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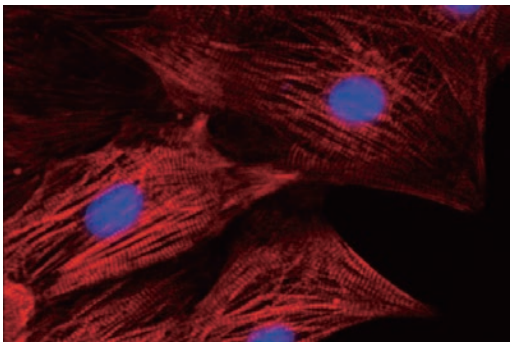
Optimized maturation of cardiomyoctyes enhances cell therapy

The Yoshinori Yoshida lab reports an important maturation stage of cardiomyocytes for cell therapies against ischemic heart.

A diseased or damaged heart is unable to replace its dead cells. Consequently, patients are often left with little option other than heart transplants, which are rarely available, or more recently cell therapies that use cardiomyocytes, which in far too many cases result in poor engraftment and thus poor recovery.

One reason for the engraftment problem is the heterogeneous maturation of the cardiomyoctyes, which are differentiated from pluripotent stem cells such as iPS cells. "Cells of different maturation will be mixed and transplanted together," said Dr. Shunsuke Funakoshi, who was first author of new study from the Yoshinori Yoshida (Associate Professor) Lab that investigated the optimal maturation stage for the transplant, "but heart cells at different stages could behave very differently." Funakoshi therefore considered if a cell population of a specific maturation stage would lead to the best outcome and grouped cardiomyocytes based on the number of days beginning from the differentiation of human iPS cells: 8 days, 20 days and 30 days.

Funakoshi found that among these three groups, cardiomyocytes at 20 days (CM20) proliferated the most upon injection into ischemic mouse heart. Three months after the injection, the cells stopped proliferating and instead began to show signs of maturation for up to six months, as they expressed markers typical of mature cardiomyocytes and also showed organized sarcomere structures. These morphological changes were accompanied by functional changes including improved fractional shortening and a smaller left ventricle compared with untreated mice.



Cardiomyocytes differentiated from iPS cells.

The reasons why CM20 were best is not clear. The authors postulate that cardiomyocytes too immature, such as CM8, do not have the proper size or surface proteins for good attachment in the host environment, while those too mature, such as CM30, are difficult to dissociate from the embryoid bodies, which would compromise their viability and survival after injection.

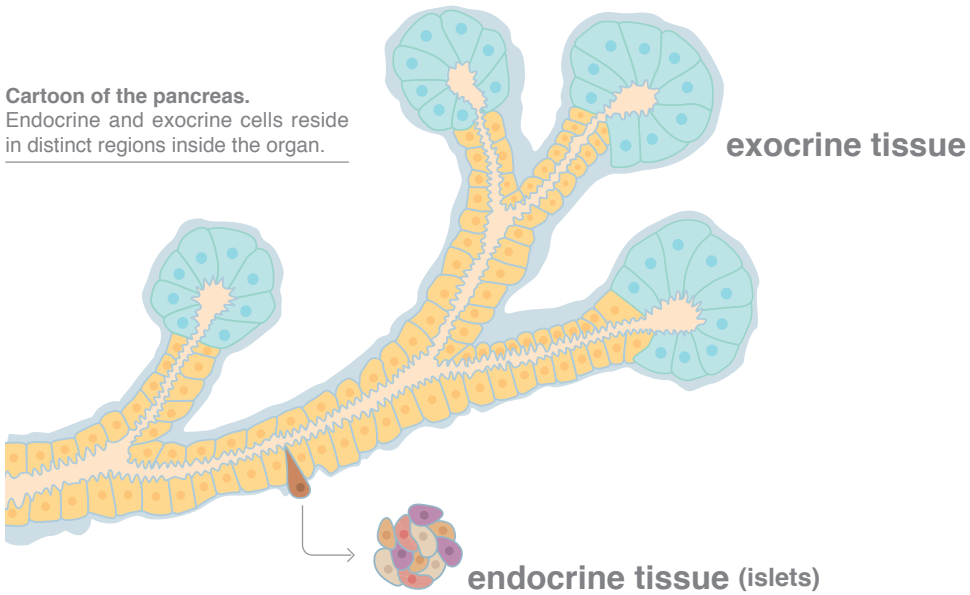
Funakoshi surmises that cell therapies for human heart will also benefit from using an exclusive maturation stage. However, he cautions any extrapolation of studies involving mouse heart, because of the different properties, especially the beating rate. "We need to test animals bigger than mice," he said.

