



World Leading Technology

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Ko-58 Mamedahon-machi  
Kanazawa, Japan  
Shibuya Kogyo Co., Ltd.

## **Advanced Regenerative Medicine Treatment for Liver Disease**

### **Patent and Technical Know-how Licensing Agreement between Yamaguchi University and Shibuya Kogyo, Co. Ltd. ("Shibuya")**

Shibuya Kogyo, Co. Ltd. and Yamaguchi University are proud to announce the development of intellectual property created both collaboratively and individually during the creation of the in vitro cell cultivation therapies described below. These therapies have been supported in part by a research grant under the Accelerated Research and Development for Clinical Application of Regenerative Medicine using iPS Cells program from the Japan Science and Technology Agency and Japan Agency for Medical Research and Development.

Background: There are an estimated 300,000 patients with hepatic cirrhosis or chronic liver disease in Japan. Over 30,000 of these are decompensated cirrhosis cases and therefore are considered to be in serious condition (requiring a transplant). In the United States approximately 36,000 deaths annually are attributed to cirrhosis of the liver. To combat these issues, Yamaguchi University began clinical trials utilizing Autologous Bone Marrow Cell infusion therapy ("ABMi Therapy"). This approach was the first of its kind in the world to administer autologous bone marrow cells (without in vitro cell expansion through culturing) into a patient and was approved as an advanced medical treatment (class B designation) by the Japanese government. This non-cell cultivation therapy requires about 400cc of bone marrow be withdrawn from a hepatic cirrhosis patient under general anesthesia. Once the extracted marrow is processed for cleaning and concentration it is drip-infused back into the patient.

In the above scenario, individuals must be healthy enough to tolerate full anesthesia. Because many patients with decompensated cirrhosis are not strong enough to withstand full anesthesia, Yamaguchi University, utilizing Shibuya's state-of-the-art aseptic technologies, developed this cell therapy whereby it is now possible to use only about 30cc of bone marrow, which can be taken from a patient using only local anesthesia. The bone marrow cells harvested from the patient are then expanded to a much more significant number of cells using cell culture under very well controlled processing conditions. The cultured bone marrow cells are evaluated for viability, quality and safety and then drip-infused back into the patient intravenously. This in vitro approach dramatically increases the quantity of bone marrow derived mesenchymal stem cells (MSC's) over a 3-week period.

Shibuya has installed its robotic aseptic chamber (or isolator) cell culture system at the Yamaguchi University Center for Development and Application of Regenerative Medicine, which is located at the Medical Creative Center campus in Ube City. Yamaguchi University and Shibuya are jointly conducting further development of cell culture methods using the combination of robotics with advanced aseptic technology.

Note: This is a joint press release by Yamaguchi University and Shibuya Kogyo Co., Ltd.  
Contact: Shibuya Kogyo Co, Ltd. Corporate Publication at 076-262-1495