

Scope

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World's First Automated iPS Cell Culture System

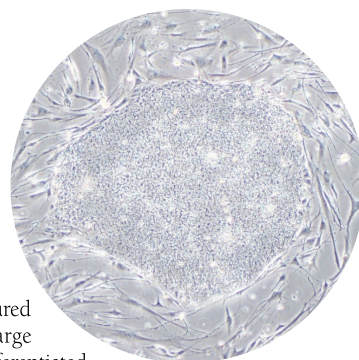
Taking Regenerative Medicine and Drug Discovery to New Heights

When scientists culture human skin cells, they usually get more of the same kind of skin cells. Yet there are some cells, known as stem cells, with the potential to become various types of body cells. Theoretically these cells could be cultured to regenerate new organs and replace a damaged heart or nerve tissue, making the dream of regenerative medicine a reality. Among these "dream" cells receiving significant attention from the scientific community is the induced pluripotent stem (iPS) cell. While an extremely promising cell type, research has only just begun to scratch its surface.

Kawasaki recently developed the world's first automated iPS cell culture system jointly with the Japanese National Institute of Advanced Industrial Science and Technology (AIST), and the Japanese National Center for Child Health and Development (NCCHD). It's a revolutionary breakthrough that has leveraged Kawasaki's advanced robotics technology to create a system that will automatically culture and supply a large volume of iPS cells.



iPS Cells Bringing Dreams to Life



Microscopic image of cultured iPS cells. A large mass of undifferentiated cells is required for research.

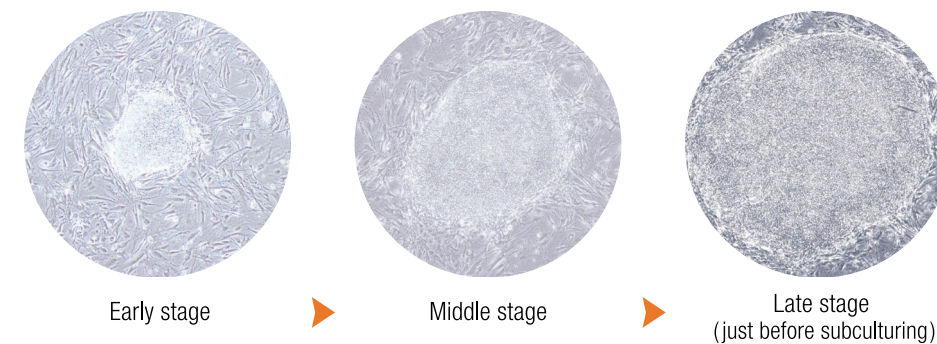
Unspecialized Cells Something Special

The cell that is most well known for having the potential to differentiate into any type of human cell, tissue or organ is perhaps the embryonic stem (ES) cell. An ES cell is derived from a blastocyst, an early-stage embryo. Cells usually acquire the particular features of a specific cell type with special functions, like liver cells, as they grow. ES cells are unique in that they do

not yet have any specialized function, so they have the potential to become any organ or tissue. Research on ES cells once required the use of human embryos that were originally created for in vitro fertilization but were no longer needed. This scientific use of human

Stages of Proliferation

These time-lapse images capture the iPS cell culturing process over a period of a week starting with the onset of cell proliferation (left) until a colony forms (right). Some of the cells are taken from the colony and transferred to another petri dish. This process is called subculturing.



embryos raised major ethical questions and sparked enormous public debate. Then in a 2006 breakthrough discovery, Professor Shinya Yamanaka of Kyoto University was able to create iPS cells with the same characteristics as ES cells, putting the divisive issue to rest.

iPS Cells Derived from Human Skin Cells

After introducing four specific genes into a human skin cell, Professor Yamanaka wound up with iPS cells capable of differentiating into any type of body cell and replicating many times

over. Differentiation is essentially the process by which a cell without any specialized functions becomes a more specialized cell type, such as the cells of our brain, liver and muscles.

