

THE AUTHOR FILE

Takanari Inoue

Sensors show calcium movement in tiny, cellular antennae

“If there is a mountain, you will want to climb it. If there is a cave, you would like to enter and see what is in there,” says Takanari Inoue, a researcher in the



Takanari Inoue

cell biology department at Johns Hopkins University. Curiosity led him from Japan to the USA and has taken him deep into cellular compartments.

Cilia are tiny hairs on cells that were once considered functionless vestiges but are now known to fulfill many roles. When cilia are absent, illnesses called ciliopathies can result, some of which cause kidney failure. In the kidney's lumen, cilia sense their environment: urine flow bends them, and they respond with an internal rise in calcium.

Inoue and his team have targeted genetically encoded calcium indicators to cilia and revealed this calcium flow, which was not previously possible. The cilia act as antennae for an environmental, mechanical cue, “which is my favorite function of cilia,” he says. They can also sense light, sound and chemicals.

These organelles are typically a few micrometers long and less than half a micrometer wide—dimensions that make them difficult to image and study. Inoue and his team had to find a way to image calcium in this tiny space, construct the DNA plasmids that encode cilia-targeted calcium sensors, and assess these sensors.

Inoue's curiosity makes him want to apply his new sensors to observe flow-induced calcium signaling in the kidneys of live mice. That work could be part of an eventual model for polycystic kidney disease. Cilia in these patients are present but just do not respond to flow, he says. He even wants to tinker with molecular actuators, which could be artificial cilia acting as the sensing antennae for cells lacking flow sensation.

Inoue likes studying compartmentalized signaling in cells. Calcium ions are multitaskers among the signaling molecules and can trigger a number of functions. He previously explored how to manipulate these signaling events in different compartments before he focused on calcium in cilia. Curiosity was the driver here, too, he says.

Inoue's curiosity rose during his PhD work at the University of Tokyo. The pharmaceutical sciences

department was multidisciplinary, with research in genetics, chemistry, structural biology and the interfaces between these fields. He continued with this multidisciplinary approach during his postdoctoral fellowship in Stanford University's chemical and systems biology department. From a distance, he watched the research atmosphere in his home country change.

Japan has traditionally had a more closed research environment. “But there are several labs that follow the open lab style in these days,” he says. Junior scientists had few options, but now there are more tenure-track positions for researchers in their 30s. At most of the Japanese universities, however, graduate students must pick their thesis lab without a trial period. “That may sound very scary for US students,” Inoue says.

In Japan, a principal investigator's salary is fully supported by the university. He sees competition for grants as “extremely tough” in the USA, where scientists must often support themselves, their lab staff and graduate students. He fears the competition might bias scientists in the USA toward projects that deliver relatively quick results.

Inoue plots his research path when attending conferences, reading papers and while driving his car, which he sometimes wishes were a Harley-Davidson motorcycle. “These are the times my brain can connect different sources of information,” he says. And he enjoys chats with members of his lab and takes care that, independent of differing scientific backgrounds and cultures, they feel appreciated as individuals.

Stanford University School of Medicine oncologist Rajat Rohatgi met Inoue during their postdoctoral fellowships, when they were baymates. Rohatgi was just returning to laboratory research after his clinical training. Of Inoue, he says that “his incessant curiosity, impeccable scientific taste, devotion to precision in experimental design and, most importantly, ebullient laugh made me realize again how fulfilling science can be.” The two men continue to collaborate.

Inoue knows that the Japanese are sometimes stereotyped as being more reserved on the sports field and in science. “We as Japanese indeed try to hide emotion in public,” he says. Some have told him he looks similar to a Zen monk who is always calm. But he finds that hard to believe. “I thought I am more like a ninja.”

Vivien Marx

Su, S. *et al.* Genetically encoded calcium indicator illuminates calcium dynamics in primary cilia. *Nat. Methods* **10**, 1105–1107 (2013).

“If there is a cave, you would like to enter and see what is in there.”