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QBiC

NEWSLETTER OF RIKEN Quantitative Biology Center

QBiTs

Symposium 2015

QBiTs thanks all of the participants and we are looking forward to next year!

Inside This Issue

PAPER HIGHLIGHTS

New microscope captures first images of sub-cellular phenomenon

Images of a newly discovered sub-cellular phenomenon were captured for the first time in a collaborative study between researchers at RIKEN Quantitative Biology Center and Olympus Corporation.

Yasushi Okada (RIKEN) and Shinichi Hayashi (Olympus) shared their groundbreaking images from a new super-resolution microscope in the journal Molecular Biology of the Cell. The article titled "Ultrafast superresolution fluorescence imaging with spinning disk confocal microscope optics," details the modifications made to a commercially available spinning disk microscope. The modifications increased both the speed and resolution of the microscope.

Yasushi Okada and Rob Cross

The new microscope captured images of the inner workings of live cells with unprecedented clarity. The researches captured images of microtubules, fast moving endosomes and mitochondria down to 120nm resolution. The extremely fine resolution of moving organelles represents a major step forward in the imaging of live cells.

The work builds upon that for which the 2014 Nobel Prize in Chemistry was awarded. In this exciting new field of super-resolution microscopy the resolution limits of the light microscope have been shattered and the remaining barrier to a new era of microscopy has been the speed of image acquisition.

Today that barrier too has been broken. Okada created a microscope that captures super-resolution images 100 times faster than microscopes used in the 2014 Nobel Prize work. This astonishing improvement was made with relative simple modifications to existing technology.

In an attempt to test the robustness of the new microscope, the researchers focused on a newly discovered and poorly understood phenomenon known as mitochondrion derived vesicle (MDV) formation. A variety of diseases including Parkinson disease have been associated with MDV and there is a great deal of interest in mitochondria in disease research.

In a eureka moment the researchers found their microscope was able to image MDVs, stating, "To our knowledge, this is the first visualization of MDV formation from mitochondrial protrusions."

HOT OFF THE PRESS

Recent publications from QBiC researchers

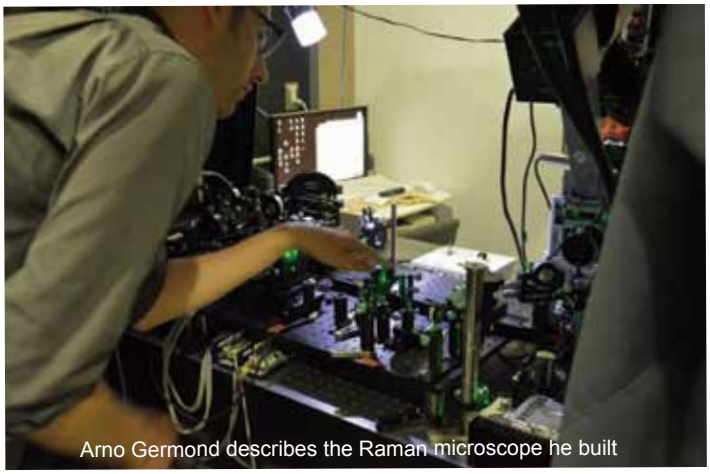
- Hanae Shimo was the lead author of a paper published recently in *PLoS Computational Biology*. The paper is titled "Particle Simulation of Oxidation Induced Band 3 Clustering in Human Erythrocytes."

- Masujima's team published a single cell analysis method in *Nature Protocols*. The paper is titled "Direct metabolomics for plant cells by live single-cell mass spectrometry."

- Morishita was lead author of a paper recently published in *Development*. The research was also highlighted in *RIKEN Research*. The paper is titled "Quantitative analysis of tissue deformation dynamics reveals three characteristic growth modes and globally aligned anisotropic tissue deformation during chick limb development."

