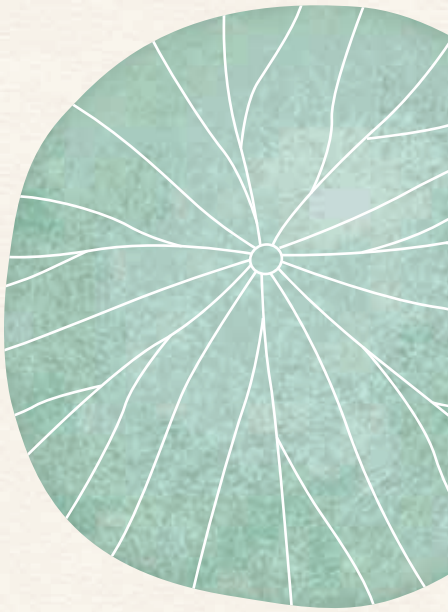
CiRA Reporter

Center for iPS Cell Research and Application,
Kyoto University



Vol.7
July 2016

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Publisher
International Public Communications Office
Center for iPS Cell Research and Application(CiRA)
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53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto
606-8507 Japan

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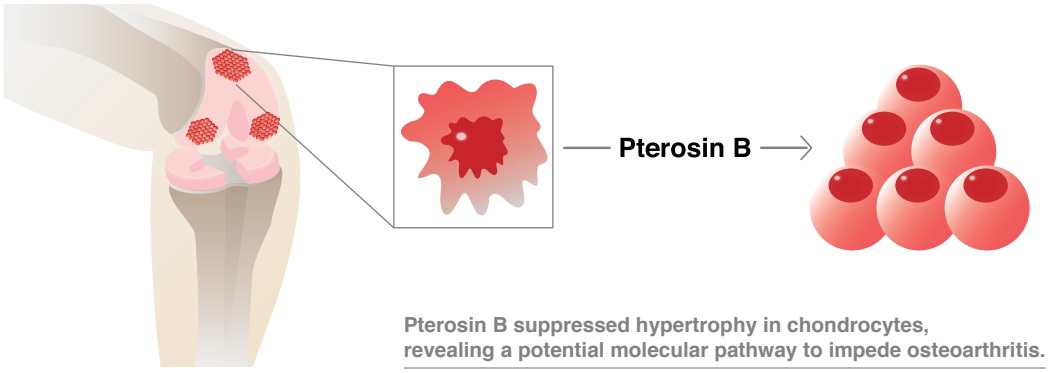
New candidate compound for treating osteoarthritis

The Noriyuki Tsumaki lab reports pterosin B as having positive effects against the progression of osteoarthritis.



Pterosin B suppressed hypertrophy in chondrocytes, revealing a potential molecular pathway to impede osteoarthritis.

Osteoarthritis is the most common form of arthritis and inflicts more than 15% of people over 60 years of age. Most therapies only treat the symptoms, thus the disease progressively worsens in most patients. The reason is that although phenotypically osteoarthritis is described by a loss of articular cartilage, little is known about the molecular mechanisms that lead to the disease. Professor Noriyuki Tsumaki and his lab, which specializes in the study of cartilage, now report a new compound, pterosin B, that shows promise for halting the disease progression.

Chondrocytes are the cells that make up articular cartilage. Articular cartilage can be divided into two zones, non-calcified and calcified. In healthy articular cartilage, only the chondrocytes in the calcified zone show hypertrophy, but in osteoarthritic articular cartilage, chondrocytes from both zones do. Tsumaki and his team wondered whether preventing the hypertrophy program could be a therapeutic measure to counter osteoarthritis. "There are many questions about what causes osteoarthritis," said Tsumaki. "We are considering abnormal chondrocyte homeostasis as a major factor."

The lab had previously reported a mouse model in which they found evidence the molecule Sik3 has an important role in activating hypertrophy. In their latest publication, the team shows how pterosin B, a compound found in certain types of fern, can inhibit Sik3 to prevent hypertrophy. The effects of pterosin B were tested in a mouse model of osteoarthritis and also in cartilage generated from human induced pluripotent stem (iPS) cells.

While their findings about Sik3 and pterosin B do not suggest a remedy for patients already suffering from severe arthritis, they do reveal a new strategy for stabilizing the disease and, in cases of early detection, preventing serious debilitation. "This gives us hope for a drug that targets the disease and not the symptoms," said Dr. Yasuhito Yahara, first author of the study.

