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QBITS

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Talking With. . .

Masashi Kimura

The professor of Design discusses his experience as a scientific illustrator and his hopes for the profession in Japan

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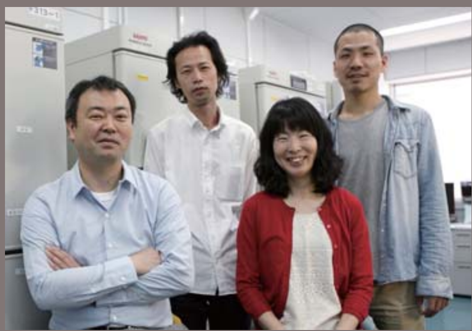
The Long Goodbye



One of the ways in which a research institute like Riken separates itself from a university is the absence of tenure. Each lab has a term limit so all laboratories will be shut down regardless of productivity. Riken still attracts excellent researchers by compensating with above average salaries and research funding packages. Nevertheless, it does mean people move on with higher frequency. That is the case for Atsuo Kawahara and his lab, as they come to an end of their time at QBiC. Atsuo is taking his research on lipid mediator sphingosine-1-phosphate in the cardiac development of zebrafish to the University of Yamanashi, about two hours west of Tokyo. Among his team, only Satoshi Ota will be joining him at Yamanashi, as Michiko Muraki and Yu Hisano have secured other positions. Along with the research at QBiC, Atsuo's group was perhaps the most active in community outreach and other non-research activities at the institute, something that he plans to continue at Yamanashi. While looking forward to his new home, Atsuo also leaves with fond opinions of QBiC. "I am very happy that we were able to study in a great research environment.

Talking with . . .

Masashi Kimura, Scientific Illustrator

If drawing is his favourite activity, then talking about drawing must be Masashi Kimura's second. The professor at Nihon University College of Art keeps a permanent smile when discussing the number of nights he has gone without sleep trying to draw a perfect replica of a specimen or even when he speaks discouragingly about the small number of art students selecting science illustration as a major.

Masashi worries that Japan is not taking advantage of its creative talents when it comes to science art. Most of his students will graduate into marketing careers and therefore see little reason to learn science. Yet his classes have managed to attract students from all sorts of design backgrounds including photography, film, and illustration, many of whom are no different from Masashi during his undergraduate days in the early 80's at the same university. It was then, nearing graduation, he had decided to go abroad, choosing a fine arts program at Washington State University, without any consideration for science or a career in it.

"I hated science. From elementary school, middle school, and high school, my teachers all taught with the intention of preparing me for exams. I loved the radio, listening to music. I wanted to be a disc jockey. I wanted to go to America and hear the music".

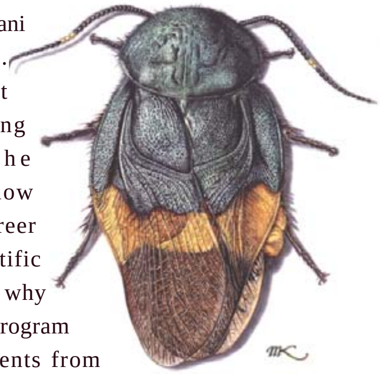
That one year at W.S.U. gave him a entirely new perspective on what it meant to be an artist. "I listened to a lecture from Buckminster Fuller. A friend of mine was a friend of his and took me to meet him for dinner. It was only until I came back to Japan that I learned how great he is". Fuller's talk showed Masashi how art is everywhere, including the sciences, and instantly made Masashi reevaluate his inspiration for art.

While that talk opened his eyes, it was not until a trip to the East Coast that he found his passion. As a teaching assistant at W.S.U., Masashi met Bradley Hower, the son of the director of the Smithsonian Natural History Museum, who suggested he come to visit. Masashi went more for the curiosity of travel, as he knew next to nothing about the Smithsonian. "I thought it was a restaurant". That perception changed, of course, when he received a comprehensive tour of the museum. It was when he visited the collection room that he "fell in love". Masashi had never appreciated the aesthetic beauty of nature like he did at that moment. Even more exciting was the scientific illustrator office, something he had never conceived. "I thought a museum just showed things. I didn't know scientists and artists work together. I never saw anything like it". He marveled at the tools and facilities, and took exceptional interest in the illustrators, who were glued to their microscopes all day drawing immaculate images.