CATCHING UP WITH

Taro Ichimura and Arno Germond from the Laboratory for Comprehensive Bioimaging



Arno Germond describes the Raman microscope he built

Taro Ichimura describes himself as an applied physicist specializing in optics and photonics, saying, "My background is in observation of semi-conductors." It should come as no surprise that applying some of the same observation techniques to embryonic stem (ES) cells takes some adjustment. Ichimura continues, "Of course when the sample type is different the design of the microscope is different; time, light and laser intensity" are reduced when observing biological samples.

When Ichimura talks microscope design he speaks from firsthand experience. Ichimura designed and built a variety of imaging devices used in the Laboratory for Comprehensive Bioimaging, also known as the Watanabe lab. And when the topic of building the imaging devices comes up Arno Germond gets excited. He too has built a Raman spectral imaging microscope with guidance from Ichimura and he is eager to show it off.

Drawing back a dark green curtain Arno gives a tour of his setup. He points out a series of mirrors and filters bolted directly to anti-vibration table that sports shock absorbers for legs. Bouncing off the mirrors and passing through the filters a bright green laser light draws the path to his sample on a microscope stage and back to a polychrometor and detector. According to Ichimura the detector is an extremely sensitive and accurate Charge-coupled device (CCD) camera. The detectors are so sensitive that during measurements the lights in the room are shut off and the dark green curtains are drawn all around the laser-microscope-detector setup.

There is a certain toy like charm to the setup. It is reminiscent of a Rube Goldberg machine built by an ambitious child with an extensive erector set and for a moment just following the path of the sparkling green light bouncing off the mirrors and around the table is a simple joy. Arno points out where he has used his business card to block stray laser light from interfering with measurements. The light reflecting off the white business card is surprisingly bright and the image of a toy is quickly replaced with that of an industrial laser deployed in a cutting edge biology experiment.

The principle of Raman light scattering has been known for nearly a century. In fact, C.V. Raman was awarded the Nobel Prize in physics in 1930 for his discovery of the Raman effect, and the discovery is one of only a handful of National Historic Chemical Landmarks from outside of the United States as declared by the American Chemical Society. The later title was imparted on the discovery for its importance as a tool for analyzing molecules. For cell biology, however, it is a new tool.

Ichimura describes how it works, "Raman scattering creates a molecular fingerprint. We use the molecular fingerprints to create cellular fingerprints." Having created a set of fingerprints to identify cells states, the Watanabe lab has been able to follow populations of differentiating ES cells through cycles of homogeneity and heterogeneity. This work was recently published in *Nature Scientific Reports* in a paper titled "Visualizing the appearance and disappearance of the attractor of differentiation using Raman spectral imaging." This and all *Nature Scientific Reports* are available free online.

Pressed to explain why they focus on ES cells, Ichimura says the techniques his team are developing are relatively new and only a few other labs in the world are doing similar work. While there are many other potential targets of the techniques, ES cells have many potential biomedical applications and the study of ES cell differentiation is of great interest. Arno concurs and adds, "Ichimura-san understates the quality of his work. It is really sugoi!"

REACHING OUT

RIKEN Yokohama Campus Open-Day

On the last weekend of summer vacation as many as three thousand people came out to visit the RIKEN Yokohama campus for the annual open-day event. There were over 80 events, including facility tours, hands-on workshops, talks, and posters. Takanori Kigawa and his Nuclear Magnetic Resonance (NMR) team, QBiC's only lab in Yokohama, presented posters of their work, challenged participants with science quizzes, and shared a family oriented attraction "What's inside a cell". The attraction inspired from their research on molecular crowding inside a cell using in-cell NMR was very popular among kids. They can dive into a 1.5 meter wide compartment full of diced sponges and floating plastic bubbles that mimics cytosol and organelles in a cell.

Another popular and interesting exhibit from Kigawa lab was a bio-battery that produces energy from oxidation of sugar. Tsutomu Mikawa a researcher in Kigawa lab invented this battery and made a sugar powered fan. Only Coke and not Diet Coke when used as fuel could produce power to rotate the fan. I knew it!

QBiC outreach activities

◆ On May 2, Shuichi Onami gave a lecture for students in Code for KOSEN at Akashi College in Hyogo prefecture. He talked about data base integration and helped students prepare for the Open Data Visualization contest that is happening in this November.