Reference

Funakoshi S, Miki K, Takaki T et al. (2016) Enhanced engraftment, proliferation, and therapeutic potential in heart using optimized human iPSC-derived cardiomyocytes. *Scientific Reports* 6:19111.

Exocrine tissue supports endocrine development in pancreas

The Yoshiya Kawaguchi lab reports a mouse model that suggests a new mechanism for the development of diabetes.

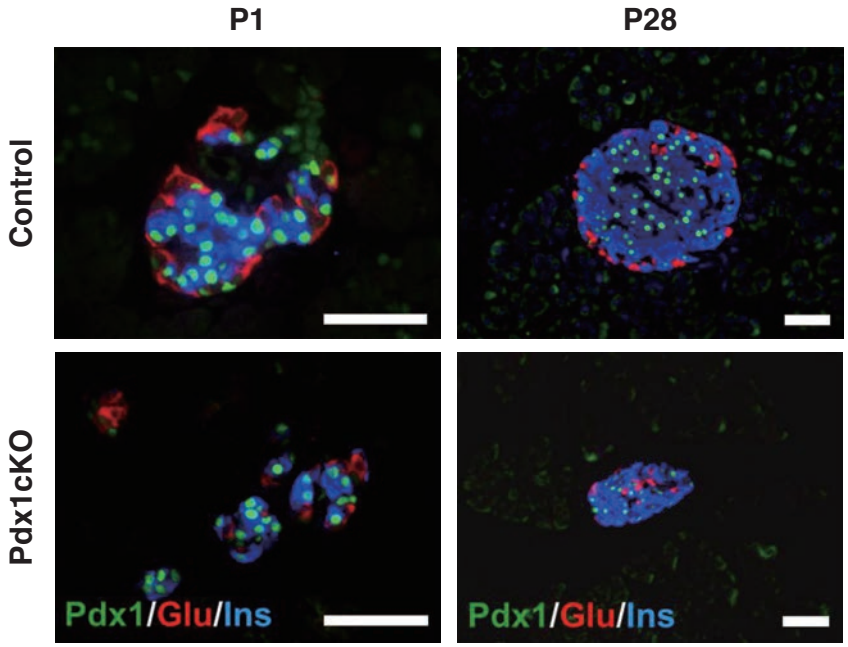


Cartoon of the pancreas.
Endocrine and exocrine cells reside in distinct regions inside the organ.

Diabetes is a disease caused by a deficiency of insulin. One cause is an insufficient number of insulin-producing cells, which are found in the endocrine tissue (islets) of the pancreas. The pancreas is also constituted of exocrine tissue, which secretes enzymes for digestion. Thus, the pancreas can be divided into two distinct structures of distinct functions, making this organ extraordinarily unusual. That said, in adult mouse models, it has been shown that exocrine tissue can stimulate the activation of insulin-producing cells in endocrine tissues after injury. However, regenerative medicines normally function by recapitulating embryonic behavior, and whether these exocrine-endocrine effects occur during development have not been confirmed.

To examine the relationship in more detail, Professor Yoshiya Kawaguchi and his lab have prepared model mice in which *Pdx1*, a gene critical for normal pancreas development, can be inactivated in embryos. The inactivation was achieved by inserting an Elastase-Cre transgene that has high specificity for cells of exocrine lineage. The effect was a smaller pancreas, because *Pdx1* inactivation caused less proliferation and more apoptosis in those cells. Further study revealed that the proportion of cells that were exocrine lineage in the control mice was much less in mice with *Pdx1* inactivated and that these cells were replaced with duct cells.