Of the many people he met at the Smithsonian, Masashi specifically remarks on the inspiration he drew from George Venable, a famous illustrator who specialized in entomology after beginning his career as a medical illustrator. Masashi was so impressed that he devoted himself to becoming Venable's apprentice. "When I came back to Japan, I wrote many letters". The irony of writing letters to a museum does not escape Masashi. "Students today haven't even seen a typewriter". It took about a year and half, but he finally got Venable to agree. "I returned to Washington D.C. for eight months". The letters were sent while Masashi was working as a graphic design artist, producing materials unrelated to science. This was a problem, because no matter how persuasive his letters, Masashi would never be able to land the internship without a portfolio, which is why he spent many nights after work producing science illustrations that were included in his posts. It was when he did land the internship that the real hardship began, because the position came with no salary.

After the internship, he came back yearning to bring scientific illustration to his home nation. “At that time I had never heard of a ‘scientific illustrator’ in Japan. There were commercial illustrators who would be used by, for example, [the Japanese popular magazine] Newton, but there were not any specialists. In America, there was the Guild of Natural Science Illustrators, 2500 people. The Smithsonian, National Geographic, when they wanted an illustrator they would contact the guild”. Masashi took advantage of these organizations to land a freelance position with National Geographic. Disappointingly, none of his illustrations were published. Nevertheless, he did not starve. It might surprise some to learn that contracts with organizations like National Geographic guarantee a minimum salary based on the production of art independent of the editorial decision to publish.

To Masashi, the United States is a model for scientific illustration that Japan has not fully embraced. He does see science illustration programs increasing in Japan, but most of those are emerging at science schools, not art schools. The reason, he believes, is that the love for the aesthetics of science is present at an early age and usually accompanies a general curiosity to how the world works. He sees this pattern most at the workshops he gives at high schools. These students will eventually enroll in science programs at university, not art, but still retain an interest in the art of science. “That is why I would rather teach at a science university”. Using that logic, Masashi believes scientific illustration can just as easily grow in Japan by converting scientists into illustrators as by training art students.



He cites Utako Kikutani as one example. Utako was a biologist who after consulting Masashi made the switch to art and now has a successful career as a freelance scientific illustrator. It is also why he is working on a program that brings art students from his university together with science students at Rikkyo University that challenges them to design material for educating and promoting science to general audiences. Some of the case studies have been in partnership with QBiC and used for high school events.

As someone who loves to draw by hand, Masashi is a bit of an anachronism. In his mind, it is the best way for the hand and mind to communicate. Unfortunately, he does it less and less. Sometimes too much passion can hurt one’s health. Sitting over a microscope and obsessing over the minutest of details did not only lead to many sleepless nights. The light from the scopes have damaged his eyes to the point that doctors have insisted he avoid them altogether. For now, he limits himself to just three hours a day, and even that is probably too much. Regardless, Masashi justifies his condition with a simple explanation, “I love drawing”.

Reunion

Last issue we reported that QBiC Director, Toshio Yanagida, was named a Person of Cultural Merit, a prestigious award given to people who advance Japanese culture. Toshio used the generous winnings to rent a banquet hall and celebrate with over 240 colleagues from QBiC, Osaka University and other institutes. Among these, 80 were individuals that had passed through his laboratory, many of whom have since become professors themselves, offering a rare reunion. Also in attendance was Toshio’s mentor, Fumio Oosawa, someone Toshio regularly acknowledges for his success. Prof. Oosawa has had a great impact on many researchers lives, as Nature granted him a lifetime achievement award in 2009 for his mentoring of future scientists. Now 92 years old and relegated to a wheelchair, he travelled from Nagoya to be the penultimate speaker. Toshio himself is sure to travel to Nagoya 3-4 times a year to spend time with his greatest role model.