◆ On June 6, Miki Ebisuya educated young and old alike at the 32nd RIKEN Day in the Synra-Dome at the Science Museum in Tokyo. Her talk titled “Reshaping the cell by swapping genes” stimulated questions of all kinds.

◆ On July 14, Tom Watanabe gave a lecture in front of 300 students at Tatsuno Super Science High School. After the lecture he held a science cafe (Café Scientifique) with some of the students.

◆ During summer vacation, students from three Super Science High Schools visited QBiC. Tom Watanabe and Chikara Furusawa showed their labs and explained their research to students from Horikawa, Kyoto. Yoichiro Kamimura, Satomi Matsuoka, gave a tour of the lab for cell signaling dynamics and Yuichi Taniguchi and Kazuya Nishimura showed their laser microscope and micro fabrication facility for students from Tatsuno, Hyogo. Tsutomu Masujima and his lab members performed single cell mass spectrometry experiments and Koichi Takahashi explained the future of Artificial intelligence for students of Nagasaki-Minami high school.

◆ On Oct 24, Onami, Ebisuya and Morishita labs participated in the RIKEN Kobe Open Day.

You probably did some outreach that we failed to notice. Please send notice of outreach activities to qbits@riken.jp with “outreach” in the subject.

Recent Science Events

Oct 22, 2015 QBiC Seminar
Andreas Hierlemann, ETH Zurich
"Highly integrated CMOS microsystems to interface with neurons at subcellular resolution"

Oct 14, 2015 QBiC Seminar
Katsuyuki Shiroguchi, RIKEN Center for Integrative Medical Sciences
"A study of higher biological organization by system-wide measurements of their components"

MEET THE LAB

Yoshihiro Morishita's Laboratory for Developmental Morphogeometry

Morishita with researcher Naofumi Kawahira

The goals of our laboratory are to understand mechanisms determining organ morphologies during their development and regeneration. To achieve this goal, quantification of tissue-level deformation dynamics with high accuracy is critical. Construction of tissue deformation maps and their geometrical analyses enable us to capture the spatiotemporal heterogeneity of deformation characteristics, especially in regions with higher growth rates and/or anisotropy of tissue stretching, which we call "morphogenetic hot spots." After such hot spots are identified, by analyzing the correlation between this tissue-level deformation and the molecular and cellular activities occurring there, inter-hierarchical relationships between events at different spatial scales are revealed. In our laboratory, for the above purposes, we are performing experiments and quantitative data analysis for limb, heart and brain development and regeneration using chick and Xenopus embryos, and also developing mathematical models that integrate inter-hierarchical relationships and reproduce/design target organs' morphologies in silico.

NEWCOMERS at QBiC

April Oga
Team Masujima
Sports: Cycling
Hobbies: Going on adventures to new places
Food: Goya Banana Smoothie

Prabhat Shankar
Team Shibata
Sports: Soccer
Hobbies: Hiking, Reading
Food: Egg Curry

Ahmed M. Ashraf
Team Masujima
Sports:Cycling
Hobbies: Gaming,
Reading Science fiction novels
Food: Rice Cooker Extraordinaire!

Yasmine Abouleila
Team Masujima
Sports: Basketball
Hobbies: Drawing
Food: French fries with cheese

Sara Amer
Team Masujima
Sports: Shopping, Reading, Biking, Watching movies
Hobbies: Basketball
Food: Anything that includes Chocolate!

Stefan Huber
Team Frey
Sports: Sadly I am not doing any sports...
Hobbies: Travelling the world
Food: Love all kinds of cheese

Recent Science Events

Sep 16, 2015 QBiC Seminar
Robert A. Cross, University of Warwick
"Strong-state kinesins inhibit microtubule shrinkage"

Aug 24-26, QBiC Symposium 2015
"High-Dimensional Data for the Design Principles of Life"

GET OUT!