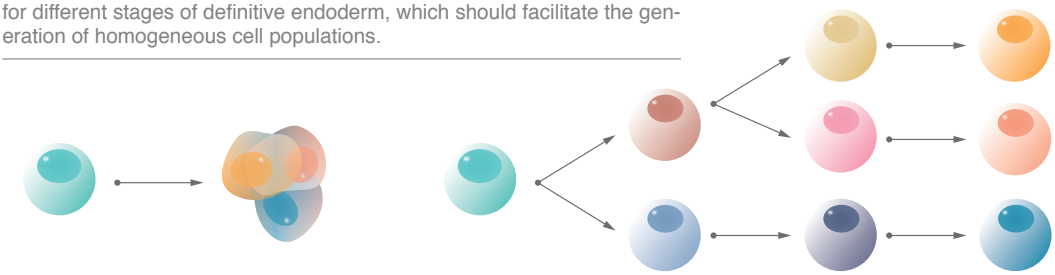
Reference

Yahara Y, Takemori H, Okada M *et al.* (2016) Pterosin B prevents chondrocyte hypertrophy and osteoarthritis in mice by inhibiting Sik3.
Nat Commun 7 doi:10.1038/ncomms10959

Endoderm-lineage organs have distinct progenitors in definitive endoderm

The Kenji Osafune lab clarifies a key debate in the development of endoderm-lineage cells.

A new substage of endoderm development.
(Left) The inability to distinguish different progenitors cells makes it difficult to generate homogeneous cells of endoderm-lineage organs, such as liver and lung. (Right) Findings by the Osafune lab suggest new markers for different stages of definitive endoderm, which should facilitate the generation of homogeneous cell populations.



Although iPS cells can be used to make any type of cell in the body, certain types have proven more difficult than others. In particular, organs such as the lung, liver and pancreas, which all originate from endoderm, have proven problematic. One reason, according to Professor Kenji Osafune, is our poor understanding of endoderm development. "It is unclear if [all] definitive endoderm cells have the same differentiation propensity," he explains. If not, then differentiation protocols using definitive endoderm cells would be ineffective on certain cell subpopulations, which could explain the difficulty in generating the desired cell type. A new study from the Osafune lab shows that, indeed, different developmental stages of definitive endoderm produce progenitors for different cell types. This finding not only has important implications on development, but also stem cell-based therapies.

Until now, the different stages of definitive endoderm had only been postulated, but never observed. Osafune's team, however, took advantage of CHIR99021, a small molecule that was previously used to show the same property is true for mesoderm. By simply changing the concentration of this drug in the differentiation protocol, the researchers were able to show that definitive endoderm derived from human iPS cells could be divided into anterior and posterior definitive endoderm, which resulted in different progenitor cells. The anterior definitive endoderm could be broken further into two groups by adding a second small molecule to the protocol. These two groups could then be differentiated into distinct cell populations that respectively resembled lung and liver cells.

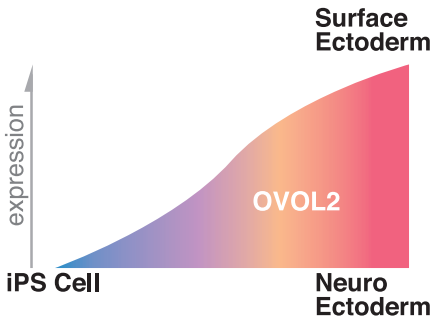
Osafune is excited about the basic scientific impact this finding should have on the study of endoderm development. Moreover, the discovery that endoderm can be divided into different populations of progenitors should also be a key step in preparing different endoderm-lineage cells in the lab for patient care.

Reference

Matsuo K, Mae SI, Okada C *et al.* (2016) Redefining definitive endoderm subtypes by robust induction of human induced pluripotent stem cells.
Differentiation doi: 10.1016/j.diff.2016.04.002

OVOL2 helps generate eye cells in the lab

The Shinji Masui lab reports that OVOL2 is a key factor for ectoderm cell fate.



Increasing the expression of OVOL2 perturbs the ectoderm fate of an iPS cell from neuroectoderm to surface ectoderm.

In its early stages, the embryo will polarize to form cell subpopulations that go on to produce specific organ cell types. The cell subpopulations are defined by transcription factors, which induce or suppress specific genes. Despite the thousands of transcription factors in the embryo, surprising very few are needed to determine a given cell's fate. The Shinji Masui lab, in collaboration with researchers at Kyoto Prefectural University of Medicine, reports that the transcription factor OVOL2 is crucial for the differentiation of human corneal epithelium (CE) cells, the cells responsible for protecting the cornea and defections in which lead to blindness in millions of people.

The discovery of OVOL2 has important implications to developmental biologists. "The ectoderm divides into the neuroectoderm and surface ectoderm," said Masui, with CE cells coming from the surface ectoderm. Cells from the neuroectoderm, on the other hand, will lead to other parts of the eye like the retina. To investigate the regulatory role of OVOL2, the researchers overexpressed OVOL2 in human fibroblasts, which resulted in the cells taking an epithelial-like cell quality. Moreover, Masui's team showed that the overexpression of OVOL2 could even change cells with neuroectoderm fate to surface ectoderm fate. Conversely, suppressing the expression of OVOL2 caused CE cells to show qualities consistent of fibroblasts. "This suggests OVOL2 uses a reciprocally repressive mechanism," noted Masui. In other words, OVOL2 functions to promote genes that stimulate surface ectoderm fate while at the same time it represses genes that promote neuroectoderm fate. This property suggests OVOL2 is a potential factor for direct reprogramming.