However, what caught the attention of the researchers was another type of cells that changed with the *Pdx1* inactivation: endocrine-lineage cells, in which *Pdx1* was not inactivated, also decreased in number. More importantly, the mutant mice showed diabetic phenotype, as less insulin was produced. Further, like the



Pancreatic cells at two developmental stages. In control cells, evidence of spatially organized islets can be seen at birth (P1). Full maturation (P28) shows a clear demarcation of different pancreatic endocrine cells, which is representative of the distinct structures of the islet. In mice with *Pdx1* inactivated, however, islets are smaller and the spatial organization is lost. Scale bars = 50 µm.

exocrine-lineage cells, these endocrine-lineage cells showed an increase in apoptosis, indicating exocrine effects on endocrine development. "This was a very unexpected finding," said Kawaguchi, "and suggests non-cell autonomous effects." Based on this result, Kawaguchi theorizes that endocrine development depends on some unknown factor secreted by exocrine-lineage cells. Identification of this factor could promote insulin-producing cells, suggesting that exocrine cells could be a therapeutic means to pancreatic diseases like diabetes.

The paper also reveals some important properties about pancreas development. The proliferation and maturation of endocrine-lineage cells was delayed following *Pdx1* inactivation, but recovered to normal levels weeks after birth. Nevertheless, the islets were not only smaller in size, but also disorganized, a phenotype likely contributing to the poorer function. The differentiation of insulin-producing cells from iPS or ES cells is extraordinarily fickle compared with other cell types, and it has been suggested that the physical structure of the microenvironment makes a significant contribution to their differentiation. While many groups are attempting to directly prepare insulin-producing cells, Kawaguchi argues that the best insulin-producing cells are those created in an environment that recapitulates the pancreas organogenesis. "Understanding how the pancreas develops is key to treating it," he said.

Reference

Kodama S, Nakano Y, Hirata K et al. (2016) Diabetes caused Elastase-Cre-mediated *Pdx1* inactivation in mice. *Scientific Reports* 6: 21211.

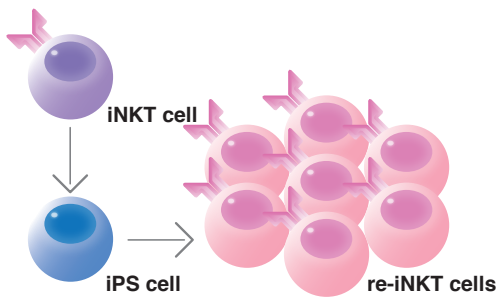
iPS cells reconstitute the immune system to attack cancer

The Shin Kaneko lab uses iPS cell technology to enhance the number of invariant natural kill T cells for future cancer therapies.

One way in which cancer cells flourish is by concealing themselves against cytotoxic immune cells. Invariant natural killer T (iNKT) cells are rare helper immune cells that activate these cytotoxic cells when cancers go into hiding. Indeed, the level of iNKT cells in the blood is a good predictor of clinical outcome.

Effective immune therapies are fastidious, as the immune cells must kill the cancer without harming healthy cells. In cell therapies, the desired immune cells are isolated, expanded, activated and transplanted to the patient. In many cases, however, and especially for iNKT cells, the original number of cells is so low that it is difficult to expand the cells to a useful amount.

iPS cell technology may be able to correct this problem, because iPS cells can be expanded indefinitely. The Shin Kaneko (Associate Professor) lab has taken advantage to prepare reprogrammed iNKT cells (re-iNKT cells), which describe iNKT cells that have been reprogrammed to the iPS cell state, expanded, and then differentiated back to iNKT cells. Importantly, re-iNKT cells show properties that would suggest they could have therapeutic effects against cancer with future study.



Reprogramming iNKT cells. iNKT cells of one type were reprogrammed to iPS cells, expanded and differentiated to iNKT (re-iNKT) cells that showed properties of another type.

Unexpectedly, although the re-iNKT cells behaved like iNKT cells, they showed properties that deviated from their origin. iNKT cells come in several types that can be distinguished by their cytokine production profile of Th1, Th2, Th17, etc. For logistic reasons, the research team reprogrammed iNKT cells that were of the Th2 type, but found that the re-iNKT cells showed properties more consistent with the Th1 type. Further investigation made an interesting observation about the increased potency of re-iNKT cells. iNKT cells are known to activate cytotoxic activity through a NKG2D pathway. While this property was true for re-iNKT cells, re-iNKT cells could also exert their activity through a DNAM-1 pathway. The implications of this finding are not clear yet, but Kaneko thinks it has something to do with re-iNKT cells not expressing TIGIT. TIGIT is thought to indirectly inhibit DNAM-1, and both are normally expressed by iNKT cells.