Osaka Aquarium

On a sunny fall morning with family in tow and sandwiches in knapsack, we set off for the tourism hotspot that is Osaka Aquarium. We took the train and subway to Osakako station and found sufficient signage there to find the aquarium, although the majority of the signs in the station read "Kaiyukan" rather than "aquarium."

We descend the stairs from the station and within a block found ourselves in front of a convenience store. Much like the animals in the aquarium, feeding time for the family occurs several times a day and so we stopped for a snack. After a ten minute walk past souvenir shops and restaurants, we were standing next to a Lego giraffe and underneath an enormous Ferris wheel. The aquarium is up a short escalator from there.

As we neared the ticket counter we were distracted by a young man juggling fire and breathlessly encouraging the crowd to get closer. And clap! When we we're finally able to move on to the ticket counter we decided on annual passes called passports. The passport cost about the same as two one-day entry fees.

Of course the passport option requires a bit more paperwork and a visit to the service counter to get our photos taken. I realized after watching some others get their photo taken that the requirements for the Osaka Aquarium passport photo are somewhat more relaxed than your government issued passport. The gentleman that got his photo taken after me, for example, did the double peace sign and a fish face. I was jealous. We were then instructed to come back later for the passports and finally we were ready to enter the world greatest aquarium!

Entering through the shark gate, where sharks swim overhead, we passed by a Halloween themed photo spot and started up a very long escalator more reminiscent of Osaka station than an aquarium. At the end of the escalator there were a few small displays including some otters and a giant salamander. The giant salamander is truly giant, as far as salamanders go and the salamander along with the other displays in the first room are worth a look if you can squeeze in to see anything. As I tried to do just that, it quickly became clear that the Osaka Aquarium is not a place to get away from people. It was crowded. The crowd was a little pushy and little overwhelming. There were many tourists and it was a crowd that inspired us to play "what language is that?"

Exiting from this small crowded room, a long downward descent began. Passing by a surprisingly large and cute sea otter caught in perpetual somersaults, we happened upon feeding time for the seals and sea lions. None of the animals is part of a formal show at this aquarium but the care takers got quite a performance from this group of pinnipeds in exchange for a healthy dose of silvery fish. Feeding time was the most interesting part of each exhibit even when the animals were not trained in anyway.
We found stamp stations along the way and started collecting the imprints in little notebooks as we went. The stamps depict many of the animals on display and there was a notebook at the gift shop specifically for collecting each of the images. Thankfully, any A6 size notepad is up to the task.

There are many tanks at the Osaka Aquarium. As we continued down the winding path I noticed that we were passing some of the larger tanks at several levels. So when we were looking at a tank of large fish we could see the sea otter from below. We could also see a scuba diver scrubbing the walls and floor of the tank. In fact we saw many scuba divers cleaning throughout the day. This helped explain why an aquarium that has been in operation for a couple of decades is fairly clean. The glass of the tanks were all clear and that is itself a remarkable

fact considering the thickness of the panes. There is a sample of the glass that makes up the walls of the tanks. It is thick heavy stuff and apparently able to resist the pressure of some 5000 tons of water in the largest tank.

The distance to the end of the walking tour is marked on the floor and it must be near one kilometer altogether. Halfway through that distance we were all ready for a snack but somehow missed the little café in the aquarium and so we rushed through to the end, got our hands stamped for reentry and went next door to the food court.

In the Tempozan market place, which is immediately next to the aquarium but appears more closely tied to the Legos and Ferris wheel, we went for the most Japanese of foods, cheeseburgers and fries. Feeling refreshed we went for a second lap around the aquarium.

The second time we found a less crowded path, a different set of animals being fed and scuba divers in different tanks. This time we entered one of the rooms not on the main route for a more in-depth education on Osaka bay including some details on invasive and native species. I couldn't help but feel some sympathy for the invaders who I imagined mean no harm but would simply like to enjoy the hospitable environment of Japan.