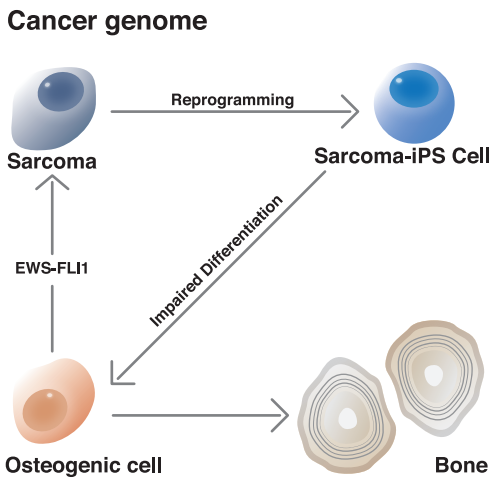
Direct reprogramming has important implications for cell therapies. For all the potential benefits of iPS cells, the time required to reprogram a cell back to the pluripotent state and then differentiating it could make the therapy ineffective if the patient is in urgent need for care, such as for a disease causing rapid vision loss. Further, the reciprocally repressive mechanism of action used by OVOL2 could also lead to the identification of other key transcription factors that determine cell fate. "We can look at which genes are repressed by OVOL2 and look for transcription factors that reactivate these genes," said Masui.

Reference

Kitazawa K, Hikcihi T, Nakamura T *et al.* (2016) OVOL2 maintains the transcriptional program of human corneal epithelium by suppressing epithelial-to-mesenchymal transition.
Cell Reports 15(6):1359-1368

Reprogramming bone tumors

The Yasuhiro Yamada lab reports a new mouse model to study how the EWS-FLI1 gene causes bone cancer.



Reprogrammed osteosarcomas have revealed new targets to obstruct disease development.

Unlike normal cells, cancer cells proliferate uncontrollably, causing their spread throughout the body. This irregular proliferation is often attributed to mutant genes. Professor Yasuhiro Yamada is especially interested in one gene related to bone cancers. "One of our projects is the EWS-FLI1 gene," he said. This oncogene is considered necessary but not sufficient for several bone cancers, which suggests it partners with other mutations to cause the cancer.

To find these other mutations, Yamada used iPS cells. "We can modify the genes of iPS cells and then differentiate them to evaluate the importance of the mutation," says Yamada, but adding, "Most sarcomas are resistant to reprogramming." Fortunately for his lab, he discovered some sarcomas that are not.

To make this discovery, his team conducted an almost desperate experiment. The researchers inserted into ES cells the EWS-FLI1 gene and then inserted these cells into otherwise normal mice. An important feature of the cells is that the EWS-FLI1 gene is not expressed unless activated with an antibiotic, but the mice failed to grow tumors regardless. "This proves that other mutations are necessary," explained Yamada. Proving this point, random mutations were added with the EWS-FLI1 gene, resulting in mice that grew tumors consistent of osteosarcomas when the EWS-FLI1 gene was activated. The researchers then attempted to reprogram the tumor cells into iPS cells (sarcoma-iPS cells), succeeding with two cell lines.

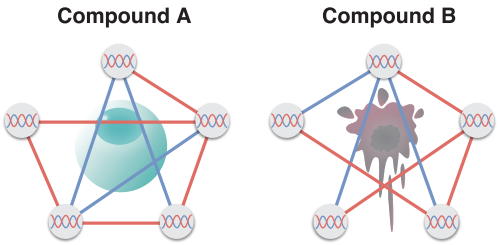
The acquisition of sarcoma-iPS cells allowed the scientists to observe how the additional mutations affect cell differentiation. In sarcoma-iPS cells in which the EWS-FLI1 gene was not activated, no tumors formed but aberrant differentiation was found. "Osteogenic did not develop properly," said Yamada. When the EWS-FLI1 gene was activated, the cells proceeded to form tumors. Yamada surmises that the unknown mutations affect the differentiation of osteogenic cells and that this mechanism is what makes the EWS-FLI1 gene oncogenic. He therefore proposes that the sarcoma-iPS cell lines could be valuable for drug discovery, as chemicals that correct the differentiation could prevent bone cancers from forming even in cases where the EWS-FLI1 gene is expressed. "This platform will be helpful to find small compounds for treatment," he said.

Reference

Komura S, Semi K, Itakura F *et al.* (2016) EWS-FLI1-induced osteosarcoma model unveiled a crucial role of impaired osteogenic differentiation on osteosarcoma development. *Stem Cell Reports* 6(4): 592-606

Machine learning measures drug toxicity

The Wataru Fujibuchi lab reports new bioinformatics that reduces the time and improves the accuracy of drug toxicity prediction.