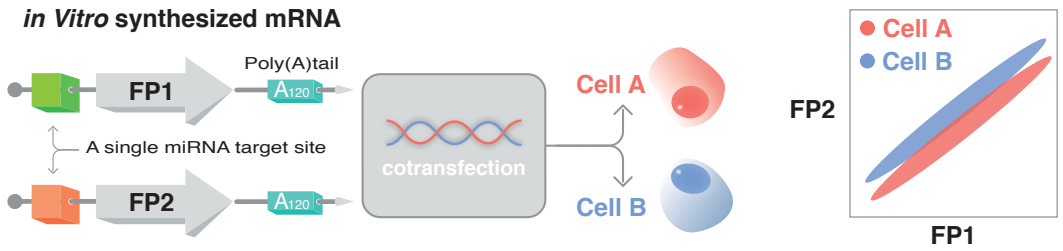
These results could suggest that to get re-iNKT cells, certain steps in normal iNKT development are bypassed. If so, this bypass could provide a new method to prepare immune cells of different potencies for cancer therapy. “Cancer patients usually have severely weakened immune systems,” said Kaneko, “The ability to make potent immune cells is very helpful.”

Reference

Kitayama S, Zhang R, Liu TY et al. (2016) Cellular adjuvant properties and direct cytotoxicity of redifferentiated Vα24 invariant NKT-like cells from human induced pluripotent stem cells.
Stem Cell Reports 6(2): 213-227.

High sensitivity cell sorting for cell therapies

The Hirohide Saito Lab shows how microRNA-based biotechnology can distinguish heterogeneities in cell populations with unprecedented precision.



High-resolution miRNA-based sorting. Two synthetic RNA strands are prepared to include RNA of fluorescent proteins (FP) and a target site for miRNA. The strands are cotransfected, resulting in a constant FP expression levels, but one that depends on the miRNA activity in the cell. This property allows different cell types to be resolved even if the miRNA activity between the cells differs by less than 50%.

The ability to make any somatic cell type from pluripotent stem cells is one reason why iPS cells have become an attractive resource for cell therapies. However, during the differentiation process, the resulting cell population is frequently heterogeneous and includes undifferentiated progenitors as well as cells of different maturation stages. Normally, antibodies and surface receptors are used to sort cells, but the production of antibodies can be both expensive and laborious, and even then the surface receptors to which they bind are rarely exclusive to the desired cell type.

Professor Hirohide Saito has accordingly been using micro RNA (miRNA) as the basis for new biotechnologies serving this purpose. “miRNA can distinguish not only cell types, but also cell states,” Saito explains. The reason, he added, is that not only are different miRNA expressed in different cell types, but their expression level changes with cell development.

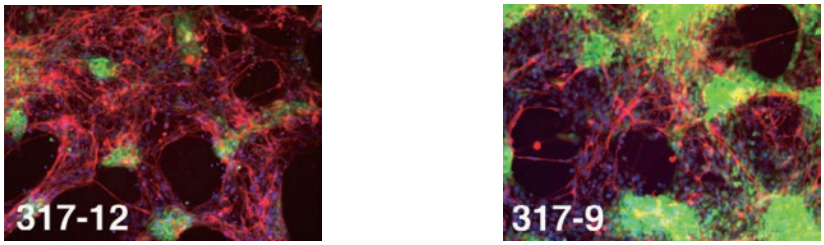
In the newest paper from his lab, Saito and his team report a method to distinguish cells that express miRNA at similar levels. The technique cotransfects synthetic RNA that each carry RNA for fluorescent proteins (FP). Because the FP RNA are cotranfected, the ratio of their fluorescence is constant regardless of the amount of RNA expressed. To separate cell populations, the FP RNA are flanked with a target site that is complementary to different miRNA. Even if the miRNA expression levels differ by less than 50% between cell populations, the researchers show their strategy can separate the cells with extraordinary precision based on changes in the FP ratio profiles due to the different endogenous miRNA expressions. Using two FP and two miRNA complements was enough to separate two different cell types, but increasing the number to three not only separated three cell types, it also separated different subgroups from one cell type. “Based on our calculations, three or four mRNAs can distinguish dozens or hundreds of cell types,” said Saito.