Leaving the aquarium we were greeted by the sun setting in the bay and the same young man juggling fire but this time for a much smaller crowd. We stopped for ice cream on the way back to the station hoping for a sugar fueled burst of enthusiasm and perhaps enough energy for a stop at the Osaka Castle on the way home. There is a stop near Osaka Castle on the same subway line but alas we couldn't muster the enthusiasm for further tourist adventures. After about an hour of standing on trains and with the sandwiches long since consumed we eyed real sustenance, however, hopes for fine dining at a conveyor belt sushi restaurant were dashed due to the two hour wait. We settled on bento from the super market and walked back home.

On the walk we played "what was your favorite part?" There were a number of animals that were unbelievably large or small and deserved honorable mention. Among the big were the salamander, a big brown fish and a disturbingly large eel and on the small side the little jellyfish that were incessantly pumping their little jelly bodies and barely making an inch despite only being trailed by four short tentacles. Of course dolphins playing, sea lions doing tricks and brightly colored tropical fish were universal favorites and the huge whale sharks for which the aquarium is famous were also impressive. But for some the scuba divers were favorite!

Location: 1-1-10 Kaigandori, Minato-ku. A 5-10 minute walk from Osakako station, just next to the huge Ferris wheel.

Transport: One-way combination Hankyu/subway tickets from Yamada station ¥500. From Yamada station take a Tengachaya-bound Hankyu Senri-line train to Sakaisuji-Hommachi, change to the Chuo (green) subway line bound for Cosmosquare to Osakako station, exit through Exit 1.

Single day entry fees: Adults ¥2,300; Grade school and middle school students ¥1,200; under five years old ¥600.

Share your story!

Do you know what's going on in Osaka? Have you got a great Kansai adventure to share? Do you know a must try restaurant? An unbelievable experience? QBiTs wants to hear your story. Whether it's a trip to the golden pavilion or the grocery store, an izakaya or the Itami airport, share your story! Contact qbits@riken.jp or pop into the Science Communication office on the first floor of building A in Furuedai for an interview.

BON VOYAGE

QBiC says goodbye to students from the University of Wisconsin

University of Wisconsin students Jacquelyn Wong (far left) My An-adirenkkun (far right) enjoying food and conversation with international Ph.D. students Vipin Kumar (center left) and Chin Yin Fai (center right).

Three undergraduate students from the university of Wisconsin-Madison have returned to the land of cheese and butter after spending the summer at QBiC. My An-adirenkkun and Leah Varner were in the Taniguchi lab and Jacquelyn Wong was in the Okada lab. The three commented on how they found out about QBiC and their time in Japan.

Jacquelyn Wong: The University of Wisconsin has an international internship program database. That is how I found out about RIKEN. I'm a genetics major, so I specifically looked for labs that did genetic based research. Spending the summer at QBiC I realized that I want to continue research and maybe work in a company like RIKEN.

My An-adirenkkun: I received a scholarship to do a molecular biology internship abroad from the Promega Corporation which is headquartered in Madison Wisconsin. This experience has expanded my awareness of scientific research and of graduate studies. The IPA program sounds interesting. Most memorable was being attacked by deer in Nara.

Leah Varner: I may come back to Japan for a graduate degree in genetics. I was born in Japan and am eager to return. I like natto and I wanted to try horse sushi but I didn't have the chance. Our most memorable trip was to Arashiyama in Kyoto.

The Chow Down

Prabhat Shankar's Egg Curry

Ingredients

-Unboiled eggs
-Potatos, onions, any other vegetable you like(mushroom, tomato, peas)
-Curry spice

Recipe

1. Boil the eggs and potatos. Peel their cover. Cut potatos into small sizes, and on a frying pan, fry for few minutes till golden brown in some oil. Also fry the boiled and peeled eggs till golden brown.

2. In the frying pan, heat oil, fry onions cut in small size for 3-5 mins. Add curry spice and fry for 1-2 more mins on low flame.

3. Add fried potato, eggs and other vegetables. Stir for 2-3 mins.

4. Add 2 cups of water. Cook for 10 mins

5. Serve with rice or nan.

Have a recipe you want to share? Contact us at: qbits@riken.jp

QBiC

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