

**FOR IMMEDIATE RELEASE**

**Successful automatic culturing of human cell sheets for regenerative medicine of the cornea and esophagus**

*- Completely-closed compact automatic cell culturing equipment prototyped -*

**Tokyo, August 29, 2012** – The Institute of Advanced Biomedical Engineering and Science of the Tokyo Women’s Medical University (“TWMU”) and Hitachi, Ltd. (TSE:6501, “Hitachi”) today announced the successful development of a compact closed automatic culturing equipment for human cell sheets<sup>(1)</sup> used in regenerative medicine. By using this equipment, external contamination is reduced and cells can be cultured automatically in a sterilized environment. The prototype developed has a capacity of 900 liters, floor space of 0.6m<sup>2</sup> and is designed compatible with the GMP<sup>(2)</sup> for safety and quality in manufacturing pharmaceuticals and medical devices. Human cell sheets for the regenerative treatment of the cornea and esophagus were experimentally cultured with the prototype developed, using human cells commercially available for experimental purposes. It was confirmed that cell sheets of equivalent quality to those cultured using conventional manual processes could be achieved.

In recent years, regenerative medicine involving the transplant of reconstructed cell-based tissues or organs is receiving attention as the next major innovation in medicine for the fundamental treatment of defective or damaged tissues or organs. TWMU has developed original technology<sup>(3)</sup> to manufacture cultured tissues as sheets (cell sheets) without damage, and is pursuing fundamental and clinical research to apply this treatment of diseases in such areas as the cornea, heart muscles, esophagus, lungs, gum, cartilage, and liver. To culture cell sheets, conventionally, processes such as the cell seeding or exchange of culture medium which contains nutrients necessary for cell culturing, are conducted manually by a technician. A need exists however, to automate the cell culturing process to raise efficiency, as it is expected that the lack of trained staff and reduction of manufacturing costs will become an issue in the future as regenerative medicine becomes more widespread. Further, as the Ministry of Health, Labour and Welfare

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guideline requires strict maintenance of a clean environment with air conditioning and a log of all processes, the automation of the culturing process within a closed sterile environment is desired.

To address this need, TWMU and Hitachi, participated in the NEDO (New Energy and Industrial Technology Development Organization)'s basic technologies research promotion project for the "Development of nano-bio interface technologies for tissue regeneration implant". In 2006, a prototype partially-closed automatic cell culturing equipment<sup>(4)</sup> was developed and used to successfully culture animal cell-sheets automatically for the first time. From 2009, TWMU and Hitachi participated in the MEXT's (Ministry of Education, Culture, Sports, Science and Technology) project on the "Formation of centers for the creation of innovative mergers of leading edge technologies: CSTE (Cell Sheet Tissue Engineering Center)" and began development of automatic cell-culturing equipment suitable for human cell sheets.

This time, a compact closed automatic cell culturing equipment capable of culturing several human cell sheets at the same time was developed, and used to experimentally culture human cell sheets, verifying its usefulness. An overview of the prototype equipment and culturing experiment are as described below.

**(1) Compact completely closed automatic cell culturing equipment using modularized circuits**

In automatic cell culturing equipment, processes such as cell seeding and medium exchange and other processes in response to cell state, are conducted within the culturing chamber which consists of a culturing vessel and fluid modularized circuits to carry nutrients to the inside of the vessel. In this prototype, processing mechanisms such as the switching vent and pump were removed outside the chamber to achieve a completely closed structure which prevents outside contamination. Further, the vessel was designed as a detachable module so that patient-dedicated vessels can be used, also preventing cross-contamination between patients.

**(2) Human cell sheet culturing experiment for regenerative treatment of the cornea and esophagus**

Using the prototype developed, human cell sheets for the regenerative treatment of the cornea and esophagus were experimentally cultured using human cells commercially available for experimental purposes. The cultured cell sheets were assessed and found to be of comparable quality to those cultured by conventional manual process, thus verifying its usefulness.

Based on the prototype developed, TWMU and Hitachi will proceed with the development of culturing equipment for clinical research to accelerate the spread of regenerative medicine.

- (1) Cell sheet: Cultured cells in sheet form similar to natural tissue
- (2) Good Manufacturing Practice (GMP): A standard established by the US Food and Drug Administration (FDA) in 1938 based on the Federal Food, Drug and Cosmetic Act (FDCA). Many countries have established similar standard based on this, and in Japan, refers to the quality control standard established for pharmaceuticals, etc. established by the Minister of Health, Labour and Welfare under the Pharmaceutical Affairs Act
- (3) TWMU has developed cell culturing dish technology based on their discovery of a thermo-responsive polymer which at reaching a certain temperature changes its solubility in water. In the cell sheet culturing process, the cell sheet can be easily peeled off without damage from culturing dish by controlling the temperature of the dish.
- (4) In the previous semi-closed culturing equipment, a structure was employed where the culturing vessel and fluid ducts were separated.



Fig.1. Prototype completely closed compact automatic cell culturing equipment (volume 900ℓ, floor space 0.6m<sup>2</sup>)

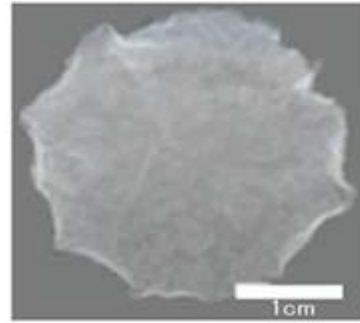


Fig. 2.Cultured sheet using the prototype equipment

**About Hitachi, Ltd.**

Hitachi, Ltd. (TSE: 6501), headquartered in Tokyo, Japan, is a leading global electronics company with approximately 320,000 employees worldwide. Fiscal 2011 (ended March 31, 2012) consolidated revenues totaled 9,665 billion yen. Hitachi is focusing more than ever on the Social Innovation Business, which includes information and telecommunication systems, power systems, industrial, transportation and urban development systems, as well as the sophisticated materials and key devices that support them. For more information on Hitachi, please visit the company's website at <http://www.hitachi.com>.

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