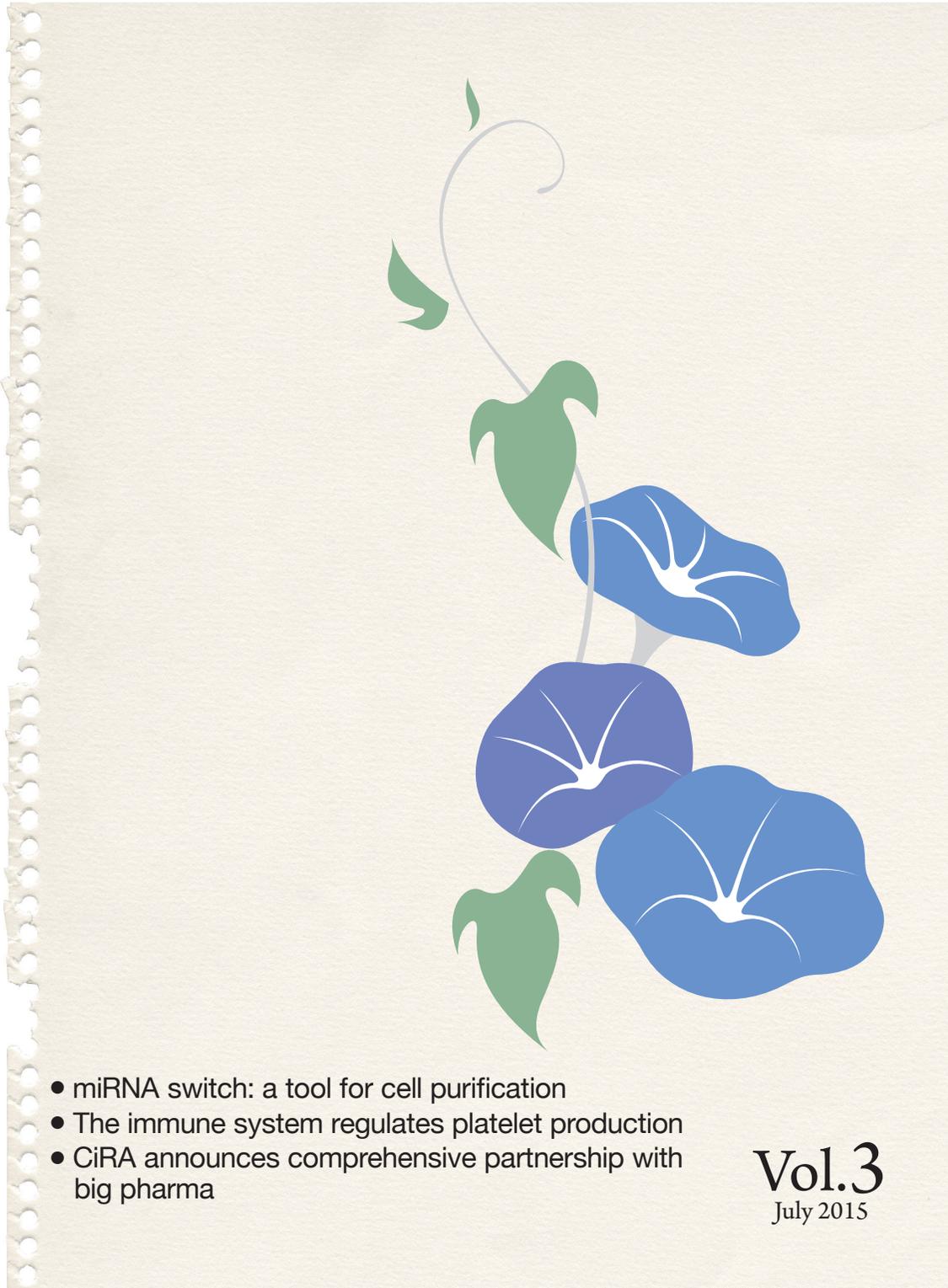


# CiRA

# Reporter

Center for iPS Cell Research and Application,  
Kyoto University



- miRNA switch: a tool for cell purification
- The immune system regulates platelet production
- CiRA announces comprehensive partnership with big pharma