Human iPS cells are made from terminally, or completely, differentiated body cells. When

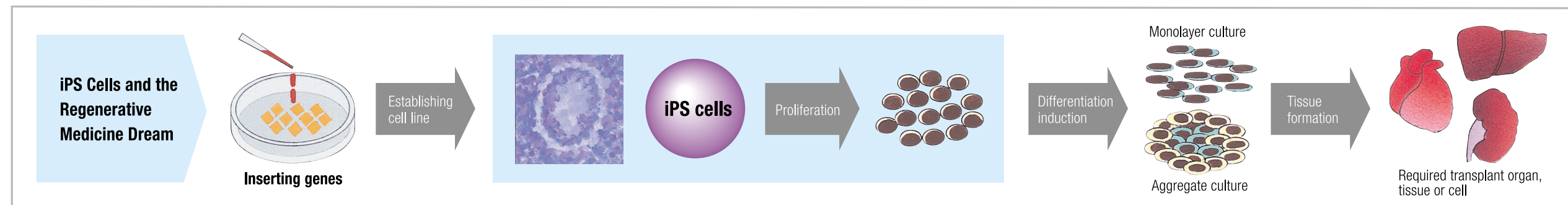


About the Cover
The clean robot performs automated operations inside the automated iPS cell culture system. See Frontline for the story.

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Scope

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the four genes are introduced into these cells, they are reprogrammed into undifferentiated cells dubbed "iPS cells." The downside to this complex process, which is very much akin to reversing time, is that the iPS cells may exhibit unstable characteristics compared to ES cells. The upside is that the discovery of iPS cells has solved the ethical dilemma surrounding stem cell research since these cells are made from skin, blood and placenta cells, rather than from blastocyst.

This pioneering work on iPS cells has made the long-held dream of regenerative medicine a possibility, turning theory into reality. Although research is off to a promising start, this is just the beginning. Further research is needed to find better ways to create iPS cells, identify ideal conditions for culturing them, and maintain their pluripotency. A universal standard for iPS cells as well as techniques for ensuring their

mass cultivation and supply must be established before they can be used in regenerative medicine and pharmaceutical development.

● **Creating Disease Models for Drug Development**

Human iPS cells are shedding new light on the research and development of new drugs. Drugs used to treat heart disease can typically cause side effects like irregular heartbeats and more. In the near future scientists will be able to proliferate, or culture, a large number of iPS cells to form pulsating cardiac muscle cells, which can be used to test a new drug in the pipeline and see if it will cause irregular heartbeats or other side effects. This means researchers will be better able to select drugs that are safe and effective. Today hopes are higher

than ever as the arrival of iPS cells is expected to pick up the pace of pharmaceutical research and development.

● **iPS Cell Culturing Tricky, Even for Old Hands**

Cell culture processing generally involves the use of cylindrical dishes, called petri dishes,



Cell culture operations are largely done manually by experienced researchers.

containing a culture medium (solution). Once the iPS cells are placed in petri dishes, they start to proliferate.

Cell proliferation is a complex and labor-intensive process. The culture media need to be replaced every day. Researchers must use a special microscope to observe the cells as they grow. Once the cultured cells reach the maximum capacity of the petri dish, some cells must be taken out of the petri dish and transferred, or passaged, to a fresh petri dish. This process is known as subculturing.

The fact that iPS cells differentiate so readily makes the already complex task of culturing that much more difficult. Even if researchers working manually can successfully complete a series of cell culture procedures once, it's almost impossible to deliver a repeat performance. That's why a reliable automated system for culturing a large quantity of cells under controlled conditions that minimizes human error is so crucial.



Automated cell processing system (2.2 m wide, 2.1 m high and 1.4 m deep)

Innovative System for Stable Mass Culturing of iPS Cells

● **Proven Effective Over a Three-Month Period**

The automated iPS cell culture system developed jointly by Kawasaki, AIST and NCCHD under an R&D project commissioned by the New Energy and Industrial Technology Development Organization (NEDO) is a revolutionary system that realizes the stable mass production of iPS

cells without the assistance of an experienced cell culture expert.

The R&D project began in the spring of 2009 in cooperation with AIST's Research Center for Stem Cell Engineering. Over the past year Kawasaki has conducted a battery of tests using iPS cells created by the NCCHD's Department of Reproductive Biology that have

successfully demonstrated the system's ability to automatically culture cells continuously and stably over a three-month period.

● **Fully Automated by Clean Robot**

Preprogrammed for a variety of culturing conditions, the automated cell culture system is

capable of processing various types of cells. It can even process cells for which culture conditions have not been preprogrammed.

Once iPS cells are manually placed in the system, a clean robot transports them to the incubator and prepares reagents and other consumables. The scheduling of cell culture operations is also done robotically. All tasks that take place inside the system, from replacing the media in the petri dishes to monitoring cell status and recording observed images, are performed entirely by the clean robot.