Different drug compounds activate different gene networks in a cell. Measuring the gene networks with machine learning provides almost 100% prediction accuracy on the toxicity of the experimental drug.

Before a drug reaches the market, it must go through vigorous testing to confirm both its efficacy and more importantly its safety. Conventionally, to evaluate an experimental drug, toxicologists rely on the quantitative structure-activity relationship (QSAR) model. However, too often, drugs that are deemed safe by QSAR in animal models fail in human ones.

The problem with QSAR, according to Professor Wataru Fujibuchi, is that it primarily considers the chemical structure and not the cell activity. "It does not consider the cell. If we switch the cell type, it should not work in many cases," he explained, adding that neglecting cell activity discounts the developmental stage of the cell.

This neglect could have important implications even if a drug passes human tests, since experimentally it is difficult to prepare cells that reflect the wide age groups the drug may serve in the general population.

In its latest work, the Fujibuchi lab shows that machine learning may be more robust than QSAR at evaluating toxic cellular effects.

Although gene expressions are one way to evaluate cell activity, the new method depends on constructing gene networks so that it further considers the interplay between genes. "We wanted to use Bayesian networks because it is more robust than gene expressions," said Fujibuchi.

The research team found that a Bayesian network consisting of just 10 genes was sufficient to predict the effects of a drug candidate. "Ten is kind of low," he said, "I am surprised."

The group tested its model on 20 drug compounds with known toxicological effects, findings its accuracy consistently scored over 97% compared with probabilities that dipped below 80% in some cases that only considered gene activities. Moreover, the results indicated that different information can be acquired by analyzing the gene expressions and networks separately, suggesting a combination of the two could provide more reliable testing.

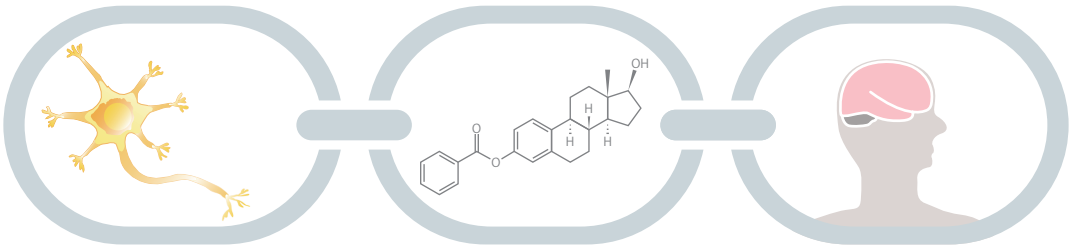
Another key outcome of the study was that the small network of 10 genes significantly reduced the computation time for one test to mere minutes. Considering that each drug needs to be tested at multiple doses and multiple durations, which adds both cost and time to a toxicology test, Fujibuchi is hopeful that this Bayesian network approach will attract collaborations with industry. "I hope many pharmaceuticals will be interested in our work," he said.

Reference

Yamane J, Aburatani S, Imanishi S *et al.* (2016) Prediction of Developmental Chemical Toxicity based on Gene Networks of Human Embryonic Stem Cells. *Nucl Acids Res* doi: 10.1093/nar/gkw450

Two reports suggest ways to improve Parkinson's disease therapy

In separate studies, the Jun Takahashi lab reports that estradiol promotes graft integration with the host and gamma-ray irradiation improves safety.

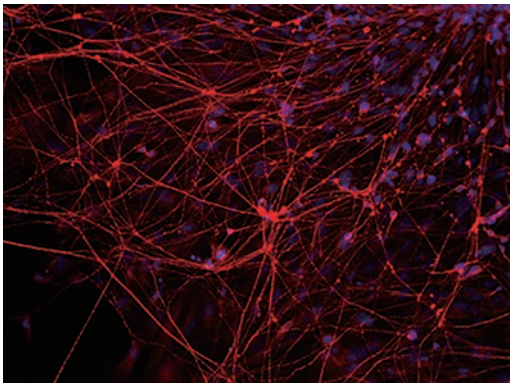


Estradiol enhances the integration of the transplanted cells to the host.

The use of midbrain dopaminergic (DA) neuron progenitors is an established cell therapy for Parkinson's disease (PD). One challenge, however, for successful transplantations is integration of the grafted cells with the host brain. The Jun Takahashi lab has dedicated itself to this problem using iPS cell technology. The lab reports that a derivative of estradiol, an important female sex steroid, offers a pharmaceutical means to promote the integration of grafted cells derived from human iPS cells in rat brain.

