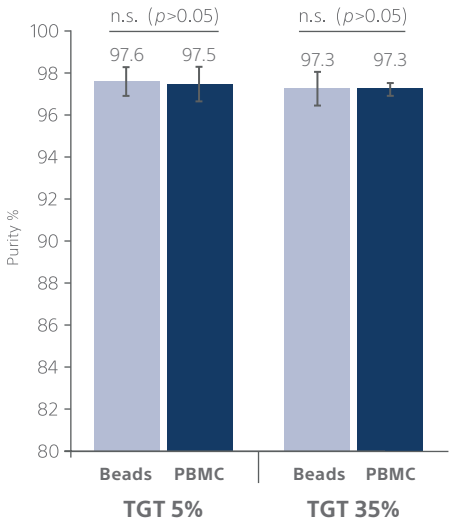


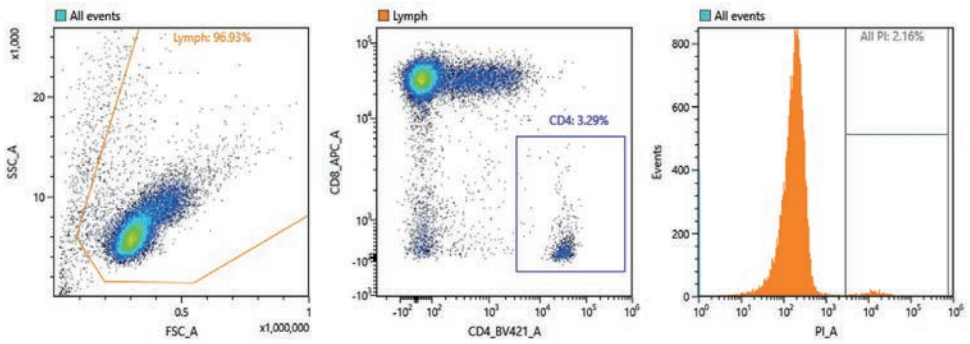
Figure 2: Evaluation of post-sorting reproducibility



In Figure 2, the average purity after sort is shown for beads and PBMCs along with error bars demonstrating the high reproducibility of purity after sort across the range of samples and target percentages considered. No significant difference between results obtained with beads and PBMCs was observed as confirmed by the result of a t-test. The error bar describes the standard deviation for each data set.

In Figures 3 and 4, dot plots depicting data from a common cell sorting experiment is shown. The data set demonstrates the high purity of more than 97% CD4 positive cells in the lymphocyte fraction after sorting a sample with approximately 3% of CD4+ cells for 6 hours at 15,000 events per second. The high viability of the sorted cells is also demonstrated. The analysis of pre- and post-sorted cells was conducted using an SA3800 Spectral Analyzer.

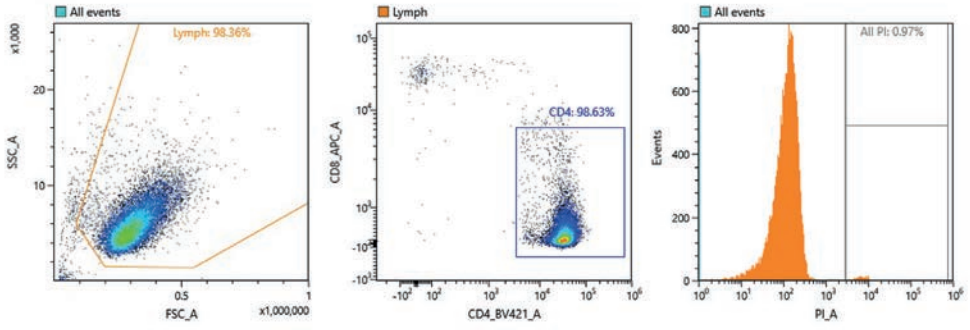
Figure 3: Pre-sort data



Gates and Statistics

Name	Events	Parent %	Total %
All events	20,000	100.00%	100.00%
Lymph	19,385	96.93%	96.93%
CD4	638	3.29%	3.19%
All PI	432	2.16%	2.16%

Figure 4: Post-sort data



Gates and Statistics

Name	Events	Parent %	Total %
All events	20,000	100.00%	100.00%
Lymph	19,671	98.36%	98.36%
CD4	19,401	98.63%	97.01%
All PI	193	0.97%	0.97%


No tubing Installed
Event Rate: 0
Agitation:OFF
Sample:4°C
Collection:4°C
405 488 561 638
Power
Menu
Maintenance
Help
Role Selection
Select your role.
Operator
By selecting this Role, you will be able to access functions reserved for operations in a controlled environment such as Standard Operation Template based sort operations, QC operations and report management.
Process developer
By selecting this Role, you will be able to access functions for process development allowing more freedom to adjust settings, such as setting up new measurement and sort experiments, acquiring compensation data, analyzing past data, creating a Standard Operation Template, running QC and manage data or reports.
Administrator
By selecting this Role (Mode) you will be able to access administrator functions such as user management, instrument settings, data and report management.
Select

Intuitive Software: Designed for All Experience Levels

The CGX10 Cell Isolation System operates with embedded software that has been designed to deliver intuitive usability for users of all experience levels, focusing on the needs of a busy laboratory. The touch screen enabled software eliminates the need to install and maintain a standalone computer and peripherals in a cleanroom or GMP setting.

The software navigation wizard available with the CGX10 system makes the workflow easy to teach, learn, and use. The software supports functions from automated setup to data acquisition and analysis, generating FCS 3.1 files which can be exported in a secure manner.

