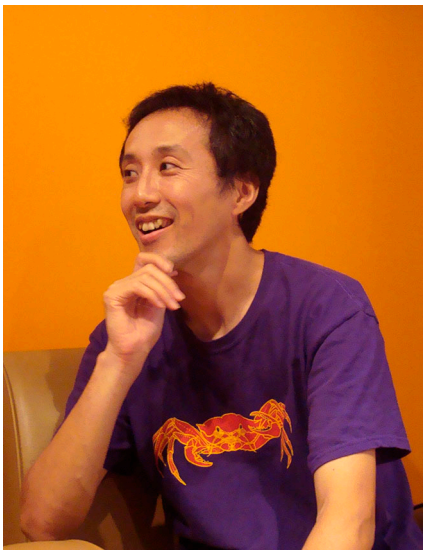
Gohta Goshima: Questing for answers on the mitotic spindle

Goshima studies spindle assembly and microtubule dynamics.

The successful execution of cell division requires the coordinated and concerted activity of myriad genes—so many, in fact, that new players are still being identified, and the roles of many are still unknown.

Seeing a question that needed answering, Gohta Goshima jumped into the search for mitosis-associated genes as a postdoc (1, 2) and has characterized several new genes involved in spindle assembly (3) and microtubule dynamics (4). Goshima has since expanded his search into new territories, seeking to understand how different organisms solve the problem of mitotic spindle assembly (5), as he told us when we reached him at his office at Nagoya University in Japan.



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Gohta Goshima

A QUESTION OF STYLE

Did you grow up in Japan?

Yes, I was born in Osaka. My interests growing up were pretty typical for a Japanese boy: I liked to play baseball, soccer, and shogi (Japanese chess). I really didn't like science at all, and my father and mother discouraged me from being a scientist because they felt that I did not have enough creativity. I think my mother also felt that science was not a very good occupation because she always had to watch my father, who was a researcher in cardiac biology, working so much harder and longer than office workers. So I nearly chose to take the nonscience track in high school, but I realized that once one is on the nonscience track one cannot later switch to science easily, whereas the reverse is not true. If I struggled in science I could always switch to a nonscience discipline. That is the main reason why I decided, at the last minute, to do a biology major at university.

You liked biology well enough to continue with a PhD…

In the Japanese system, real research starts in the last year of college, and most students go on to graduate school, often staying in the same laboratory where they do their undergraduate research. So I entered Mitsuhiro Yanagida's laboratory as an undergrad and studied how kinetochores affect spindle morphology via their interactions with microtubules.

I very much liked doing experiments, and I was good at getting data. I published several papers during my graduate work. But psychologically this was a difficult time for me because Yanagida-san, like my parents, felt that I lacked creative vision. I thought I would probably have to quit science before becoming a researcher, but I decided that, if this was so, then I should work my hardest and accomplish as much as I could before I had to quit.

Then the American professor Andrew Murray visited our lab, and I took a three-hour train trip with him to a Japanese conference. We started talking about science, and he said scientists do research in order to understand something that is not understood. This was a revelation for me, because this was exactly my style. I may not have any grand philosophy, but I am pretty good at solving the problem in front of me. Even small questions can be worth addressing. But I still was not convinced that I should stay in science until I was maybe 30 years old.

> "This was a revelation for me, because this was exactly my style."

MAKING A COMMITMENT

What eventually convinced you to stay in a research career?

I was quite successful in terms of my publication record and enjoyed doing research, so I thought, why not do a postdoc? My postdoc interviews were only on the west coast of America. I looked at San Diego, San Francisco, and Seattle for a very simple reason: all have major league baseball teams and a lot of good Asian restaurants. [Laughs] I joined Ron Vale's lab in San Francisco.

When I got to Ron's lab, I had the idea to investigate the roles of different motor proteins in mitosis using RNAi, which at that time was a newly developed technique. My friends all thought this was a boring approach, but I knew I could do it quickly. So I did it anyway and observed some unexpected phenotypes in that screen. I thought Ron would think this was a boring paper and wouldn't be interested in publishing it, but he was actually quite enthusiastic about it. This became my most frequently cited paper.

After that, I returned to my main project, which concerned organelle transport in neurons. For two years I was unsuccessful with this, whereas my side project on the mitotic spindle was going very well and generating a lot of data. Clearly I should focus on the spindle! [Laughs] But I was worried that most of the big questions in the mitosis field had already been answered or were about to be solved. Then in the summer of the third year of my postdoc I went to Woods Hole and mentioned my concern to Ted Salmon, who had been in the mitosis field for 30 years. He said he thought the very same thing back when he was a student! He said, "Don't worry, Gohta. Just pursue what you are interested in."