Reference

Endo K, Hayashi K and Saito H (2016) High-resolution identification and separation of living cell types by multiple microRNA-responsive synthetic mRNAs. *Scientific Reports* 6:21991

Protocol for safe and stable gene integration

A new protocol for precise integration of a transgene by the Knut Woltjen lab allows for reproducible transgene expression across different iPS cell lines.



Neurons differentiated from iPS cells. Homozygous alleles (317-9) showed twice as much GFP expression (green) as heterozygous alleles (317-12).

Technically, the easiest method for researchers to integrate an exogenous gene into a cell's genome involves viral or transposon systems. However, these systems integrate in random locations with random frequency. While not a problem when comparing populations, such unpredictability can compromise experiments when comparing individual iPS cell clones. Associate Professor Knut Woltjen and his lab in collaboration with other CiRA groups have recently reported a detailed method that explains how to eliminate the risk of this randomness.

The method depends on genome editing technologies, such as TALEN or CRISPR, to integrate reporter genes, such as GFP and luciferase, into the AAVS1 locus. Importantly, the expression of GFP was sustained after differentiating the iPS cells into different somatic cell types including neurons, cardiomyocytes, neural crest cells and mesenchymal stromal cells. Luciferase adds the potential to track these cells in vivo following transplantation. The protocol was verified in three standard human iPS cell lines.

Besides the reliability of the integration position, the study also shows that the intensity of the expression is scalable if employing the CAG promoter; homozygous iPS cells expressed twice as much reporter as heterozygous iPS cells. Furthermore, the zygosity of the locus had no effect on the pluripotency or differentiation of the cell line, and the expression of the transgene was sustained after 6 months of culturing, indicating long-term stability. Heterozygous iPS cell lines were verified to have retained one normal AAVS1 allele, which allows researchers to target the second allele with a gene of interest.

Woltjen expects that the protocol and materials will be a big aid when reliable transgene integration is required across multiple cell lines. "The reproducibility of gene expression is truly impressive," he said.

The reporter cell lines and gene targeting materials are expected to be available at the Riken BioResource Center later this year

Reference

Oceguera-Yanez F, Kim SI, Matsumoto et al. (2015) Engineering the AAVS1 locus for consistent and scalable transgene expression in human iPSCs and their differentiated derivatives. *Methods* DOI:10.1016/j.ymetho.2015.12.012

Measuring patient motivation in cancer therapy

New criteria provide a method to recognize best treatment options for cancer patients.

It is a dreaded diagnosis – cancer – but one which touches almost every family. Surprisingly, Japan had a tradition of not informing the patient the true diagnosis when cancer was found, instead providing other reasons for the treatment. The country has since become more progressive, but a declaration of cancer does not always result in full cooperation from the patient. There exists evidence that some patients may actually be less inclined to participate in the therapy if aware of their status. This reaction has implications on the recommended treatment strategy, but there remains no reliable way to identify which patients will eagerly participate from those who will withdraw. "Less motivated patients have other priorities. They want to live as they always did. On the other hand, highly motivated patients are ready to discuss all treatment options in detail," said Taichi Hatta of the Uehiro Division for iPS Cell Ethics at CiRA. Hatta, along with other researchers at Kyoto University, has written a report that introduces criteria to distinguish such patients. The authors call these criteria the Achievement Motive Index for Medical Treatment (AMI-MeT).

To examine the validity of AMI-MeT, the authors looked at three Japanese populations: cancer patients themselves, people who take regular health checks, and university students. The AMI-MeT consists of 10 questions, which can be broken down into two categories of equal size. The first describes Self-derived Achievement Motivation (AMS). AMS only assesses the self and ignores any implications on the wider community. On the other hand, Achievement Motivation Derived from Other (AMO) assesses factors like how one's own treatment could benefit others: for example, motivation to collect data that would help medical care practitioners decide which cancer therapy is best in which circumstances.

The study shows that AMS does not differ between the three groups, but that AMO is lower in the university students than in the other two. These results did not surprise Hatta, since university students are generally healthy and do not need medication. The value in the data, he believes, is that they could provide a baseline for recognizing patients who need more encouragement and support to undergo therapy. "AMI-MeT should be useful for physicians to make a strategy for communicating with their patients," he said.