**Vol.3**  
July 2015

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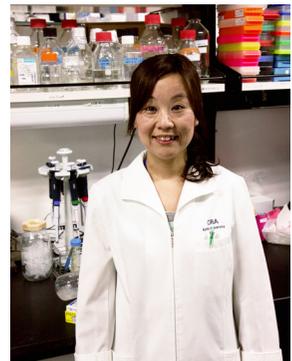
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## An iPSC cell model to study muscle degeneration in infants

Spinal muscular atrophy (SMA) is an autosomal disease that is often recognized in the first six months of life and is considered a leading genetic cause of infant mortality. The disease causes progressive muscle weakness and eventual death. While some patients can survive for decades with the assistance of an artificial respirator, quality of life is severely compromised. Most frustrating to patients and their primary care givers is that SMA is a ravaging disease with no treatment. “SMA patients are intellectually normal but cannot move,” explains Prof. Megumu Saito at the Dept. of Clinical Application, who led a project that included five different CiRA labs and has resulted in a recent report that gives insight about the early phases of SMA progression based on an iPSC cell-based model.



Michiko Yoshida

Although historically the disease has been diagnosed by a loss of motor neurons, the new model suggests that the first defect in SMA is due to an absence of acetylcholine receptors (AChR) clustering at the myotubes. The lack of clustering disrupts communication between the neuron and muscle at the neuromuscular junction, resulting in atrophy of the muscle and consequent motor neuron death.

At the genetic level, SMA is recognized by insufficient production of the SMN protein. In humans, SMN is synthesized by two gene isoforms, *SMN1* and *SMN2*, with approximately 90% of the body's SMN level produced by *SMN1*. However, SMA patients have a deleted *SMN1* isoform, which explains their deficient SMN levels. Lead author and neuro-pediatrician Michiko Yoshida therefore investigated ways that could amplify SMN production from the *SMN2* isoform in iPSC cells derived from SMA patients. She found that AChR clustering could be improved by treating the cells with valproic acid, which increases the *SMN2* expression, or by applying to the cells phosphoro-diamidate morpholino oligonucleotides. These observations “show SMA is not a neuro-degenerative disease but maybe a developmental one,” she suggests. The implications of this finding argue for genetic tests at the fetal stage, since disease onset will have already progressed by birth.

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### Reference

Yoshida M, Kitaoka S, Egawa N et al. (2015) Modeling the early phenotype at the neuromuscular junction of spinal muscular atrophy using patient-derive iPSCs. *Stem Cell Reports* 4(4):561-568.

Online publication: March 19, 2015

## **New biotechnology for high purification of live human cells**

One of the reasons stem cells are so popular in medical research is that they can be differentiated into different cell types. However, typical differentiation protocols lead to a heterogeneous population from which the desired type must be purified. Normally, antibodies that react to surface receptors unique to the desired cell are used for this purpose. However, in many cases the purification levels remain poor and the cells can be damaged. New RNA technology produced at CiRA may avoid these problems.

Prof. Hirohide Saito at the Dept. of Life Science Frontiers is a bioengineer who makes tools to study reprogramming. His latest technology, the microRNA (miRNA) switch, is designed to detect and sort live cells not by surface receptors, but by miRNAs. miRNA is a better marker of cell types and can therefore improve purity levels. His miRNA switch consists of synthetic mRNA sequences that include a recognition sequence for miRNA and an open reading frame (ORF) that codes a desired gene, such as a regulatory protein that emits fluorescence or promotes cell death. If the miRNA recognition sequence binds to miRNA expressed in the desired cells, the expression of the regulatory protein is suppressed, thus distinguishing the cell type from others that do not contain the miRNA and express the gene marker.