The robot also has the ability to perform delicate operations during the subculturing

process, like carefully removing iPS cells that are prone to proliferation at the bottom of petri dishes without damaging them. Employing imaging analysis to automatically identify whether a cell is differentiated, the system effectively proliferates only undifferentiated cells needed for research.

● **Fueling iPS Cell Research**

Kawasaki's new state-of-the-art automated system is providing easily reproducible conditions that deliver stable cell culturing performance and cell quality. It saves not only on labor but also cost, as it enables

researchers to focus their energies on important research work.

The automated iPS cell processing system is currently in operation at the NCCHD, where it is being used to culture iPS cells as NCCHD researchers assess its performance.

Kawasaki has received top honors for its automated cell processing systems. It took home the Robotics Society of Japan's 15th Technical Innovations Award and was one of the twelve first-prize winners at the 4th Robot Award ceremony jointly sponsored by the Ministry of Economy, Trade and Industry and the Japan Machinery Federation.



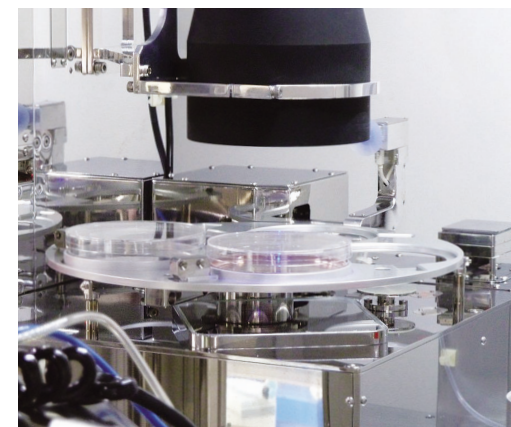
Reagents and consumables are placed in the system's room-temperature storage unit.



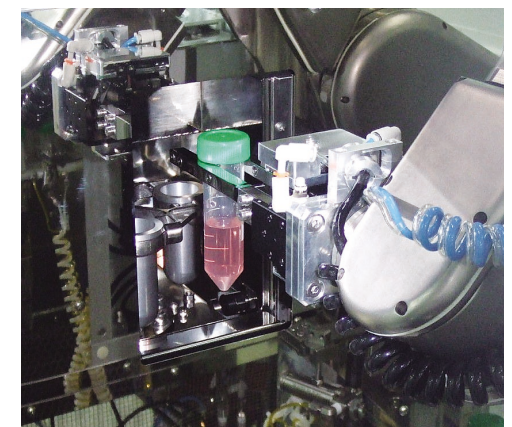
▶ Culture medium (solution) operations performed by the built-in clean robot.



▶ All normal operations performed by the self-contained system's clean robot ensure a class 100 clean environment.



▶ Cultured cell conditions monitored via the system's image processing function eliminate the need to remove cells from the system.



▶ A centrifugal separator is used for subculturing procedures. The robot efficiently performs delicate operations without damaging cells.



▶ Proliferated cells are collected and readied for retrieval by researchers.

How Forestry Waste Is Fueling a Greener Future



Inside the Woody Biomass Fluidized Bed Gasification Power Generation System

Woody biomass, composed of diseased trees, fallen branches, logging refuse and other wood waste, can be found spread out over vast tracts of forest. While it's nearly impossible to efficiently harvest large volumes of this renewable energy source, small amounts are perfectly suited for small-scale distributed power generation.

The woody biomass fluidized bed gasification power generation system developed by Kawasaki Plant Systems, Ltd. (now the Plant & Infrastructure Company) is a compact small-scale woody biomass distributed power generation system. The system was adopted as an energy conversion system for a pilot project overseen by Japan's New Energy and Industrial Technology Development Organization (NEDO). Installed in the town of Niyodogawa in Japan's Kochi Prefecture, the system was tested over a three-year period beginning in April 2007. The project aimed at building a comprehensive community-based biomass energy system, covering everything from the harvesting and utilization of forestry waste for fuel, and was designed to promote the widespread use of biomass energy. Today the system is running full-swing under the management of the Niyodogawa municipal government.

