

# Yusuke Nakamura

Yusuke Nakamura might not win any popularity contests in his homeland, but friends and rivals agree that his unique blend of scientific skill and financial savvy makes him the most influential force in Japanese research.

It's easy to see that Yusuke Nakamura is one of the most powerful men in Japanese science. The University of Tokyo's Human Genome Center, of which Nakamura is director, is sleek and modern, in complete contrast to a dilapidated research building next door. Each floor of the center's new building is shared by two researchers, but Nakamura occupies two floors.

Including his laboratory at the RIKEN SNP Research Center in Yokohama, Nakamura leads 130 students, postdocs and technicians. As his compact frame weaves through the labs, men in suits and women in lab coats spring to their feet and bow. There is gleaming steel everywhere, and every lab has fingerprint scanners for security. Not even the director of the university's prestigious Institute of Medical Sciences (IMS) has access.

Much of the equipment is part of Japan's Biobank project, which aims to collect serum and DNA samples from 300,000 Japanese. The five-year project was controversial, in part because of privacy and discrimination issues, but brought \$180 million to Nakamura's already brimming coffers.

Nakamura also heads Japan's piece of the International HapMap Project, which is documenting single nucleotide polymorphisms (SNPs), and he is responsible for 25% of the world's data. His team has thus far contributed more SNPs to the project than any other.

"He's a very strong leader. Without him, Japanese genomic research will not perform at the same speed," says Ryosuke Takahashi, a researcher at the RIKEN Brain Science Institute in Wako. "In my opinion, he's doing great things for Japanese science."

Many people expected Nakamura to succeed Ken-ichi Arai as director of the IMS last year. But Nakamura says he is too busy with research. "I'm not interested in that kind of thing," he says. "In Japan, if you say 'yes' or 'no' clearly, you would make enemies. To not make enemies is important to be a good administrator—I'm not that kind of person."

Although Nakamura's name is now inextricably linked with genomics, he first became famous for his work on DNA markers and for isolating various disease-related genes. He says his primary motivation even now is to translate the results of genomics to the clinic, particularly for cancer.

Nakamura began his career as an abdominal surgeon. Frustrated by the limited options to treat cancer—he lost his mother to colon cancer—he became a postdoc at the University of Utah. After publishing a series of articles on DNA markers in the late 1980s, he returned to Japan—mostly, he says, for the sake of his children's education.

At the time, the Japanese government had little interest in genomics, but in response to international competition, in 2000, it launched the Millennium Genome Project (MGP). "If that hadn't happened, I might have left Japan already," Nakamura says.

In Japan, it is impossible to mention Nakamura without sparking conversation about his grants. With funding for the Biobank, the MGP and his slice of Japan's massive cancer project, he has averaged about \$50 million per year. One year, he topped \$120 million. In a country where the average researcher is lucky to net ¥5 million (about \$45,000) per year, the money has understandably created some friction—something Nakamura is intensely aware of. "There's lots of jealousy and envy," he says.

Most of the money from the projects has gone toward infrastructure and salaries, Nakamura says. He adds that people often mistakenly accuse

him of funneling SNP money into his new company, OncoTherapy. "People [are] mixing up everything," he says.

Experts such as Francis Collins, director of the US National Human Genome Research Institute, say genomics projects don't come cheap. But many Japanese scientists criticize the research without realizing its importance, Nakamura says. "Superficially they're quite friendly, but under the desk, they kick my leg," he says. "If I ask which parties [are] skeptical, I get no answer. I prefer the open discussion, even quite aggressive—that is quite important to science."

Collins and others in the US say they appreciate Nakamura's forthright approach. In Japan, however, Nakamura is notorious for being outspoken and for challenging authority—both rare qualities among the Japanese.

"[Nakamura] was sort of Japanese in America, but he is much more American in Japan," says David Cox, chief scientific officer of Perlegen Sciences. "I'm not saying he's not Japanese, he's very Japanese. But he does business like an American," says Cox, who has known Nakamura for nearly 20 years. Nakamura admits to much the same thing. "Genetically I'm Japanese, but my thinking is American," he says.

That philosophy has not won him many friends in Japan. Some Japanese scientists describe him as a "bulldozer" and a "big boss."

"[Nakamura] is not a president, he's an emperor," says Yoshiyuki Sakaki, director of the RIKEN Genomic Sciences Center. "He asks everybody to obey his orders, it's true."

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Nakamura just has high expectations for himself and for others, says Cox. "There are a lot of people like that who don't have friends or loyal supporters," Cox notes. But after a recent visit to Nakamura's lab, he says, he was struck by the lab members' loyalty to Nakamura and his work. "They do that not because Yusuke beats them with a wet noodle but because they care as much as he does," Cox says. "He's not a jerk. He just doesn't have time not to get it done—yesterday."

Sakaki says Nakamura has had to face tough questions, but that is inevitable when sizable grants are involved. "He is using big money. It's not clear how big the outcome will be," Sakaki says. Because common diseases are complex, he adds, "I'm not sure such a large amount of population genetics can extract genes related to diseases."

Nakamura says he fears that funds for his projects will not be renewed next year. Even if funding is reduced, he says, it will be difficult to stay competitive with international teams, but would free him to go back to the US. "I still have some hope of playing in the major leagues."

Nakamura's comment is telling of the impossible standards he sets for himself, says Cox. "Here's a guy who has arguably the most impressive genotyping operation in the world ... and he feels he's not playing in the big leagues," Cox says. "Which planet does this guy want to go to? This guy is the big leagues."

Apoorva Mandavilli, Tokyo