Senior Lecturer Yoshinori Yoshida is a cardiomyocyte specialist also at the Dept. of Life Science Frontiers who immediately saw the potential of this technology. He has been studying how iPS cells can be used to combat cardiac diseases, but has been stymied by unsatisfactory purity levels. Cardiomyocytes are especially difficult to purify, because they do not express unique surface receptors. He and Saito therefore collaborated to investigate the effectiveness of miRNA switches for these cells. By applying the miRNA switches to a defined cardiomyocyte cell line, they were able to identify miRNAs unique to cardiomyocytes. From there, miRNA switches that contained sequences



Hirohide Saito and Yoshinori Yoshida

complementary to these miRNAs were constructed. The result was far better purification than that achieved by standard methods. Furthermore, because this technology is RNA-based, it does not integrate into the genome, which makes the cells safe for clinical application.

Yoshida sees this tool as remarkably simple and something that can be used by stem cell researchers studying any organ. “It is just synthesizing RNA and transfecting them. It is not difficult,” he said. To prove this point, he and Saito extended their application of miRNA switches to the purification of hepatocytes and pancreatic cells, which like cardiomyocytes also lack unique cell surface markers, finding miRNA switches effective there too.

Intriguingly, the performance of different miRNA switches varied with cell development, suggesting that strategic selection of miRNAs could separate cardiomyocytes at different developmental stages. Yoshida believes this property could make cell therapies even more effective. “We may find that certain cell subpopulations give better results,” he said. Saito is optimistic that with further development, miRNA switches will be applicable to all cell types at all cell stages. “We want to make an active miRNA dictionary for each cell type, so that if we want to isolate this kind of cell type, we know to use this kind of switch,” he said.

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**Reference**

Miki K, Endo K, Takahashi S, et al. (2015) Efficient detection and purification of cell populations using synthetic microRNA switches. *Cell Stem Cell* 16(6):699-711.  
Online publication: May 21, 2015

## The immune system may regulate platelet synthesis



Koji Eto

In the standard model of thrombopoiesis, thrombopoietin (TPO) initiates a series of events that leads to the differentiation and maturation of megakaryocytes and finally the shedding of platelets into the blood stream. However, quantitative studies suggest that while this model explains homeostatic levels of platelets in the body, it does not adequately explain how the body rapidly produces the necessary number of platelets in response to acute wounds. Recent work by Prof. Koji Eto and his lab at the Dept. of Clinical Application gives new insight on this question. In collaboration with researchers at the University of Tokyo and Jichi Medical University, the group used two-photon microscopy to directly observe platelet production in the body, finding

there exists a previously unknown TPO-independent mechanism that depends on the immune system and activates upon acute trauma.

The mechanism operates using the caspase-3 signaling pathway and is triggered by the cytokine interleukin (IL)-1 $\alpha$ . IL-1 $\alpha$  is an inflammatory signal and offers a clue as to why acute inflammation is accompanied by an increase in platelet levels. “It remains a mystery why inflammation is associated with platelet numbers,” Eto says. In the TPO-dependent mechanism, megakaryocytes grow in size and extend proplatelets, which penetrate into the blood stream where they are eviscerated into smaller fragments – platelets – by the blood flow. In the TPO-independent mechanism found by Eto and his colleagues, IL-1 $\alpha$  causes irregular changes in the morphology of the megakaryocyte, which leads to the cell rupturing and releasing platelets much faster than otherwise. The rupturing is attributed to a weaker membrane and results in a 20-fold increase in platelet count within an hour of the mechanism’s initiation. IL-1 $\alpha$  also promoted megakaryocyte ploidy and maturation, two phenotypes thought to correlate with platelet numbers. Although the platelets generated from this caspase-3 system tended to be larger than those generated by the TPO-dependent mechanism, they nevertheless demonstrated good function.