Steady Synthesized Gas Flow Fuels Turbine

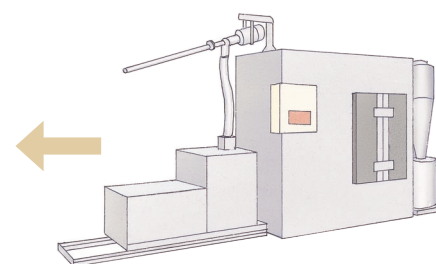
The system, incorporating Kawasaki's proprietary low-calorie gas burning technology, features a fluidized bed gasifier and gas turbine. This unique system is the world's first small-scale woody biomass distributed power system.

Biomass is converted into gas as it is fluidized in the air fed from a double-walled fluidized bed gasifier. Gasification occurs at a relatively low temperature of approximately 650°C. The synthesized gas (syngas), containing combustible gas and tar, flows toward the turbine combustor at an even temperature and pressure. Maintaining the temperature and pressure eliminates the need to remove the tar, which would normally be required in conventional systems, as well as problems associated with tar solidification due to cooling. Tying everything together is the gas turbine, the main engine driving this innovative power generation system.



Pellet utilization

The wood pellets provide an alternative to heavy oil for nearby facilities, including a heated public swimming pool as well as accommodation facilities.

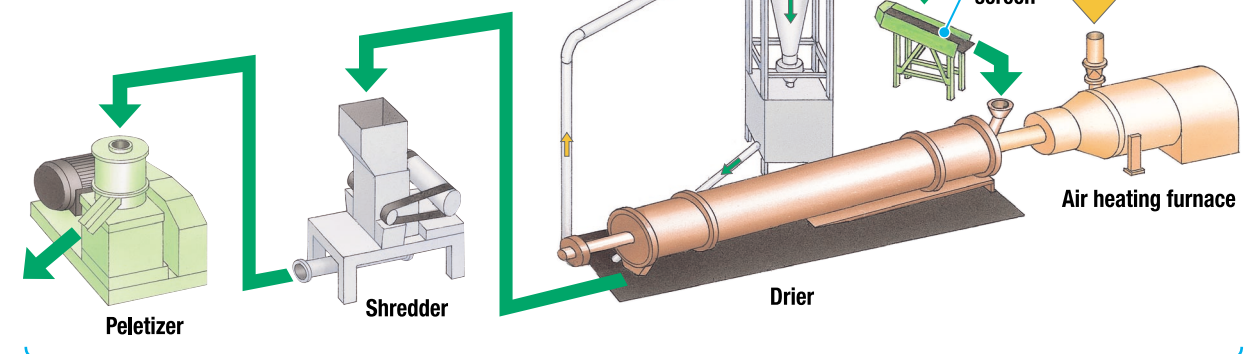


Pellet boiler



Pellets

(6 mm or 8 mm in diameter, 20 mm long, 10% moisture content)



Pellet production unit

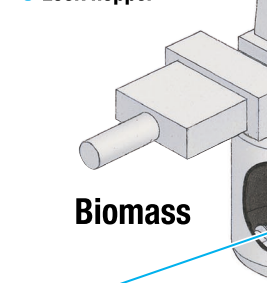
This unit produces 600 tons of wood pellets a year using waste heat from the heat recovery boiler as well as some electricity from the power generation system.



Biomass hopper

Highly-compacted biomass material composed of collected forestry waste ground into pieces of 30 mm or less is fed into the system.

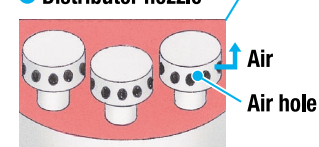
Lock hopper



Screw conveyor

Woody biomass is supplied to the gasifier at 450 kg per hour.