Paper Highlight

Stem Cell Fingerprinter

At its most ambitious, the ultimate goal of stem cell studies is the ability to control the cell's stemness, i.e. the likelihood the cell proliferates or differentiates, and the type of somatic cell it eventually becomes. Normally these investigations consider molecular signals and markers and are genearlly qualitative. In a recent paper published in *PLOS One*, the Watanabe lab describes a quantitative method based on Raman spectroscopy, which may offer a simpler and more robust way to evaluate stem cell potential and quality. The report, first authored by Taro Ichimura, applies Raman spectroscopy that uses confocal scanning in combination with principle component analysis (PCA) to evaluate the morphology of a cell, finding that the resulting spectrum acts as a fingerprint that can be used to identify the cell type and potentially the cell fate.

The authors show how Raman spectra can distinguish fibroblasts, epithelial cells and hepatocytes. PCA further quantified distinct maps of the three cell types, which could be interpreted as different cell states that could potentially be used for predicting cell fate. To investigate whether the same technique could be used to distinguish undifferentiated and differentiated cells of the same type, the group observed two cell lines, finding that cytochrome C could be used as a decisive marker. Again, PCA could separate the two types into distinct regions on the PC1 and PC2 maps.

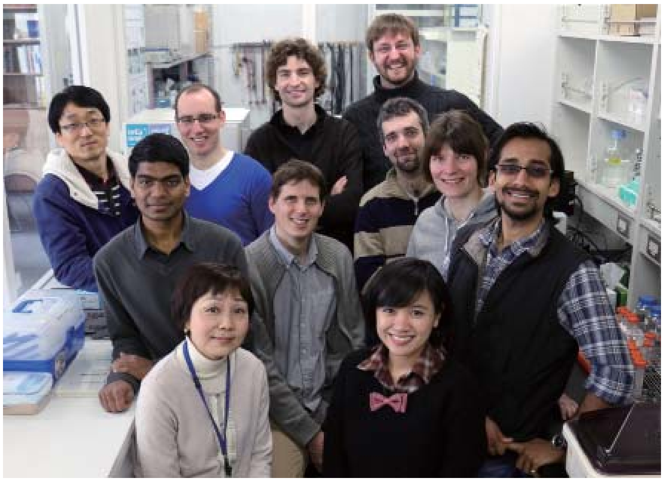
As a final challenge, the team investigated mouse embryonic stem cells (ESCs), since the cell lines used above may have had certain properties that would not apply to endogenous stem cells. Their Raman spectroscopy successfully detected an iterative fate, as the distribution of the PCA narrowed over time in accordance with the progression of differentiation.

The molecular implications of the spectra still need to be explored. Nevertheless, Taro believes that these results argue Raman spectroscopy could have a pertinent role in future stem cell science, as it could be used for quality control and cell sorting, two major obstacles in the field because of frequent heterogeneities in stem cell cultures. However, in his mind, the most exciting potential of the technique is its potential in predicting cell fate. "If we apply this technique to many kind of conditions, we expect to find many pathways that become somatic cells. We may be able to predict the somatic cell." Moreover, he hopes that such predication capabilities will be instrumental in guiding effective external perturbations to direct the cell into a desired fate.

In a related project from the lab, Sayaka Higuchi is the first author on a report seen in the *Journal of Bioscience and Bioengineering* that investigates mechanical effects on cell reprogramming. While the effects of biochemical factors on cell fate are quickly clarifying, the authors show the importance of mechanical properties like the use of soft substrates for culturing, which can initiate reprogramming properties. The suppression of actin stress fibres in cells cultured on the softer surface may provide some evidence of the reversal mechanism. Project leader Hideaki Fujita is cautiously optimistic about the potential of this approach. "We are planning for full reprogramming, but it is not that easy".

Meet the QBiC Lab. . .