In PD therapy, grafts are transplanted in the striatum of the brain. Therefore, to evaluate the effectiveness of the grafts, the authors looked at the activation of striatal neurons post transplantation. They found that successful innervation depended on the expression of integrin α5β1, which has a role in synaptogenesis and synaptic plasticity. Integrin α5β1 operates during development to promote cell adhesion with fibronectin, which could be a way to promote connection between the grafted and host cells. It is also activated via the reelin pathway, which can be modulated by estradiol. Accordingly, the authors experimented with the possibility of activating integrin α5β1 with estradiol-2-benzoate (E2B), finding that doing so further promoted the attachment of striatal neurons with fibronectin and synapse formation with the grafted cells.

Along with these physiological changes in rat brain, the authors also observed behavioral changes. Although all rats showed recovered rotational behavior, a standard measure of PD, with the transplantation of iPS cell-derived DA neuron progenitors, those that also received daily injections of E2B recovered much faster. "It is important to confirm that the rats too show improvement and not just the rat brains," explains



Neurons differentiated from iPS cells.

Dr. Kaneyasu Nishimura, who first authored the report and started a post doctorate position at the Karolinska Institutet (Sweden) earlier last year.

The realization that integrin α5β1 can improve cell therapy outcomes gives invaluable insight on the molecular mechanism in which PD cell therapies function. Other studies have suggested that integrin α5β1 levels are preserved in PD patients, giving hope that activating this molecule will provide therapeutic benefits in humans.

In any stem cell therapy, an important risk factor is the emergence of tumors. Immature progenitors formed by the stem cells have an unacceptably high proliferation rate. It is therefore essential to identify these cells and either remove them from the transplant or suppress their proliferation capacity. Takahashi believes that cell sorting is adequate, but an auxiliary method should also be considered, saying that, "We have never observed tumor formation using our cell sorting protocol, but we want a fail-safe therapy." His group shows such a fail-safe therapy for PD by demonstrating gamma-ray irradiation removes from the graft progenitor cells that could cause tumors.

A graft actually consists of many types of proliferating cells, but it is those that make up neural rosettes that cause the greatest concern. "Neural rosettes are the main contributors to tumor formation," said Takahashi. On the other hand, other proliferative cells will go on to make mature neurons, which will replace those lost by PD. The study shows that the cells constituting neural rosettes are distinguishable by their expression of two protein markers, SOX1 and PAX6. It also reported that the rosettes emerged by 4 weeks after transplantation in rats, but vanished by 14 weeks, giving the scientists a clear time window to conduct the irradiation therapy. Whole-brain radiation treatment on rats at 4 weeks after the transplant inhibited the proliferation of the $SOX1^+$ $PAX6^+$ cells in the graft, but did not affect those that would become mature neurons. "We think it is partly due to a slow proliferation rate" of the other progenitor cells, explained Takahashi.

Takahashi is excited about the implications of this fail-safe therapy for the first iPS cell-based neurosurgery. "We hope to start in the next couple of years," he said.

Reference

Nishimura K, Doi D, Samata B *et al.* (2016) Estradiol facilitates functional integration of induced pluripotent stem cell-derived dopaminergic neurons into striatal neuronal circuits via activation of integrin α5β1. *Stem cell reports* 6(4): 511-524

Katsukawa M, Nakajima Y, Fukumoto A *et al.* (2016) Fail-safe therapy by gamma-ray irradiation against tumor formation by human induced pluripotent stem cell-dervied neural progenitors. *Stem Cells and Development* doi:10.1089/scd.2015.0394

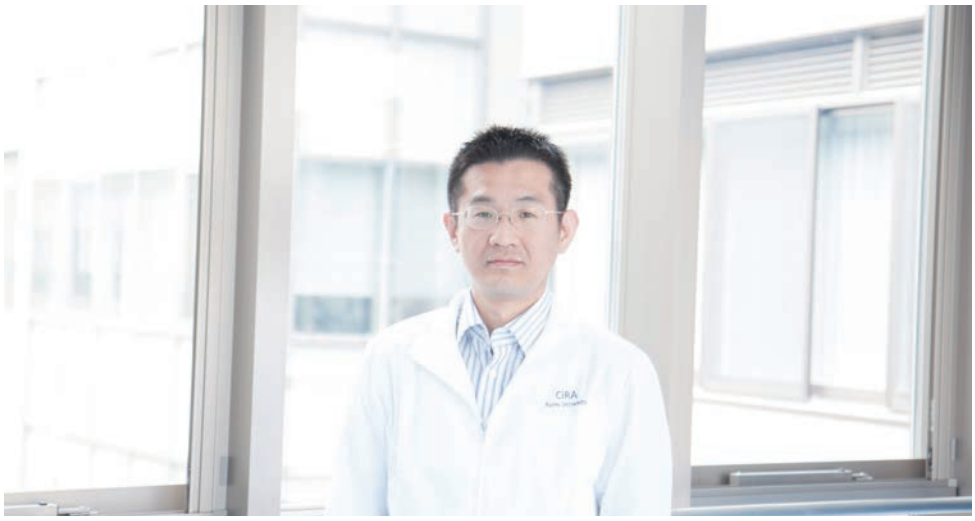
Greetings from the
Yasuhiro Takashima Lab