Text and Interview by Caitlin Sedwick
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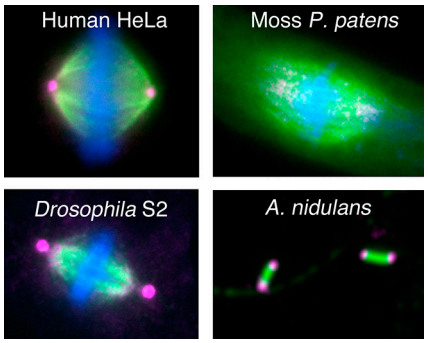

IMAGES COURTESY OF GOHTA GOSHIMA (TOP LEFT AND BOTTOM LEFT); YUKI NAKAOKA (TOP RIGHT); AND TOMOYA EDZUKA (BOTTOM RIGHT)

Spindles under study in the Goshima lab. Labeling: microtubules, green; DNA, blue; γ-tubulin, magenta.

So that's when you committed to studying the spindle?

Right. After talking with Ron, I decided to do a genome-wide RNAi screen for genes involved in mitotic spindle formation in fly S2 cells. Again, this may not be a very creative approach. What I did was simply mixing cells with 14,425 different RNAs and observing 3,950,818 spindles. But as my parents foresaw, I am good at doing this type of routine work. [Laughs] After about six months I had several interesting genes to follow up on, and then I got a group leader position at Nagoya University.

In our screen we had found several genes that gave rise to the same phenotype. So I took those genes and did a quick experiment to look at where those proteins are and whether they interact with each other. We found that they formed a stable, eight-subunit complex, which we named augmin, that is important for microtubule amplification and organization of the mitotic spindle. We showed—first in fly S2 cells but later and more vividly in plant cells—that centrosomes can largely compensate for a lack of augmin but that cells lacking both augmin and centrosomes have very defective spindles. In plants the centrosome was lost during evolution, so when we knocked down augmin the spindle was completely defective. We're now looking at augmin in filamentous fungi, where it seems to play a somewhat different role.

KEY WORDS

Another interesting gene in your screen was Sentin…

Disruption of Sentin gives rise to a short spindle phenotype that is similar to that of cells lacking the microtubule polymerase XMAP215. Then we saw that, like the microtubule-associated protein EB1, GFP-tagged Sentin localizes to the plus ends of microtubules. We found that Sentin directly binds to EB1 at plus ends and helps recruit XMAP215 to facilitate microtubule polymerization. Sentin also has a role in inducing microtubule catastrophe.

One of the key words in my lab is "reconstitution." We would like to reconstitute the dynamics of the microtubule plus end in vitro using a bottom-up approach. Tubulin has some dynamic behavior without any other proteins as long as there is GTP, but that behavior is quite different from the in vivo dynamics. Adding Sentin, EB1, and XMAP125 can produce, to some extent, similar behaviors to what we see in vivo, but we don't see all the characteristic features yet. We must be missing some proteins.

"Another key word in my lab is 'diversity.'"

How did you come to start working with plants?

Another key word in my lab is "diversity." When I was in high school I contemplated studying agricultural science at university, so I have a long-standing interest in plant biology. As a group leader I was finally free to choose my own projects, and I decided to start working with plants. I wanted to do RNAi screens in plants similar to the ones I had already done in fly cells, and the moss *Physcomitrella patens* was a very attractive model system because a draft genome was available and RNAi was already established in this plant. I wanted to develop a conditional RNAi system in *P. patens,* and that took quite a while, but eventually I was able to combine this with live imaging to do some gene hunting studies. My first focus was on kinesin motors because plants have unusually high numbers of kinesins. We think plants use many of these motors during spindle organization to compensate for the absence of centrosomes and of cytoplasmic dynein.

What advice do you give to students who are interested in a career in science?

Many Japanese students quit graduate school after getting a master's degree. I encourage all my graduate students to get a PhD because the heart of a PhD is to publish a research paper and having a paper as a first author is a great thing. It will be yours forever, even after you die. It is such a wonderful feeling.

Afterwards, it's their choice whether they go to industry or continue as a postdoc. But if they decide to do a postdoc, I advise them, based on my own experience, that they should decide within three years whether to go to academia or take another path.

1. Goshima, G., and R.D. Vale. 2003. *J. Cell Biol.* 162:1003–1016.
2. Goshima, G., et al. 2007. *Science.* 316:417–421.
3. Goshima, G., et al. 2008. *J. Cell Biol.* 181:421–429.
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Goshima lab members under cherry blossoms.