Distributor nozzle



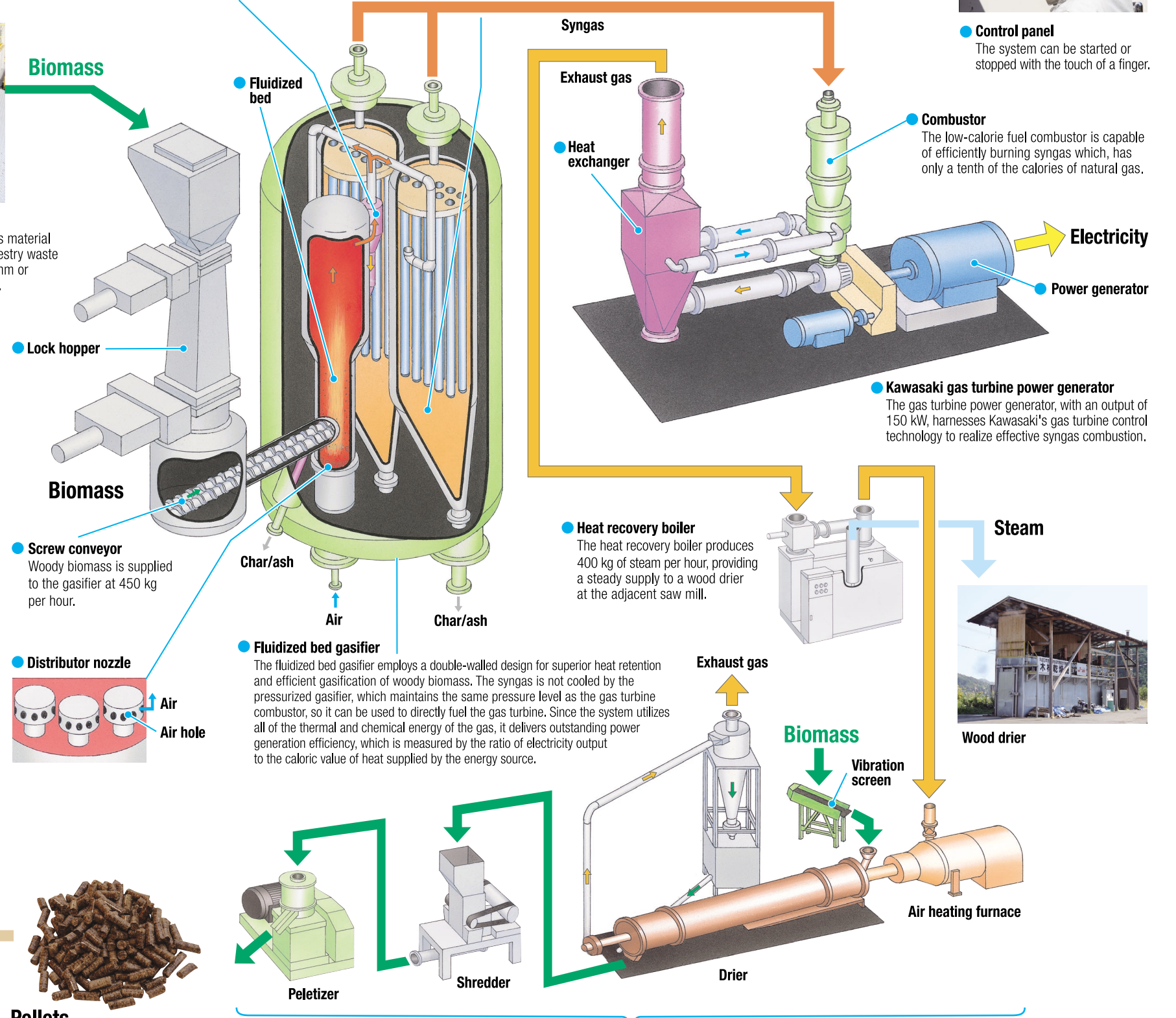
Air
Air hole

Cyclone
Air flows in a spiral pattern inside the cyclone to separate out the char/ash, ungasified carbon material that will be used on organic farm crops, during the primary collection process.

Filter
The high-temperature filter is used for the secondary collection of char/ash. It is made of a flame-resistant material so the char attached to the filter surface can be removed by combustion. The filter is thoroughly cleaned during the combustion process. This eliminates the need for frequent reverse washing, where gas is fed in the reverse direction to remove dust clinging to the filter surface.



Control panel
The system can be started or stopped with the touch of a finger.



Big Send-Off for New Bulk Carrier



The cord holding the vessel is cut and the bulk carrier slowly slides down into the water as the thunderous applause of the crowd is carried away on the wind.

Over 2,000 People Fete Ship's Launch

The mood was festive at Kawasaki's Kobe Shipyard on the morning of August 2010, as everyone prepared for the launch of the new bulk carrier developed by the company. About 2,200 people, including the ship's owners, members of the local community, former and current Kawasaki employees as well as their families, took part in this spectacular event. The scene was a familiar one at the shipyard, where

newly minted ships are named and launched with a celebratory splash several times a year.