Dept. of Life Science Frontiers

Although human pluripotent stem cells exist, their pluripotency capacity suggests that they are more differentiated than mouse pluripotent stem cells. The different capacities are commonly referred to as primed and naïve pluripotency, respectively, with the former showing properties that are consistent with mouse epiblast stem cells. In terms of development, mouse naïve pluripotent stem cells, which include mouse ES and iPS cells, resemble the pre-implantation embryo, which can be used to create chimeras. In contrast, epiblast stem cells have more restricted potency and are not capable of forming chimeras. Therefore, intensive research has been devoted to producing human naïve pluripotent stem cells, which would represent the pre-implantation stage and provide a preferred model both for understanding the earliest moments of development and for new regenerative medicine.

With respect to embryogenesis, both mouse and human embryos share pre- and post-implantation stages. However, morphology studies have revealed that the two species have different temporal dynamics in the pre-implantation stage, with implantation occurring later in humans, and different spatial dynamics in the post-implantation stage, with the blastocysts showing different cellular organization. We are investigating these dynamics using culture systems to see if we can uncover clues on how to promote the naïve state from human iPS cells. Our strategy involves working with human and mouse models, as we expect comparative analysis will help reveal which signals are critical to maintaining the naïve state. We also expect this analysis to improve the quality of cells differentiated from human iPS cells. Already, we have created stem cells that are consistent with the pre-implantation state, but the culture conditions used are not optimal for maintaining human naïve cells. Identifying the optimal culture conditions is a major goal of the lab.

We are the newest and a relatively small group at CiRA, with this past April marking our first anniversary. Our lab should therefore be especially appealing to scientists who seek to enter a project from its beginning and drive its direction.

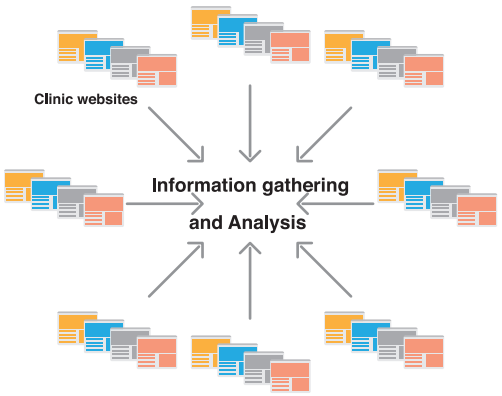


Yasuhiro Takashima

Advertising stem cell therapies in Japan

The Uehiro Research Division for iPS Cell Ethics investigates marketing strategies used by private clinics in Japan.

Inappropriate marketing of stem cell therapies is a high concern among scientists. The unrealistic expectations created could cause public hostility towards these therapies when miracle cures do not arise. The Uehiro Research Division for iPS Cell Ethics at CiRA has been particularly interested in how private clinics in Japan, at which costs are covered 100% by the patient, advertise their services. In its most recent publication, the team shows that clinics tend to give an imbalanced impression, with high emphasis on the positives of stem cell therapies and little elaboration on the risks.



CiRA bioethicists reviewed clinic websites and their compliance with e-health Code of Ethics.

The group did a web search of 24 clinics and evaluated how their webpages describe the offered treatments. They found that not one clinic satisfied the e-Health Code of Ethics (eHCE) prepared by the Japan Internet Medical Association. "Ethicists use these ethics, but the public does not know about them," explains Hidenori Kashihara, first author of the paper, suggesting that the public does not seek any mark of approval from the association when viewing the pages.

In terms of services, a plurality of clinics offered cosmetic therapies, such as anti-aging, but in total one could find treatments for a comprehensive list of illnesses including cancer. Websites also tended to claim that the treatments could be customized to the patient. "We found webpages wrote 'personalized medicine' to make it sound more promising," said Kashihara, who worries that patients could misconstrue these claims to conclude that stem cell therapies are more effective than anything covered by the national insurance plan. More concerning was the absence of any conflict of interests. The eHCE stipulate that sponsorships should be disclosed, but not one of the investigated clinics reported any. On the other hand, the names of universities that collaborated with the clinics for research purposes were easy to find. As too were the names of any media that may have covered the clinics and their services.

Currently, adhering to policies on medical information is primarily voluntary. Kashihara wants his work to be a basis along with similar studies investigating medical information in other nations for internationally consistent guidelines. "Bad stem cell therapies can harm public support and stifle stem-cell based clinical applications," he warns.

Reference

Kashihara H, Nakayama T, Hatta T et al. (2016) Evaluating the quality of website information of private-practice clinics offering cell therapies in Japan. *Interact J Med Res* 5(2):e15.