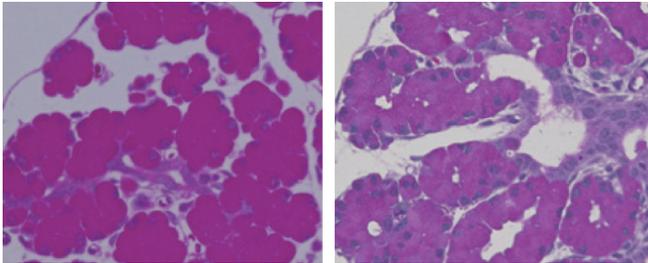
The work is the first to show direct evidence that inflammation-related cytokines, and by extension the immune system, regulate thrombopoiesis. Eto is curious about how strong this relationship is. “It will be interesting to see if other interleukins have similar effects,” he says.

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### Reference

Nishimura S, Nagasaki M, Kunishima S et al. (2015) IL-1 $\alpha$  induces thrombopoiesis through megakaryocyte rupture in response to acute platelet needs. *Journal of Cell Biology* 209(3):453-466.  
Online publication: May 11, 2015

## Notch signaling promotes centroacinar cells



Normal development of acinar structures show homogeneous structures (left). Knockout of Notch ligands causes loss of centroacinar cells, leaving holes in the impaired acinar structure (right).

The pancreas regulates both glucose levels and digestion, which are respectively endocrine and exocrine processes. Structurally, islet cells are responsible for the former, while acinar and duct cells operate the latter. Accordingly, many researchers view these functions and the respective structure of the pancreas as distinct. However, Prof. Yoshiya Kawaguchi at the Dept. of Clinical Application thinks the pancreas is oversimplified when treated this way. “The endocrine and exocrine pancreas are specified and form at the same time in development, yet we know much less about the exocrine pancreas,” he explains.

In a study that gives insight into exocrine pancreas development, Kawaguchi reports a new role of Notch signaling. Kawaguchi’s strategy was to focus on centroacinar cells, as some believe these cells function as progenitor cells in the pancreas. Centroacinar cells are located at the junction of the ductal tree and the acini, acting as a boundary between the two structures. It is believed that the formation of the boundary is regulated by *Dll1* and *Jag1*, two Notch ligands. Careful examination of the expression of these two factors showed that both are expressed in centroacinar cells, but not in acinar cells. The expression of *Sox9*, which functions to maintain cells in an undifferentiated state, followed the same pattern.

To further investigate the roles of *Dll1* and *Jag1*, the scientists used single and double knockout mouse models (sKO and dKO, respectively). While no phenotypical changes were seen in sKO cells, suggesting *Dll1* and *Jag1* have redundant function, dKO cells lost their expression of *Sox9*, had reduced proliferation potential and showed a stronger propensity to undergo apoptosis. Additionally, these effects compromised acinar construction, literally leaving holes in the structure. This defect was due not to abnormal growth but rather the absence of specific cell populations, namely centroacinar cells, indicating that Notch signaling regulates specific cell populations during pancreas development.

Kawaguchi believes that these findings are an important component to generating functional pancreas for transplantation in the laboratory. “Targeting the expression of these factors could help us develop treatment methods for pancreas damage,” he says.

### Reference

Nakano Y, Negishi N, Gocho S et al. (2015) Disappearance of centroacinar cells in the Notch ligand-deficient pancreas. *Genes to Cells* 20(6):500-511.

Online publication: April 27, 2015

## DNA demethylation promotes colon tumor cells to differentiate and escape carcinogenesis

One way to describe cancer is as dysfunctional cell proliferation. Increasing evidence has shown that this dysfunction is in part due to the repression of tumor-suppressive genes. More research has shown that these genes are methylated at their promoter regions when repressed. Accordingly, agents that demethylate the genes are currently used in several treatments to combat cancer. Yet despite their benefits, there is surprisingly much not understood about how these agents function.