An Ocean Colossus is Born

The clock struck 11:00 a.m. and everyone focused their attention the podium. The ceremony began with the Japanese national anthem, played by a brass band, while the flags were hoisted overhead. The minute the person standing on the ship's foredeck proclaimed, "I name thee *Ocean Colossus*," the audience erupted in thunderous applause as a

red and white banner fell, unveiling the magnificent name painted across the ship's bow.

The vessel was then prepared for launch. A whistle blew and like clockwork the safety locks, called dogshores, and blocks were removed one by one. Next the cord that held the ship in place was cut. This was the moment everyone had been waiting for.

The instant the cord was cut, the remaining safety locks, a.k.a. triggers, were released and the vessel started to slide down the slipway.



After the vessel's name is pronounced, the red and white banner is lowered to unveil the name *Ocean Colossus*.



The minute the cord is cut a bottle of Japanese sake is broken over the vessel's prow amid a shower of streamers, and the latest Kawasaki cargo ship begins its descent.

After a bottle of sake was broken over its prow, the ship descended into the water. A ball above the prow burst open in a shower of streamers while balloons in a rainbow of different colors were released into the clear blue sky. The bulk carrier continued its slow slide down the 157 m slipway until it finally touched the waters of Kobe Harbor.

Once again the crowd broke into a deafening round of applause as they witnessed the dramatic birth of the *Ocean Colossus*.

protective coatings (PSPC), ensures the highest quality paint.

The *Ocean Colossus* employs the latest in technology to achieve maximum fuel economy, including an energy-saving main diesel engine, highly efficient propellers, the Kawasaki rudder bulb system with fins (RBS-F) installed behind the propellers, as well as a bow designed to reduce wave resistance. These all add up to optimal propulsion performance.

Kawasaki's new cutting-edge 58,000 DWT

bulk carrier has all the outstanding features of its popular 55,000 DWT bulk carrier and more. It boasts not only increased deadweight capacity but also enhanced propulsion performance, making it a market favorite. Kawasaki has already received orders for fourteen 58,000 DWT bulk carriers, including the *Ocean Colossus*.

After being outfitted at the Kobe Shipyard quay, the bulk carrier was completed and delivered to its new owner in October 2010.

Fully Compliant with New Hull Strength Rules and Coating Performance Standards

The *Ocean Colossus*, built for "K" Line Pte Ltd (a Singapore-based company), is the second 58,000 DWT state-of-the-art bulk carrier to be developed by Kawasaki, but the first to be built at the Kobe Shipyard. The vessel has five holds that are designed for optimum transport of various types of ore, coal, grain and steel products. Its four 30 t deck cranes enable operators to load and unload in ports lacking cargo-handling facilities. The vessel is fully compliant with the new bulk carrier hull strength rules (IACS Common Structural Rules) for enhanced safety. Its anti-corrosion coating, meeting the new performance standards for ballast tank



The *Ocean Colossus* the slipway and glides into Kobe Harbor.

First Test of BPS for International Railways a Success

Kawasaki successfully completed the first overseas test of its Battery Power System (BPS) for railways recently. The BPS employs Kawasaki's proprietary large nickel-metal hydride GIGACELL® battery. The company's Yonkers, New York-based subsidiary, Kawasaki Rail Car, Inc., conducted the test in cooperation with New York City Transit (NYCT) after receiving a grant from the New York State Energy Research and Development Authority (NYSERDA) for the development of new technologies that will increase energy efficiency and reduce CO₂ emissions.

There is a growing need for energy-efficient products to combat a host of problems related to chronic electricity shortages across the U.S. Transit operators like the NYCT need products

and technology that can safely move railcars to the nearest station in the event of voltage drops and blackouts due to electricity shortages.

The three-month-long testing process, which involved installing a BPS between two substations along a stretch of the NYCT's A Line, running through New York City's borough of Queens, demonstrated that the energy generated via the test cars' regenerative braking system could be effectively stored for later use. Energy discharged by the BPS was able to compensate for power loss along the catenary, preventing voltage drops as well as minimizing and stabilizing fluctuations in supply voltage from substations to cut power consumption. When a BPS is installed by a commercial rail service

operating trains that use regenerative braking, the stored energy can effectively compensate for line voltage drops during startup as well as normal and rush-hour operations.

The BPS offers rail operators a sure way to lower overall power consumption and utility expenses, including the cost for new substations. The NYCT gave the BPS high marks during the much-anticipated power outage test for its ability to move a 10-car train a distance of approximately 2.5 km and still keep the air conditioning and lighting systems running while charged to only about 11% of its full capacity. Calculations based on these test results indicate that a fully charged BPS could move a 17-car train to an adjacent station located a distance of 1.2 km away.