ISSCR invites CiRA to teach about science communication

Ayaka Nakauchi

The International Society for Stem Cell Resarch (ISSCR) has a webinar series for career development intended to inform young scientists of job options besides scientific research. For one of its latest webinars, the ISSCR invited Ayaka Nakauchi, a science communicator at CiRA, to discuss how she transitioned into this career. Nakauchi was deemed an excellent spokesperson, because she holds a Ph.D. in health sciences, but went straight to communications after graduating from the University of Tokyo in 2014. Her decision to pursue science communication came somewhat late in her studies. “Even when I entered my masters course, I thought I would be a researcher,” she said. During her graduate studies, however, Nakauchi began to reconsider and did several internships both domestic and abroad. These experiences made her realize where her passion lies. “I really like science. I really like communication. For my career, I decided to do both.”

In the webinar, which happened June 3, Nakauchi introduced her work at CiRA and the skillsets she believed crucial for communication, emphasizing imagination. While imagination is important to conceive clever experiments for a scientist, Nakauchi says that having another kind of imagination is important for a science communicator. “I mean the imagination is about how people will react to what you say or write, and we need to realize the best approach,” adding that to understand the audience, “I suppose it is important to remember what was difficult when you studied the science for the first time.”

Despite the extra work and effort presenting in her second language, Nakauchi was very happy to be involved. “I hope – it might be tiny – but I hope my talk could be a little help to young scientists, because when I was a young scientist I was wondering what else I could do.”

New Collaborations

To expedite the use of iPS cells in the clinic, CiRA has been working closely with the Japanese Red Cross Society for the past three years to find donors who will volunteer their cells for the iPS cell stock project. As of April 1st, the Japan Bone Marrow Bank has joined this initiative. By adding this third party, CiRA hopes to recruit a wide range of HLA donors for immune matching, thus expanding the number of patients eligible to receive the iPS cell-based therapies expected in upcoming years.

Japan remains the only country to have conducted a human operation involving the transplantation of iPS cell-derived tissue. The patient, who suffers from age-related macular regeneration, had her skin tissue reprogrammed into retinal cells via iPS cells. Despite the encouraging results, the cost of this autologous operation is prohibitive. To explore allogeneic iPS cell-based surgeries, CiRA formally announced a partnership with Riken CDB, Kobe City Medical Center General Hospital and Osaka University on June 6.

Contemporary Einsteins

To celebrate the 100th anniversary of the general theory of relativity, the Albert Einstein Foundation is publishing the world's first 3D printed book, Genius: 100 Visions of the Future. The Foundation has invited what it considers the 100 greatest minds to contribute. The list is comprehensive and includes artists, scientists and innovators. To express the importance of including CiRA Director Shinya Yamanaka among the 100, the Foundation sent a delegation to Kyoto to extend the invitation in person. The book is scheduled for print and celebration September 2017. The ceremony is planned to have six Nobel Laureates speak and will be held at the Smithsonian Institution in Washington D.C.

Delegates from the Albert Einstein Foundation with members from CiRA

Awards

Junior Associate Professor Masato Nakagawa and Assistant Professor Akitsu Hotta were recognized by MEXT (Ministry of Education, Culture, Sports, Science and Technology) on April 20 for their research. Nakagawa won a prize for Science and Technology in the Development category for his establishment of feeder free culture for ES and iPS cells. Hotta won a Young Scientist's Prize in recognition of his gene editing work to study muscular dystrophy. Both were flattered by the recognition. "I am delighted for the award," said Nakagawa, "and have many people to thank." Akitsu responded similarly. "My research is still at its initial stages. This award will help me push my research to forward."

Masato Nakagawa (Left) and Akitsu Hotta

Cell Symposia

10 Years of iPSCs

September 25-27, 2016, Berkeley, CA, USA

To mark the 10th anniversary of iPSCs, Cell Press will host the symposium: 10 Years of iPSCs in Berkeley, California, from September 25-27, 2016. The invited speakers include CiRA faculty Shinya Yamanaka, Kazutoshi Takahashi and Koji Eto.

For once, the interviewer

Professor Shinya Yamanaka is quite accustomed to being interviewed. On the other hand, he has far less opportunity to hone is interviewing skills. He had a recent chance, however, on Japan's public broadcaster NHK show, "Switch Interview Specialists," which has two famous people of disparate professions interview each other about their careers. Yamanaka appeared last April in a two-part episode with one of Japan's most recognized film stars, Ken Watanabe, who is known for his roles in Batman Begins and Godzilla. Watanabe, like many Japanese, has been captured by the magic of iPS cells. He is also a cancer survivor. Conversely, Yamanaka has been captured by the magic of Watanabe and his films. To film the first episode, Watanabe visited CiRA January 22, where he was given a tour of the facilities by Yamanaka and discussed iPS cell science. They then enjoyed an unusual Kyoto lunch of hot dogs before visiting a local cinema. Yamanaka took advantage of the format to inquire about Watanabe's battle with cancer, their common experience and appreciation of the United States, and baseball. Although he is from Niigata, which is several hours north of Tokyo, Watanabe is a rabid fan of the Hanshin Tigers, the local baseball team of Osaka and Yamanaka's hometown. The team is nationally recognized more for the enthusiasm of its supporters than its performance on the field.