To elucidate this matter, Prof. Yasuhiro Yamada and his group at the Dept. of Life Science Frontiers investigated methylation effects in colon cancer using a mouse model and human cell lines. Based on the expression of goblet cells in mice, they found that DNA hypomethylation suppressed the proliferation and initiated the differentiation of tumor cells. Consistent with these observations, hypomethylation shifted the transcriptome to a more differentiated state. In particular, the researchers found that the expression of *Cdx1*, a critical transcription factor in intestine development, was suppressed in tumor cells, but increased with decreasing DNA methylation levels. Interestingly, *Cdx2*, which like *Cdx1* is thought to have a crucial role in intestine development, did not follow this pattern; although its expression was suppressed in tumor cells, its promoter region in tumor cells was unmethylated. “This was an unexpected finding and suggests that colon cancers have various causes,” explains Yamada.

That conclusion is supported by the different responses seen in three human cell lines (HCT116, SW480 and HT-29). Interestingly, decreasing the methylation levels only deterred growth in two, even though cells from all three lines showed an increase in the expression of differentiation-related genes and heterogeneous morphologies, suggesting that they were transitioning from a proliferative to differentiated state. One explanation for the difference is that *Cdx1* is not suppressed in the HT-29 cell line, but is in the other two, which like the *Cdx2* findings, points the finger to distinct tumor-promoting mechanisms. It is not surprising then that other groups had previously classified HT-29 as a separate colon cell line subgroup.

These findings bring some light to how demethylation agents operate. Yamada also believes they also affirm a need for better gene targeting. “Current approaches can only give us limited information, because they are not specific. We need agents that control DNA methylations at specific sites,” he says.

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### Reference

Hatano Y, Semi K, Hashimoto K et al. (2015) Reducing DNA methylation suppresses colon carcinogenesis by inducing tumor cell differentiation. *Carcinogenesis* 36(7):719-729.  
Online publication: May 4, 2015

## NXPH3 improves the survival of neural cell grafts

Although the quality of the cells is critical for successful cell therapy, so too is optimization of the environment in which the cells are injected. Prof. Jun Takahashi and his group at the Dept. of Clinical Application, in a study first authored by Kaneyasu Nishimura, have now reported the benefits of neurexophilin 3 (NXPH3), a secreted peptide that binds to neural surface receptors, for the survival and functional development of grafted neurons. Takahashi expects this finding to be an important step in his soon anticipated clinical research using iPSC-derived dopaminergic (DA) neurons for the treatment of Parkinson's disease.



Jun Takahashi and Kaneyasu Nishimura

The identification of NXPH3 came after considering a number of candidate proteins that could improve the outcome of transplanted DA neurons. "Inflammation is a major problem in any transplantation, because by definition we are traumatizing the tissue," explains Takahashi. "In addition, the brain of a Parkinson's disease patient is under chronic inflammation. Therefore, it is even a bigger problem in Parkinson's disease and causes a large number of cells to die and compromises efficacy." The authors examined Parkinson's disease mouse models under several inflammatory conditions. They prepared DA neurons differentiated from mouse iPS cells and transplanted them into the models, finding that the DA neurons were more likely to survive under acute inflammation than chronic inflammation. The question intriguing the researchers was whether any specific factor was responsible for this difference.

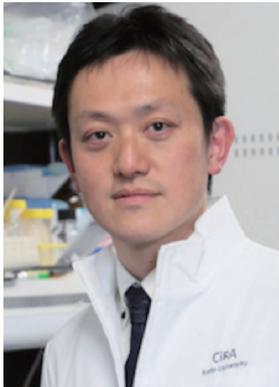
They therefore took a closer look at changes in gene expressions between conditions, finding several candidates that were expressed at higher levels in the acute condition compared with the chronic one. Among these candidates, only NXPH3 improved the survival of DA neurons when injected with the graft. More importantly, NXPH3 showed significantly lower expression in the postmortem brains of human Parkinson's disease patients compared with healthy subjects.