Owing to the success of this verification testing, Kawasaki began tests to assess the actual introduction of the BPS for subway lines using the central transformer station for the Manhattan area, which is subject to a serious power shortage, in order for BPS usage to be extended to the various lines in NYCT.

The BPS successfully passed a test run on an Osaka subway line in November 2007 as well. Kawasaki will now leverage these latest test results to market the BPS in Japan, the U.S. and around the world. Also, by working to bring the BPS to the smart grid, an innovative grid technology that maximizes the use of renewable energy, Kawasaki is finding new ways to realize a low-carbon society. ::

*'GIGACELL' is a trademark, or registered trademark of Kawasaki Heavy Industries, Ltd. in JAPAN and the U.S.



Taitar No. 4 LNG Carrier Delivered

Kawasaki delivered the *Taitar No. 4* LNG carrier to NiMiC No. 4 S.A. on October 1. This 289.5 m long carrier (Kawasaki hull No. 1626) is the 12th in a line of internationally acclaimed 147,546 m³ LNG carriers boasting state-of-the-art facilities developed by Kawasaki.

The ship is equipped with four independent Moss spherical tanks with a total cargo capacity of 147,546 m³. The tanks feature excellent thermal insulation performance due to the Kawasaki Panel System, which achieves a boil-off rate of 0.15 percent per day, and are protected against direct damage by double hulls and double bottoms.

Engineered for centralized, single-operator ocean navigation, the wheelhouse is equipped with a state-of-the-art integrated navigation system as well as a 360° view window for enhanced operability. Monitoring and control of cargo handling is done from the cargo control room, which is positioned for the best

view cargo-handling operation. The room is equipped with an integrated monitoring and control system (IMCS) that monitors and controls cargo-handling operations as well as machinery

system conditions. Kawasaki engineered the IMCS for optimal operability by incorporating lessons learned in actual operations and feedback from ship operators throughout the design stage. ::



Marine Diesel Test Engine to Enhance Green Technologies

Kawasaki recently completed construction of a new two-stroke diesel test engine aimed at research and development to boost the environmental performance of its marine diesel engines. Technological development is now underway using the test engine.

The IMO (International Maritime Organization) Tier III NO_x regulations, slated to go into effect in 2016, will make an 80% reduction in present NO_x emissions from marine diesel engines mandatory for ships operating in Emission Control Areas. As a result, engine manufacturers are urgently developing technologies to meet these new regulations.

Kawasaki's new test engine was built at the Kobe Works not only in response to these requirements, but also to meet upcoming regulations that are expected to be increasingly stringent and to use the testing in future engine performance research.

The diesel test engine—an electronically controlled two-stroke engine with twin cylinders 50 cm in diameter—makes it possible to conduct tests under the same

conditions as an actual working engine. Since coming on line in July 2010, the engine has been undergoing testing to determine the



ideal operating conditions to improve the trade-off between the reduction of NO_x and that of CO₂. Development is expected to accelerate in the future as testing is undertaken on engine emissions and performance using the NO_x reduction technology.

Kawasaki will work to quickly incorporate the results achieved with this test engine into its current product lines even as it continues to make further contributions to a better environment through its ongoing development of marine-related technologies. ::

Diesel Test Engine Specifications

Cylinder bore diameter: 500 mm
Cylinder stroke length: 2,000 mm
Turbocharger:
 Variable turbine nozzle ring area
Electronic control system:
 Variable fuel injection control,
 variable exhaust valve timing

World's First Water-Emulsion Fuel System to Undergo Long-Term On-Board Testing

Kawasaki Kisen Kaisha, Ltd., and Kawasaki have jointly developed a new water-emulsion fuel supply system intended for eventual commercial deployment. It was installed in January on a Kawasaki-built 58,000 DWT bulk carrier and will be the world's first to undergo long-term operational testing.

International Marine Organization (IMO) Tier III emissions controls for nitrogen oxides (NO_x) ship emissions go into effect beginning 2016. In Emission Control Areas (ECA), NO_x emissions from diesel marine engines must be reduced by 80% over Tier I levels. To meet these requirements, the companies have jointly developed the water-emulsion fuel system ready for on-board testing. In conjunction with

other NO_x-reducing technologies, this water-emulsion fuel technology will enable ships to meet Tier III controls effectively.