Ken Watanabe (Left) and Shinya Yamanaka ©NHK

iPS Cell Research Fund

This past fiscal year marked the most successful yet for the iPS Cell Research Fund, with donations reaching almost 2.5 billion yen. "We had more than three times donations than fiscal year 2014," gratefully notes Fumitaka Watanabe, who leads the team responsible for the fund. Watanabe attributes the success to a number of reasons, including more media coverage. The increased coverage has pushed a stronger international mandate by the fundraising team. In April, Watanabe visited organizations in New York to discuss the work being done at CiRA and ways to contribute to the institute. "We hope to strengthen our support outside Japan," said Watanabe.

Donations are always welcome through Give 2Asia. Residents of Hong Kong and the United States are all eligible for tax credits.

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

The Temples and Shrines of Kyoto

Ninnaji Temple

Despite its size and recognition as a World Heritage Site, Ninnaji Temple is an often forgotten temple, humbled by neighbouring temples that lie on the same street and attract far more tourists. For the same reason, of the many impressive temples in Kyoto, few offer the same peaceful feel one gets here due to the smaller crowds. The highlight of the temple is easily the Omuno Palace, which holds a vast Japanese garden. The palace was originally constructed over a thousand years ago, but has undergone several renovations due to destructions caused by war and fire. Outside the palace but within the temple grounds is a plantation of cherry blossoms, which a causes a brief surge of visitors in early April. The main gate of the temple is guarded by two menacing deities that each stand over 3 m tall, but now do more to attract tourists than keep them away.

Entrance to Ninnaji Temple

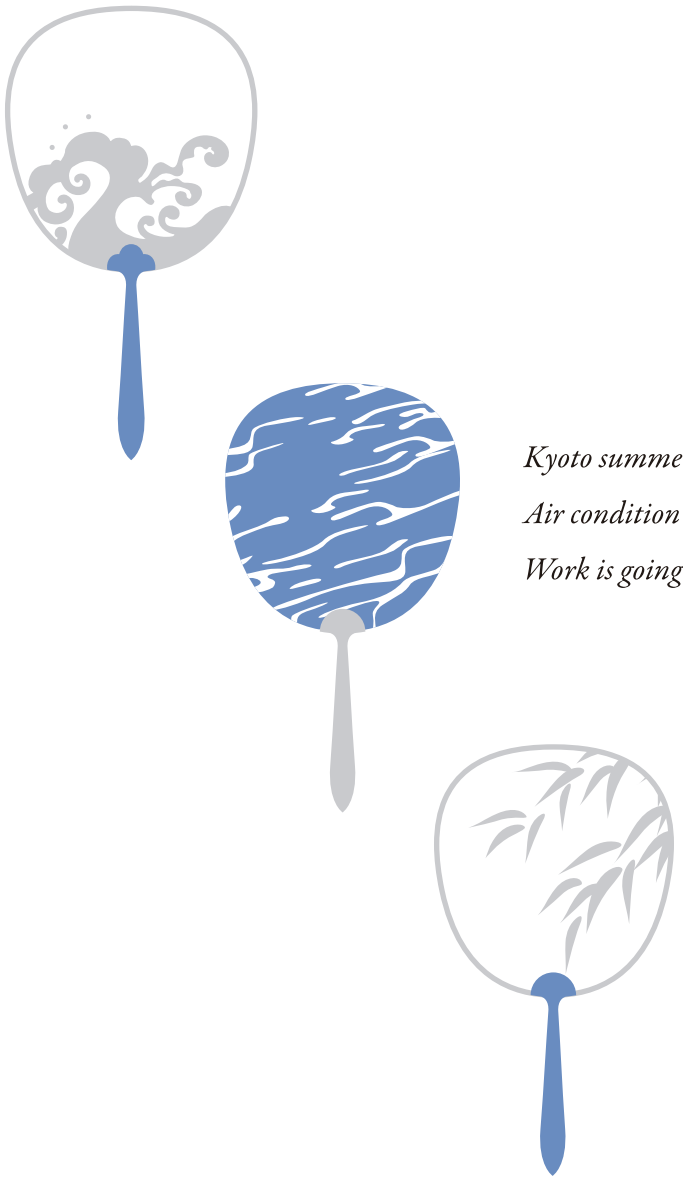
Omuno Palace

CiRA-ISSCR

For those unable to attend the CiRA-ISSCR symposium last March 22-24, Development has published a Meeting Review summarizing the event. The article covers the presentations given by all the invited speakers.

Reference

Karagiannis P. and Eto K. (2016) Ten years of induced pluripotency: from basic mechanisms to therapeutic applications.
Development 143:2039-2043.



Kyoto summers
Air condition in the lab
Work is going well

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Vol.7 | July 2016