Taichi Hatta

Reference

Hatta T, Narita K, Yanagihara K et al. (2016) Measuring motivation for medical treatment: confirming the factor structure of the Achievement Motivation Index for Medical Treatment (AMI-MeT).
BMC Med Inform Decis Mak Decis Mak 16(1).

Greetings from the
Noriyuki Tsumaki Lab

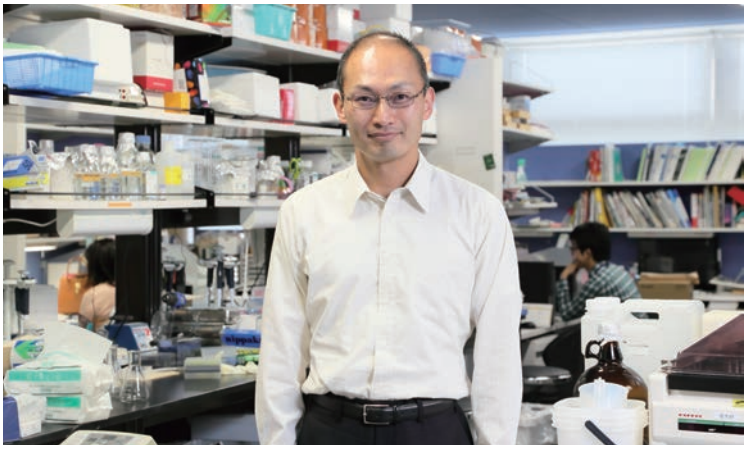
Dept. of Cell Growth and Differentiation

Cartilage wear is a common problem among the elderly and also those who have had trauma to their joints. When articular cartilage, which is the cartilage that lubricates the joints, is damaged, the body's repair system generates fibrous cartilage. The result is painful and less mobile joints. Currently, cell therapy strategies for patients with unbearable or debilitating pain due to insufficient articular cartilage is to take biopsies of chondrocytes, the cells that generate cartilage, from another part of the body and transplant them to the damaged area. The benefits of this approach are limited, however, because the size of the transplant is normally too small. Thus, the chondrocytes must be expanded, but this causes their degeneration, which results in fibrous cartilage formation in the repaired tissue. Plus, the procedure damages the patient's cartilage from which the biopsy was taken.

We are therefore examining iPS cells as an alternative way to produce articular cartilage for cell therapy. We are using iPS cells and differentiation protocols developed in our lab to produce sufficient amounts of curative cartilage without a dependency on biopsies. We have already shown preliminary success of this strategy in rat and pig models and are now investigating more animals with the aim of patient care in the next few years.

Another advantage of iPS cells for cartilage study is drug discovery. Several bone diseases are related to abnormal cartilage development. Because body growth is critically dependent on proper development of cartilage, we are using iPS cells from patients with related diseases to study molecular perturbations and seeking drug compounds that can convalesce the cells. As an example, we found that statins, which are well known for their effects on cholesterol levels, can compensate for abnormalities caused by mutations in the fibroblast growth factor receptor gene 3, which is associated with skeletal dysplasia. Similar studies have revealed other compounds that switch chondrocytes from generating fibrous cartilage to articular cartilage, thus indicating a potential to treat osteoarthritis.

Our iPS cell model is also allowing us to understand the molecular mechanisms regulating chondrocytes. Detailed understanding of these mechanisms, in combination with drug discovery and cell therapy studies, is leading us to a new generation of treatment for cartilage-related diseases.



Noriyuki Tsumaki

Communicating science to the public

Associate Professor Yoshimi Yashiro, Uehiro Research Division for iPS Cell Ethics

At the most recent meeting of the Japan Society for Regenerative Medicine last March, we conducted a discussion about how researchers in the field are communicating their findings to the general public. It is increasingly clear that there exists disconnect between the two groups. Scientists are primarily concerned with conveying their results, which involves explaining complex ideas in a manner that can be grasped by the wider public. The public itself, however, is more interested in understanding how regenerative medicine will impact society at the daily level.

This past January, Japan approved of new policy that considers the relationship between science and technology and society along with promoting new science and technology innovations. Recognizing the importance of strong and sustained public support, the policy puts emphasis on communication. However, as I alluded to above, the content of the communication will need to be adjusted in order to satisfy the information the public demands.