The Frey Initiative Research Unit



Our lab designs custom integrated circuits and employs micro- and nanotechnology to fabricate novel transducer devices for the purpose of quantitatively measuring biological processes. One example of our technology is a high-resolution microelectrode array that can be used to study the electrophysiological behavior of mammalian cells, in particular neurons. This array can achieve subcellular resolution extracellular recordings and, at the same time, network-level analysis of neuronal activity in acute slices and organotypic or dissociated cultures. Ultimately, we aim to elucidate the effect of dendritic arborization shapes on dendritic calcium spikes and complex spiking activity in the developing cerebellum. We have also established a method that combines this technique with patch-clamping, which allows us to manipulate individual neurons and observe their communication in real time. In a different project, we are designing microsystems that feature nanoscale sensor elements like carbon nanotubes to study molecular events, such as DNA hybridization and protein dynamics. We are integrating these sensor elements on custom CMOS chips using a dielectrophoresis technique.

Overall, our research can be summarized as the design and application of bioelectronics and biosensors, which requires a multidisciplinary approach that is at the interface of engineering, biology, and nanotechnology. Accordingly, we are an international team that is always seeking to increase our number of experts in engineering or the neurosciences.

Briefs

Parallel experiments are often employed when seeking to identify which phenotypic and genotypic changes are necessary for evolutionary dynamics during laboratory evolution. A major limitation to these experiments, however, is the culturing of the observed microbes, as current methods are often unstable, costly, or both. The Laboratory for Multiscale Biosystem Dynamics has published an automated culturing method that minimizes these demerits. The report, first authored by Takaaki Horinouchi, shows how the system can maintain hundreds of cultures in the exponential growth phase independently and can be seen in *the Journal of Laboratory Automation*.

Biological systems have to operate with a lower bound of noise when conducting chemical reactions, because of the small number of molecules providing information. The Berg-Purcell limit is a standard description for this limit. However, it assumes that the reactions are diffusion limited, which is often not the case for binding reactions. In collaboration with AMOLF, Kazunari Kaizu and Koichi Takahashi proposed a new model and use Green's function reaction dynamics to simulate reaction-diffusion systems at the particle level, finding that the Berg-Purcell limit can be extrapolated. The report can be seen in *Biophysical Journal*.

Bacteria deliver virulent proteins via a needle complex, which structurally and functionally resembles the flagellar basal body, which is the better studied of the two. Drugs targeting the needle complex are preferred, as they impede protein transmission without compromising bacteria survival, which reduces the likelihood of drug-resistant mutations. The two structures differ, however, in that the needle complex lacks a C ring, which may or may not be due to purification methods. Akihiro Kawamoto and other QBiC members show by in situ cryoelectron tomography that the absence of the C ring is not an artifact, providing new theories on the mechanism used by the ATPase to inject the pathogenic material. The report can be seen in *Scientific Reports*.

Interesting People

Play Ball

Baseball is Japan's national sport. There are far more diamonds than soccer fields and basketball courts, and every child it seems dreams of becoming the next baseball legend. Tomohiro Shima was no different. When it came to his decision for university, he considered his interests in science and baseball. An excellent student, but only a very good player, he found a convenient place nearby home, Tokyo University, one of the best universities in the country and literally a short bicycle ride away.

Todai, as the university is more commonly called, is part of the Tokyo Big6 League, along with five private universities in the region. All games are played at Meiji Jingu Stadium, which is also where the professional baseball team the Tokyo Yakult Swallows play. Although Todai emphasizes the student in student-athlete, the other five teams view their players somewhat differently, which is why Todai was never serious competition during Tomo's reign. In fact, they finished last place each year. Tomo points out, however, "they are even worse now".

