

# Innovative systems for advancing regenerative medicine

Shibuya Corporation is promoting **THE INDUSTRIALIZATION OF REGENERATIVE MEDICINE** and contributing to society through its aseptic and automated technologies

**The enormous potential of regenerative medicine** to treat diseases and save lives is just starting to be tapped. Based in Kanazawa, Shibuya Corporation is playing a key role in unlocking this potential through pioneering systems for producing sterile drugs and biologics — pharmaceutical products made from biological systems.

## From sake to stem cells

Shibuya began in 1931 by making bottling equipment for Japanese sake breweries. Over time, it expanded its focus, developing customized automatic bottling and packaging systems for many other industries. Shibuya has now grown into a global business with 3,500 employees and has a global presence in almost all industries requiring aseptic manufacturing and advanced contamination control.

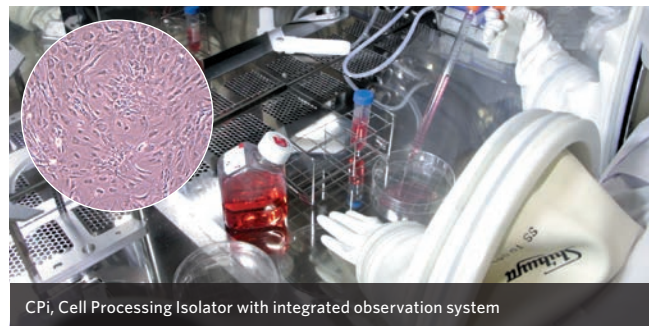
Shibuya's three decades of experience in manufacturing systems for producing pharmaceuticals and biopharmaceuticals can be traced back to the early 1990s

with the demand by drinks manufacturers for aseptic bottling systems, notes Hidetoshi Shibuya, the managing director of Shibuya Corporation and grandson of its founder. This led to the company introducing its isolator technology, which is fundamental to most regenerative medicine systems, and developing the first truly large-scale isolator-based aseptic processing systems for drugs and combination products in Japan.

"Our isolator system is completely closed, and so provides a very safe environment for culturing and processing cells," explains Shibuya. Unlike conventional systems like safety cabinets, where human users are in contact with bioproducts, Shibuya's systems completely isolate people from cells, reducing the risk of contamination to very low levels and thereby minimizing the risk to patients. "Safety is paramount, especially for applications to humans," Shibuya says. "Our isolator is



Shibuya's Advanced Cell Processing Factory



CPI, Cell Processing Isolator with integrated observation system

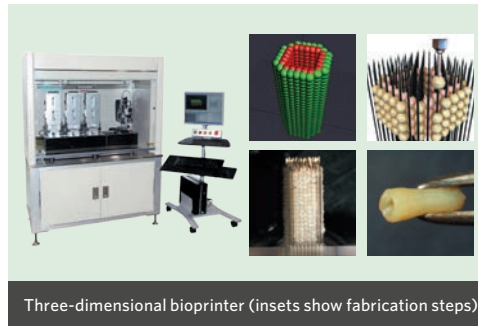
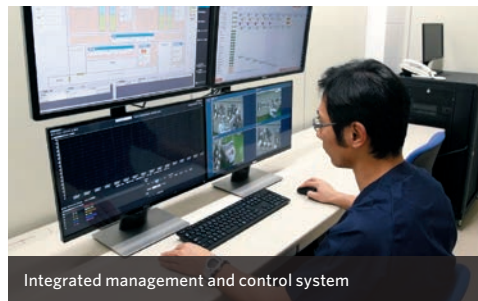
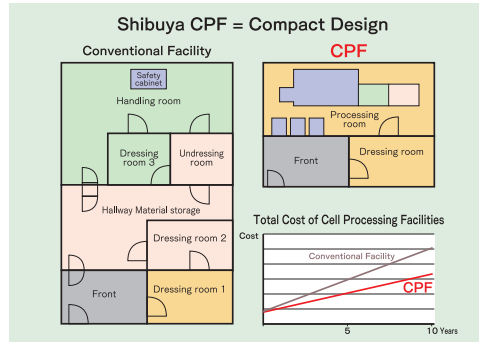
essential technology for those wanting to commercialize their cell products."

In 2004, Shibuya manufactured an isolator for the aseptic processing of embryonic stem cells. The company is now striving to accelerate the industrialization and commercialization of regenerative medicine through its advanced technologies. Its systems for producing cells are used for the entire gamut of cellular therapies under research and development.

## Using robots to manipulate cells

Reducing the role of the human operator even further,

in 2008, Shibuya developed the world's first robotic cell-culture system, which reduces the risk of contamination to unprecedented levels through innovative engineering and creative input from Shibuya's customers. The robot can be sterilized and installed inside the isolator. It can then be programmed to automatically perform cell processing. "This robotic system is being used in a collaborative project with Yamaguchi University for treatments that involve culturing bone marrow from liver cirrhosis patients," says executive officer, Kazuhiro Miyamae.



induced pluripotent stem cells, producing an automated system for culturing mesenchymal stem cells taken from patients with liver diseases (Yamaguchi University) and developing a clinical-grade cell-processing system in conjunction with Promethera Biosciences in Belgium. Shibuya also participates in other research projects by investing in select bioventures.

### Accelerating the safe commercialization of regenerative medicine

Shibuya's isolator-based cell-processing systems provide the highest level of contamination control and product safety that current technology allows. Its systems also significantly lower facility, utility and consumable costs. Furthermore, they reduce the likelihood of product loss, improve space utilization and enhance operator efficiency and comfort. These advantages are making the isolator systems the de-facto standard for cell cultures because of their many technical, regulatory and economic advantages.

In regenerative medicine, the ability to safely, efficiently, reliably and consistently culture cells is essential. Shibuya's long experience in aseptic processing gives it the ideal foundation for developing state-of-the-art aseptic systems for culturing cells. Its technologies are all geared towards advancing and accelerating research and commercialization of cell-based regenerative medicine. ■

### Printing cells in three dimensions

In conjunction with researchers at Saga University, Shibuya has developed a three-dimensional (3D) bioprinter, which has been installed at major universities and research centres around the world. Using an accurate positioning system, the bioprinter can manufacture 3D structures of cells without employing a scaffold. "Our 3D bioprinter just uses stem cells taken from the patient," explains Shibuya. The 3D bioprinter is being used to study the regeneration of bone, cartilage, nerve, bladder and other tissues. And clinicians

will soon start evaluating tissue-engineered blood vessels manufactured using the bioprinter.

### Cell-processing facility

To further improve regenerative medicine, Shibuya has built its own cell-processing centre, which has received approval from the Japanese government. The facility enhances the company's ability to work with collaborators and to continuously improve its products. "We built this facility to support bioventures and research centres that can't afford their own cell-processing facilities. Our facility provides

substantial cost reduction compared to conventional cell processing facilities because of its compact design and integrated management and control system," says Shibuya. "We have also received requests from university researchers to provide cell-culturing support for industrialization of their treatments."

### Combining forces

Shibuya has forged strategic partnerships with research institutions and bioventures in Japan and abroad, including Healios, Cyfuse Biomedical and Promethera Biosciences. These collaborations include culturing

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