Japan's attention to regenerative medicine took a significant leap in 2013 with new laws. The Pharmaceutical Affairs Law aims to expedite the development of regenerative medicine by putting an emphasis on safety, whereas beforehand translation from the bench to the clinic was viewed as exceptionally slow. Importantly, the law was revised to expand the regulations that applied to medicines and medical equipment to cellular and genetic therapeutic products as well. These changes have garnered large attention around the world and have made Japan an interesting case study to see how regenerative medicine proceeds compared with other nations. However, the emphasis on communication indicates the need for establishing good relations and trust with the public regardless of the scientific outcomes.

Uehiro Ethics Workshop

In its effort to keep the general public informed about the latest in stem cell research, the Uehiro Research Division for iPS Cell Ethics held a workshop, "iPS cell research and iPS ethics," on February 10. Conditional of its support, the Uehiro Foundation on Ethics and Education asks the ethics unit at CiRA to prepare annual events like this one. This year's was held at the Kyoto University Museum, where four of our bioethicists spoke about their research to the 40 people in attendance. Talks included discussion about stem cell science, how stem cell research is conducted throughout the world, and the use of stem cells in private clinics.

Uehiro Research Division for iPS Cell Ethics

Another Marathon Best

The fifth annual Kyoto Marathon was run February 21, and as always CiRA had a number of representatives. Included was Professor Shinya Yamanaka, who ran his third consecutive personal best marathon time. The run was also the last for Kentaro Azuma as a member of CiRA. Azuma had been on loan from the Ministry of Health, Labour and Welfare as a policy expert on regenerative medicine. He returned to Tokyo a week after the run, bringing his three-year tenure at CiRA to an end. He summarized his experience simply, "CiRA was wonderful." Joining the above two were Professor Junya Toguchida, who has run several marathons representing CiRA, and Professors Jun Takahashi and Hirohide Saito, who made their debuts. Donations to these runners is one way in which the public can financially support CiRA.

In fact, beginning this year, CiRA has introduced a new website for donations. Donors can contribute directly through our website, iPS Cell Research Fund, which now accepts donations in English. One can also contribute by visiting Give2Asia. Donations through the CiRA webpage are eligible for tax deductions in Japan, while those through Give2Asia are eligible for tax deductions in the United States and Hong Kong.

1) iPS Cell Research Fund
http://www.cira.kyoto-u.ac.jp/e/about/fund.html

2) Give2Asia
http://www.give2asia.org/ku-ips

Kentaro Azuma (left) and Shinya Yamanaka

iPS Bar in Nagoya

CiRA partnered with Nagoya University to host CiRA's first iPS Bar in Nagoya, Japan's automotive capital, on January 22. Following a brief introduction about iPS cells and CiRA from science communicator Dr. Ayaka Nakauchi, Associate Professor Hidetoshi Sakurai spoke to the 30 people attending the event about Duchenne muscular dystrophy and his use of iPS cells to study the disease.

Hirohide Sakurai at the iPS Bar in Nagoya

Ritsumeikan High School

Along with being home to countless temples and shrines, Kyoto is also home to an inordinate number of universities, which makes the people of the old city rather young. One of the universities is Ritsumeikan University, which has associated with it an international high school. The Akitsu Hotta lab invited 11 students from the school to tour CiRA and see iPSC experiments first hand. “It was great for our students to speak with scientists to gain a better understanding of what a career in science might be like,” said Dave Bohn who coordinated the visit from the Ritsumeikan side.

The Hotta Lab and Ritsumeikan students

UC San Diego-Kyoto University Symposium

Building on the success of last year’s inaugural UC San Diego Kyoto University Symposium in Kyoto, the two institutes teamed again to hold their second, this time in San Diego. The two-day event attended three themes that have grabbed the attention of science policy in the respective nations: alternative energy, cancer and regenerative medicine. This year’s event was highlighted by keynote talks from two Nobel Prize winners, Professors Shinya Yamanaka and Roger Y. Tsien, who won the Nobel (Chemistry) in 2008 for his discovery of green fluorescent protein. Other invited CiRA speakers included Professors Jun Takahashi, Hirohide Saito and Haruhisa Inoue. “It was really interesting to hear about the different diseases they study in San Diego compared to CiRA,” said Chikako Okubo, a graduate student in the Yoshinori Yoshida lab who attended the symposium.