Baseball is a demanding sport in Japan. Tomo had practice or games on all but one day of the week, and those practices would last four hours on weekdays and eight on weekends. Furthermore, students were expected to prioritize class, as professors made no favours to athletes. Rather, coaches exempted their players from practice if class ever conflicted (games were on weekends). Yet the grueling schedule does not appear to have been detrimental to Tomo's academics. In his last year of studies, he joined the laboratory of Kazuo Sutoh, who at the time was glowing over promising experimental results about producing the first active dynein recombinant. Tomo's work late in project was sufficient to get his name on the breakthrough paper, which has since directed his research to the study of the molecular mechanism for dynein motility.

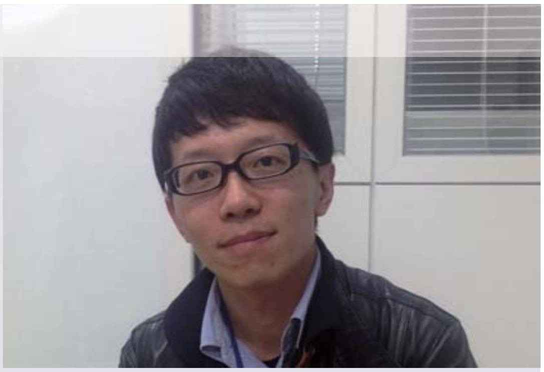
Baseball continued to influence Tomo's decision for graduate school when a teacher at his high school, Tsukuba Daigaku Fuzoku Komaba, invited him to manage the high school team. Tomo agreed while negotiating with the lab of Hideo Higuchi, a specialist of single molecule microscopy, to pursue his masters and doctorate degrees at Todai. Asked which he decided first, the coaching position or the lab, Tomo admits, "I guess it was becoming the coach. But they were pretty much at the same time".

Dynein is a very challenging molecular motor for single molecule microscopy experiments compared to more popular models like myosin and kinesin, which is what drew Tomo to the work. Dynein is far more massive than the other two. It also, despite the similar function, has a distinct evolutionary ancestry, as dynein is a member of AAA proteins like helicases and chaperones, whereas myosin and kinesin derive from small G proteins. Also, dynein has 4 ATP binding sites on its motor domain unlike the one in myosin and kinesin.

The opportunity to study dynein using advanced microscopy was the primary reason he decided to move to Osaka and join Yasushi Okada's lab at QBiC. "The microscopy is very good, hard to find elsewhere. Plus, until I came I had only been working on proteins. Here I can work on cells". His baseball skills, however, are rarely used at QBiC.

While Tomo does not deny the team struggles at Todai, neither does he see the experience in a negative light. He is quick to remark that some of those teams did win one or two games a season (forgetting sometimes they won none). More importantly, those struggles also helped prepare him for his time in the lab. "All that losing, it's a lot like the feeling you get when doing experiments". Well said.

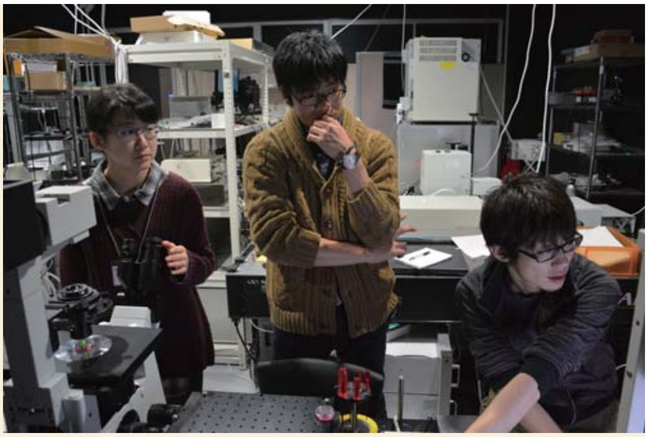
Talking Business



One of the goals at QBiC is to strengthen industry-academic collaborations, which lag in Japan relative to other nations like the United States. QBiC PI Tsutomu Masujima, was invited to speak at the Kansai-Hiroshima Business Network on January 22nd, an event attended by 200 people from the two sectors and interested in larger medical and diagnostics projects. Tsutomu made an ideal speaker, since he had spent many years advocating for Hiroshima but is now committed to the Kansai area with his move to QBiC. Nevertheless, he still wants the best for his hometown. “I love Hiroshima and would like to do something for the Hiroshima prefecture”. Tsutomu stressed that Hiroshima would be unwise to follow the actions taken by richer regions like Kanto (Tokyo) and Kansai. Rather, Hiroshima needs to wisely evaluate the technologies in which they invest, which he believes will be the primary determinant to attracting companies to the Hiroshima region.