Takahashi is optimistic that the identification of NXPH3 will go a long way in priming the host for cell transplantation. "We have made good progress optimizing the differentiation protocol of iPS cells to DA neurons. The bigger challenge now is preparing the host tissue to accept the graft," he says.

### Reference

Nishimura K, Murayama S, and Takahashi J (2015) Identification of neurexophilin 3 as a novel supportive factor for survival of induced pluripotent stem cell-derived dopaminergic receptors. *Stem Cells Translational Medicine* 4(8):932-944  
Online publication: June 3, 2015

## Greetings from The Shin Kaneko Lab Dept. of Cell Growth and Differentiation



Shin Kaneko

Many cancers are able to thrive because our immune system is unable to recognize them. At the same time, other cancer cells are readily detected by the immune system, but persist. The reason is that the T cells are exhausted ( $T_{ex}$  cells), a state in which T cells are able to recognize their cognate antigen but unable to eliminate the pathology.  $T_{ex}$  cells are intriguing because even though they cannot kill the cancer, they still selectively target it and often infiltrate the cancer environment. Therefore, if there was a way to reactivate their cytotoxic activity, a population of rejuvenated  $T_{ex}$  cells should make effective cancer therapy.

We have discovered that iPS cell technology is a promising way to achieve this rejuvenation. Using cell reprogramming methods, we can dedifferentiate  $T_{ex}$  cells back to the pluripotent state. Unlike other cell therapies, which can begin with a totally different cell type, such as a fibroblast or blood cell, we must begin with T cells in order to preserve the TCR rearrangement. From there, using appropriate cultures and cytokines, we can advance the cells through lymphopoiesis and capture T cells in the memory state. Memory T cells are important for adoptive cell therapy against cancer, as they lead to better outcomes. Because the source of the rejuvenated T cells were T cells that had TCR rearrangement for the cancer antigen, the rejuvenated T cells too are responsive to the original target peptides. Importantly, because we can reprogram the cells to the pluripotent state, we can massively expand T cells numbers.

While our initial focus has been the rejuvenation of CD8+ T cells, we are applying our iPS cell technology to rejuvenate other immune cells, with the ultimate aim of recapitulating the entire immune system for a comprehensive attack against pathologies, especially those that cause chronic infection. Combining our methods with other technologies, such as exogenous TCRs and chimeric antigen receptors, should allow us to produce an adequate number of T cells even for those infections and cancers in which the number of responsive T cells are low and cannot be harvested for reprogramming.

## Gene editing human embryos



**By Associate Prof. Yoshimi Yashiro, Uehiro Research Division for iPS Cell Ethics**

Recently, genome editing of human embryos was reported. Since biotechnology had already enabled researchers to conduct genome editing of embryos from other animals, the ability to do so in humans was long awaited but with anticipated bioethical concerns. As biotechnology improves, so too will our ability to selectively manipulate the embryo to produce a human being of our liking. Current genome editing methods are viewed as too risky to be done in human embryos, since they would almost certainly lead to undesired mutations. However, ambitious scientists have sought to push the boundaries of these limitations. The obvious concern that emerges from modifying the human embryo with gene editing technology is designer babies, where parents can literally select for traits in their offspring before birth. Beyond the societal implications, there are also personal ones, as the baby itself cannot be consulted on how it wants to be designed.

The paper that reported this genome editing used fertilized eggs from fertility clinics that could not be used for impregnation. Therefore, these experiments avoid the possibility of human embryos reaching birth. Importantly, a number of off-target mutations were observed in the paper, demonstrating that from a safety perspective genome editing of human embryos in its current state is ethically untenable. Nevertheless, with continued advancements in gene editing and developmental biology, including that of iPS cells, the ability to manipulate viable human embryos with high precision is inevitable. In anticipation of these experiments, the International Society for Stem Cell Research (ISSCR) has condemned these efforts, arguing it is far too early to be using human embryos. However, as demonstrated by the already reported efforts, the ISSCR cannot prohibit these experiments. Instead, countries must set the rules.