Water-emulsion fuel is fuel throughout which fine water particles have been dispersed. As the fuel is burned in the engine combustion chamber, these fine water particles evaporate and thus capture ambient heat. This reduces the burn temperature, thereby decreasing the production of NO_x.

Ahead of the on-board testing, a reduction in NO_x emissions was already verified last July during shop test operation of the ship's diesel engine using marine diesel oil water-emulsion fuel. The on-board test is using heavy fuel oil water-emulsion fuel for ships.

The on-board testing is intended to verify NO_x and other emissions gases, engine performance, and engine and fuel system durability under long-term use. It will also enable actual operation by the crew. Testing will consist of sea trials prior to the ship's completion, as well as long-term on-board testing once it is commissioned. On-board testing began in January 2011 and continue for four years to evaluate performance and verify durability.

Kawasaki Kisen and the Kawasaki Group are engaged in the active development of new technologies that will contribute even further to improving the global environment. ::

Corrections: The article entitled *A Distinctive Aerodynamic Nose and Bold Crimson-Red Top*, which appeared in the In Focus section of Scope 85, contained several errors. We deeply regret any inconvenience this may have caused. The second paragraph should have read as follows: "The Akita Shinkansen runs on the dedicated high-speed Tohoku Shinkansen Line between Tokyo and Morioka, and continues to Akita on a conventional local line. Because it runs on both the high-speed line and the conventional line, the train is referred to as a 'through-operation type Shinkansen'." On page 9, the first sentence of the second paragraph under *Newly Developed Heater to Melt Snow During Winter* should have read as follows: "Kawasaki has manufactured many through-operation type Shinkansens, such as the Series E3, that run on both Shinkansen and conventional track in snow country." The article entitled *WMATA Orders Series 7000 Rail Cars* on page 10 also contained an error, for which we apologize. The second sentence of the article should have read: "The \$880 million contract covers the manufacture, outfitting, assembly and testing of the subway cars at KMM's Lincoln Plant (Nebraska), with delivery scheduled between 2013 and 2016."

Kawasaki Gallery Heizo Kanayama's World



Mogami River in Oishida, Ca. 1948, 60.8 x 91.0 cm, oil on canvas, from the collection of the Hyogo Prefectural Museum of Art.

A Stroke of Genius

Shusaku Sagara, Assistant Curator, Hyogo Prefectural Museum of Art

Oishida, a tranquil town straddling the Mogami River in Yamagata Prefecture, was one of early modern Japan's most bustling transportation hubs. While waterway transport has given way to today's high-speed Shinkansen train, the town's neat rows of quaint riverside houses testify to its former commercial prosperity.

Oil painter Saburotsuke Okada is credited with turning Oishida into something of a mecca for landscape artists after mentioning it in a travelogue he penned in 1917. Among the many artists who visited the town was Heizo Kanayama, who made his first trip in 1923 and quickly fell under the spell of this charming locale. During the '30s and '40s Kanayama would return time and again to capture the Oishida environs

on canvas in what became practically an annual pilgrimage. After befriending the renowned local poet Mokichi Saito, as well as countless townsfolk, Kanayama finally made the town his official home.

This painting captures a view of the Mogami River as seen from the Ohashi Bridge that connects Oishida with the neighboring town of Yokoyama. Kanayama has drawn from the broad palette of artistic techniques at his disposal to accurately bring the scene to life. The vivid depiction of the trees growing along the river bank and snow-capped mountain ridge in the distance, all reflected on the flowing river's watery surface, come together in a work of art that is, in a word, exquisite.



Heizo Kanayama and Kawasaki

Heizo Kanayama (1883 -1964) went to Europe in 1912, after graduating at the top of his class from the Tokyo University of the Arts. He won the second prize at the Ministry of Education Art Exhibition in 1916, and went on to create many masterpieces in which nature is a recurring theme. Kanayama left an indelible imprint on the history of modern art in Japan.

The Shipyard, exhibited at the Ministry of Education Art Exhibition in 1917 (and featured in *Scope 83*), is the work that first brought Kawasaki and Kanayama together. Toward the end of Kanayama's life, Kawasaki agreed to the artist's request to permanently house 138 pieces of his artwork. Kawasaki has since donated a major portion of this collection to the Hyogo Prefectural Museum of Art.