The software offers several advanced features to ensure safety and security of electronic records such as authorized user access, password protected login, recording of audit trails, and generating the reports in a secure non-editable format to enable 21 CFR Part 11 compliance. The CGX10 software offers three different modes of operation (roles), ensuring smooth transition through various stages of cell and gene therapy development.

The three roles are: **Administrator** for configuring the system settings and managing data, a flexible **Process Developer (PD)** mode enabling the user to create and optimize the protocol such as gating strategies and visualization parameters and **Operator (OP)** mode allowing the user to simply execute previously created protocols. In the Operator mode, all the operations are recorded in the audit trail, so the user can still adjust flow rate and gates while keeping track of all changes. The Operator mode offers a Sort Report or summary at the end and enables compliance with 21 CFR Part 11 guidelines. An overview of the CGX10 system software mode capabilities is provided (Table 1).

The CGX10 System and software are designed to enable walk-away cell sorting operation by offering automation at multiple steps from setup to analysis, such as automated chip positioning, optical axis adjustment, automated sample line cleaning and end-of-sort detection. One of the key features of this instrument is the automatic clog detection and recovery capability. During sorting, any clogs that may be formed during sample flow are automatically detected by the system through the profiling of the scatter of the sorted cells and are automatically disintegrated by controlling the fluidics, through making multiple adjustments as needed. This ensures robust operation over long sorting times and promotes walk-away operation.

Table 1: Overview of CGX10 system software capabilities

Function	Operator (OP) Mode	Process Developer (PD) Mode	Administrator Mode
Sort operation	✓[1]	✓	
Compensation		✓	
Quality control	✓	✓	
Sort SOP creation		✓	
Settings			✓
Report management	✓	✓	✓
Data management		✓	✓

[1] With Sort SOP, user generates a Sort Report for 21 CFR Part 11 compliance

Fit for Purpose, Single-Use CGX10 System Consumables

Key features of the CGX10 Cell Isolation System and Accessory Products

- Sterile (compliant with relevant ISO standards) and single-use accessory products
  - Accessory products which may come in contact with biological material produced in ISO 13485 compliant facilities
- Biocompatibility evaluation completed for the Sterile Tubing Kit (Standard Operation) and Sterile Tubing Kit (Process Development) per ISO 10993 compliance

The CGX10 Cell Isolation System is designed for use in GMP-compliant manufacturing of Advanced Therapy Medicinal Products (ATMP) and regenerative medicine applications, including cell and gene therapy. Related accessory products are supplied with harmonized documentation such as Certificates of Analysis, Certificates of Origin, Product Information Files, and access to authorization letters for the Device Master Files (MAF).

All the fit for purpose consumables offered with the CGX10 Cell Isolation System are single-use kits designed for enabling fully closed, high speed, high purity, multiparametric, fluorescence-based cell sorting from process development to clinical/commercial manufacturing.

The accessory products which may come in contact with biological material include the Sterile Tubing Kit (Standard Operation), Sterile Tubing Kit (Process Development), Sterile Sheath Bag, and Sterile Buffer Bag.

These accessory products are designed to be single use and sterile, and are made using biocompatible materials.

Single-Use Kits

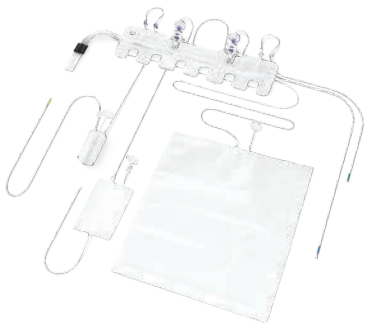
Sterile Tubing Kit (Standard Operation or Process Development) includes a preconnected assembly of:

- Microfluidic Chip
- Sample Reservoir
- Sort Collection Bag
- Waste Bag

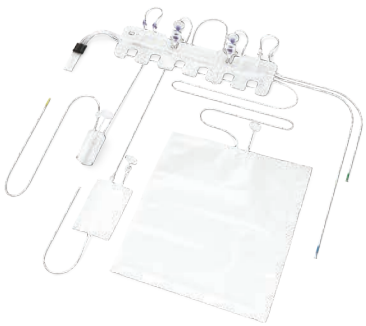
This kit also includes:

- 1 Tubing Extender Kit for Sheath and Buffer Bag connection
- 1 Sterile Sample Preparation Bag (only for Standard Operation Kit)

Sterile Tubing Kit (Standard Operation)



Sterile Tubing Kit (Process Development)



Comprehensive Services and Support

With the CGX10 Cell Isolation System, we offer comprehensive service agreements to protect your investment. Our service plan packages are created to meet your budget and compliance needs. In addition to the standard service agreement which includes comprehensive technical service and support, diagnostics, and repair as well as the preventive maintenance, we also offer Comprehensive Qualification services including IQ and OQ.

CGX10 Cell Isolation System Installation and Operational Qualification (IQ/OQ) services include numerous experiments for the system to ensure critical components are tested and validated, have cut-off metrics, and to confirm these metrics show the system is operating in accordance with specifications.

Our IQ service provides documented verification that the instrument is installed according to our specifications and safety regulations. During the IQ, a trained engineer verifies the latest supported firmware and software versions were installed, verifies instrument setup checks that physical and environmental safety conditions are met, and provides a signed audit-ready report.

Our OQ service follows a comprehensive, well-defined protocol to verify the system functions according to preset and validated operational specifications. We update the OQ protocol following each instrument hardware and software release, ensuring your laboratory receives the most up-to-date service.

We strive for excellent customer relationships. Our customer service and technical service teams are available to answer questions, help expedite orders, and to provide the assistance needed for you to get the most out of your Sony Biotechnology products.

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