Coincidentally, it was a discovery made by Prof. Atsuo Nakata and fellow Japanese researchers in 1987 that lay the foundation for genome editing. Thus, with its history in the field, it would be nice to see Japan take a lead role in setting the framework.

## CiRA Retreat

The 4<sup>th</sup> annual CiRA retreat took place on May 19-20 along the shores of Lake Biwa. Accolades are deserved to all who organized the event, with none more deserving than Yoko Miyake of the Director's Office. While discussions about science were central, the retreat is also an opportunity for CiRA's best and brightest to showcase their lesser known talents and take on some of the most advanced engineering problems known...in a high school. This year, groups were challenged to preserve two eggs from a 7 meter fall using nothing more than 1 meter worth of plastic wrap, two sheets of A3 paper and a pair of scissors. Impressively, several teams managed to save the eggs. More impressively, one had managed to smash theirs before the drop.

The retreat also welcomed four guest speakers, Prof. Irving Weissman, Director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, Prof. Hongkui Deng, Director of Stem Cell Research Center, Peking University, Dr. Chikara Furusawa, Team Leader at Quantitative Biology Center, RIKEN, and Dr. Ann Tsukamoto, Executive Vice President at StemCells Inc. Because of her experience in the biotech industry, we spoke to Dr. Tsukamoto about her career development.

### ***What enticed you to join a biotech startup?***

I decided to go to Systemix because I was very interested in purifying hematopoietic stem cells to potentially treat blood diseases and cancers. The founding scientists at Systemix had also developed a good model for growing HIV that could be used to test and develop treatments. The work involved basic and applied science without the burden of teaching or writing grants. It worked out very well for my career; much of the work done by the scientists at Systemix has been foundational for the stem cells field.



Dr. Ann Tsukamoto

### ***How did the job transition into an executive position?***

When you are in a small start-up with limited resources, you wear many hats and have the opportunity to be involved in many aspects of running a company. As head of R&D, the scientists and I had to formulate the research plans, timelines and determine the best pathway forward for starting clinical studies. We also had to establish collaborations with academic groups with expertise in the particular clinical target.

When we needed funding, the CEO would take me on trips to speak the science. We had to build the infrastructure, and that takes lots of money and a lot of meetings to get the money. That's how I got exposed to the business world. There really was no education than on-the-job training. This really is unlike what I saw in many friends who joined big companies like Genentech, Amgen, or Roche. They had less opportunity to be involved in many endeavors simultaneously.

### ***What people thrive in this kind of environment?***

Honestly, we look for the qualities that make up any good scientist. Skills are most important. Do you have a background in the types of cells we produce? Assays we conduct? Manufacturing? You have to be able to do what needs to be done and work well in a team environment! That kind of personality type means hard working, diligent, and careful.

People who want to make big money are probably not well suited, because cell therapy takes such a long time. I have been with my company for 17 years, which is unheard of in Silicon Valley where we are based. You have to commit. We do the research, development and clinical trials. Lots of scientists in academia are interested in this kind of work, but most scientists never experience the complete process from basic research to development of the project suitable for early clinical testing because they usually have no idea this world exists.



Egg Engineering



CiRA rocks

## Takeda and CiRA announce a 10-year collaboration



Christophe Weber and Shinya Yamanaka

*Last April Takeda Pharmaceutical Co. Ltd. and CiRA signed an agreement to form T-CiRA, a large-scale project in which Takeda will invest hundreds of millions of dollars to advance iPS cell research.*

One of the first destinations Christophe Weber visited after being appointed President of Takeda, Japan's largest pharmaceutical company, was CiRA and its Director Shinya Yamanaka. At the time, Yamanaka planned little more than a handshake and smile. "I was just going to say, 'Hi. Welcome to Japan,'" Yamanaka said. Instead, the meeting was the catalyst for a partnership that made international headlines. Takeda and CiRA announced T-CiRA, a 10-year collaboration for which Takeda has

pledged 20 billion yen for research funding and another 12 billion yen for infrastructure.