Like any large research organization, Riken has an office devoted to procuring patents and promoting them to the private sector. The Technology Transfer Office was accordingly asked to invite presentations to two events this past February, Nanotech 2014, an international conference on the latest in nanotechnology, and the Riken-Industry Conference, an exclusive meeting attended by 500 people, to publicize recent Riken technology. In both cases, it invited Hiroyuki Moriguchi of the Yo Tanaka lab to discuss his new microfluidics devices. In one, the device has a series of wells that can be placed on a rotor, which allows for automated and periodic stimulation. In the other, a series of different experiments can be done simultaneously at the single molecule level to compare reactions. These events were opportunities for Hiroyuki to find partners who could mass-produce his product. “We are talking to companies about manufacturing”.

Spring Course 2014



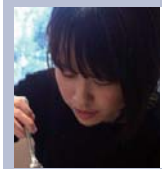
In the first week of March, QBiC had its 3rd annual Spring Course, which invites university students from across the nation to attend one day of lectures and three days of experiments. Although the course is partly intended to recruit f uture graduate students and researchers to the institute, that 1st year students were welcomed demonstrate it is also intended to introduce students to the world of quantitative biology. Organizer Takaaki Aoki was especially happy to see that several of the 77 participants were returning from the previous year. On the last day, students gave 10 minute presentations of their 3-day lab work, which in Takaaki’s mind reflected well the changes made to the program. “It was a success. The student presentations definitely improved from last year”.

Red, White, and Gold

I promised myself never to use QBiTs as an editorial, but I make an exception this time. About one month before the Canada-Sweden gold medal game in Sochi, I coincidently met a Swede who had been living in the U.K. for a year. Hearing that I had been in Japan for ten, he asked me how I have handled a very difficult matter for anyone migrating from an arctic nation, “Where do you watch hockey”? I explained I don’t except once every four years. That one time, of course, was this past February, which is why I was awake in the early hours on a Saturday to see the men’s semifinals and then late Sunday night to watch the gold. I did not watch the women’s finals, however, a game that had one of the most incredible finishes in memory. If cheering national hockey teams is silly patriotism, then Canada is a nation of silly people. Even in Japan the pride triumphs, as Canadian friends were answering their phones with, “We won the gold”. (For the record, I did not).

As for a photo of the champs, Riken unfortunately did not agree with my argument that I should be posted in Sochi as a photographer. So instead I include a picture (albeit blurry) of my goddaughter that shows what a typical high schooler does even on an August evening in the Great White North.

Newcomers at QBiC



Me: Ayumi Kishimoto
Lab: Team Ueda H
Hobbies: Restaurants, coffee art
Cheers: HANSHIN TIGERS

Me: Imran Fanaswala
Lab: Team Frey
Hobbies: Running, hiking
Cheers: HANSHIN TIGERS

We are now on the web!
Download past issues of QBiTs at http://www.qbic.riken.jp/

THE CHOW DOWN

Sicilian Style Bass

Have a recipe you want to share, contact us at: **qbits@riken.jp**

Ingredients

2 slices of Japanese seabass
(スズキ ; other fish can be used)
2 slices of lemon 2 cm thick
2 cloves of garlic thinly sliced
1 stick of rosemary
teaspoon of olive oil
salt and pepper

Recipe (very easy)

1. preheat the oven to 180℃
2. place the fish on a cooking rack with the lemon and garlic below
3. rub the top of the fish with the salt and pepper
4. place the rosemary and olive oil on top
5. cook for 20 minutes

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