Diplomats

Last February, three dozen diplomats, including ambassadors and science and tech consuls, welcomed Professors Shinya Yamanaka and Noriyuki Tsumaki to Tokyo to discuss the latest in iPS cell research. Accompanying the two CiRA representatives were Gifu University’s Associate Professor Ken-ichi Tezuka and Riken Center of Developmental Biology Project Leader Masayo Takahashi. The event was part of a series that aims to inform the international community of Japan science and technology. Seeing that one of CiRA’s goals is to globalize iPS cell research, it was a rare opportunity for the scientists to appeal to an audience that influences policy in so many countries.

CiRA / ISSCR Symposium

This year, to celebrate the 10th anniversary of iPS cells, CiRA partnered with the International Society for Stem Cell Research (ISSCR) to hold the international symposium, Pluripotency: from Basic Science to Therapeutic Applications. The event was held at Kyoto University and welcomed over 500 scientists to discuss the science of pluripotency, new technologies to study this science, and applications towards disease modeling and new therapies. “I am honored ISSCR chose to celebrate iPS cells in Kyoto,” said Prof. Shinya Yamanaka, who gave the special lecture.

Despite the distance, Kyoto’s place in the field was reason enough for many leading scientists to travel half way around the world even though the symposium only lasted three days. “Every talk was excellent. It was very impressive to see how far stem cell therapy has come and very nice to see the labs,” said Dr. Luc Douay, one of the guest speakers, who came from Paris to discuss his work on red blood cell therapies.

The symposium had been in planning for over two years and was easily the largest CiRA has hosted. “We did not expect such strong interest,” said Etsu Noguchi, who was the lead planner. “The ISSCR put in a great effort to attract so many scientists from overseas.” Along with the talks and 200 posters, the symposium included a Meet the Expert lunch, where four dozen attendees had a chance to discuss their research with the speakers over lunch.

The symposium marks the first in Japan hosted by the ISSCR since 2012, when it had its annual meeting in Yokohama. Nancy Witty, Chief Executive Officer of the ISSCR, commented on the importance of the society’s relationship with the country. “There is a lot of outstanding research here. We benefit from coming to see it firsthand and we hope to hold ISSCR meetings in Japan in future years,” she said.

CiRA / ISSCR 2016 Symposium Speakers

The Temples and Shrines of Kyoto

Heian Shrine

The Heian Shrine has easily one of the most striking appearances to be found in the city. The main entrance sits almost like royalty at the end of a wide, flat road. Immediately inside is a large bare yard of stones in which the only sign of life is a couple of small trees. At the opposite end is a modest entrance to a massive garden (several tens of thousands of square meters) that juxtaposes the yard with its Zen design.

The emperor's move to Tokyo in 1868 is still viewed by some as an affront to Kyoto, which held the honor for over 1000 years. To memorialize the prestige of the city, it was decided the Heian Shrine would be made. Enshrined at the shrine are Emperor Kammu, who had created the city of Kyoto, and Emperor Komei, the last emperor to reside in the city.

The shrine is only a 15-minute walk from the institute, offering both a break from an arduous day of experiments and ideas for new ones.

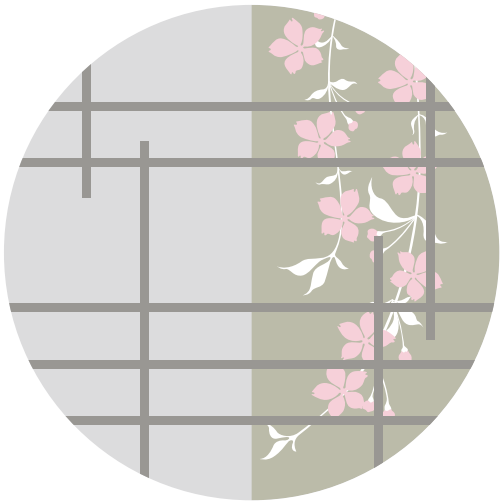
Main gate of the Heian Shrine

pathway to Heian Shrine

Summer Internships

Last year CiRA inaugurated its internship program, which welcomes students of all levels to work at CiRA labs for two months. The internship program will run again this year, with the deadline for applications May 10. Applications and details can be found on our website. The program is funded by the iPS Cell Research Fund.

http://www.cira.kyoto-u.ac.jp/e/education/internship.html



The cherry blossoms

End another winter and

Begin a new year

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