The aim of the program is to combine the knowledge of iPS cell technology at CiRA with the drug discovery resources at Takeda in order to hasten the innovation of iPS cell-based medicines. The program is expected to employ at least 100 researchers, with the two institutes directly hiring half each. However, all will be located at the Takeda Shonan Research Center, which is much closer to Tokyo than it is to Kyoto, the home of CiRA. The reason, explains Yamanaka, is that he wanted a wall between the science done at T-CiRA and that done at CiRA alone. "I wanted a clear separation between T-CiRA and any other efforts. The way is to physically separate them," he said. Yamanaka expects T-CiRA to be a model for partnerships with other companies. Creating a clear demarcation between the two organizations he hopes will alleviate any worry about encroachment when making agreements with different parties.

Even though formal discussions only began in January, the agreement was signed on April 15. Yamanaka credits much of the fast work to the staff at Takeda and at CiRA, particular naming Naoko Takasu and Atsushi Onodera of the Medical Applications Promoting Office in making the partnership official. "T-CiRA is extraordinary in view of scale, time, and budget," said Onodera. "We had to consider a new agreement structure. We were in the major meetings and really understood what was important for this project." Yamanaka envisages T-CiRA to initially focus on clinical applications that are strengths of CiRA, but hopes to see the breadth of research expand to currently unexplored fields. Principal investigators at CiRA involved in these projects will keep their primary labs in Kyoto, but have the option to hire additional staff that will operate out of Shonan. Yamanaka too plans to travel there with some frequency.

Wherever T-CiRA leads, Yamanaka is excited about the opportunity to hire bright minds that will expand the reach of iPS cell applications. "Any scientist will be [considered] as long as he or she wants to use iPS cells," he said.

## Briefs

### Prof. Haruhisa Inoue awarded Gold Medal

Each year, the Yomiuri Shimbun, through its subsidiary, the Yomiuri Research Institute, awards three exceptional young scientists gold medals for their work. This year's winners were announced on April 16 and included CiRA Prof. Haruhisa Inoue. He is the third CiRA member to receive the Gold Medal Award, the others being Prof. Shinya Yamanaka, who won it in 2004 prior to his invention of iPS cells, and Dr. Kazutoshi Takahashi, who won it in 2010 for his work on cell reprogramming. The announcement was in recognition of Inoue's work using iPS cells to study neurological diseases.



Haruhisa Inoue

### Prime Minister Abe speaks to scientists

Prime Minister Shinzo Abe visited the Gladstone Institutes in San Francisco, where Shinya Yamanaka is a senior investigator and has an active laboratory, on April 30. Prime Minister Abe was there to recognize the importance of Japanese-American scientific collaborations, with Yamanaka as the paramount example. Many Japanese expatriates are working in the Bay Area on leading scientific problems, which the prime minister hopes will benefit Japan and the world. "I believe you should introduce wisdom from Japan to the United States and vice versa... and I hope that new innovation which will enrich people's life will be generated," Prime Minister Abe said.

Yamanaka is also a big advocate of this Pacific partnership, frequently citing the impact Japan and America have had on his career. "I hope others see the benefit in exploring the opportunities that can come from a Japanese-American scientific exchange," he said.



Yamanaka and Prime Minister Abe at the Gladstone Institutes

### The importance of science communication and journalism

In June, Prof. Yamanaka gave a Keynote lecture at the World Conference for Science Journalists (WCSJ) 2015 in Seoul, South Korea. The biennial event is the largest conference for science journalism. Because he recognizes the important roles of science communicators and journalists to fill the communication gap between the public and scientists, Yamanaka prioritized this invitation among the hundreds he receives annually. "I found Professor Yamanaka's talk inspiring...because he is so straightforward about not only the promise but also the potential issues with what he's doing," commented Dr. Ivan Oransky, who chaired the lecture.



Yamanaka at WCSJ 2015



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## **CiRA Reporter**

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