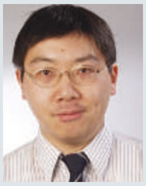
# Abstractions



**FIRST AUTHOR**
When the Huygens spacecraft descended into the atmosphere of Saturn's largest moon, Titan, in January 2005, the data it recorded suggested it had encountered a fine mist of rain. But this was no ordinary rain — it was a methane mist. Some researchers thought methane condensation to be unlikely in Titan's frigid environment (its surface temperature is −180 °C). However, according to the data collected by Huygens, which allowed an international team of scientists to calculate a profile of Titan's relative humidity, there is condensation on Titan. Tetsuya Tokano, a geophysicist at the University of Cologne, Germany, and his colleagues used Huygens' data to characterize Titan's clouds (see page 432). He tells *Nature* about methane rain on a distant moon.

**Had you always had a fascination with Titan?**
Clouds on Earth were the subject of my master's thesis. I then moved on to study Titan, developing climate and atmospheric-circulation models. I was interested to know whether, if rain arrives at the moon's surface, there would be a hydrological cycle. As it turns out, there is.

**How often does it rain on Titan?**
We believe that it was raining during the descent. In contrast to sporadic clouds observed near the South Pole, this rainfall is permanent for at least the season, which lasts several years on Titan. There are 30 Earth years to every one Titan year.

**What does methane drizzle suggest about the geological features of Titan?**
The rivers on Titan's surface were probably not caused by this drizzle because the rainfall is too weak. But the presence of drizzle does not rule out the occurrence of thunderstorms and heavy rain storms at other times.

**How do your results compare with those of Hueso and Sánchez-Lavega (page 428)?**
They believe that rainstorms are rare but violent, whereas we feel that rain is ubiquitous but weak. However, I think both can occur on Titan, although not simultaneously.

**Has such drizzle been documented on other planets and moons?**
Methane clouds have been identified on some other planets, but, so far, no actual rainfall has been observed.

**Do your results have any relevance for the hydrological cycle on Earth?**
This paper would definitely be of interest to terrestrial meteorologists. The comparison of methane and water condensation provides a better idea of how condensation works. ■

# MAKING THE PAPER

## Antonio Iavarone

**How a simple protein sent researchers on a long journey.**

Sometimes, finding out how proteins interact with each other, trigger other reactions and affect development is more complicated than the biochemical process itself. Such was the case for two cancer biologists from Columbia University, New York. While Antonio Iavarone and his colleague Anna Lasorella were exploring the role of a family of proteins in brain cancer, their research led them from gene expression to basic cell-division processes, and on to neurobiology. During the course of this journey, which is detailed on page 471, they collaborated with two separate groups, eventually learning that a family of proteins essential to the basic processes of cell proliferation and cancer also exerts influence beyond cell division in nervous-system development.

Iavarone and Lasorella had been studying a family of proteins to find out whether they were turned off or on during brain development and in brain cancer. These proteins, particularly one known as Id2, were already known to prevent stem cells from differentiating into adult cells. But the experimental data showed a paradox. Id2, which had been thought to be an inhibitor, actually seemed to be stimulating the development of axons — slim fibres that carry signals from nerve to nerve. "We couldn't figure out what it meant," says Iavarone. "We had the result for a year without really knowing how to follow it up."

Meanwhile, Lasorella and Iavarone had been using proteomics to identify the partners of Id2 in neuronal cells. They discovered that Id2 interacts with the anaphase promoting complex (APC), a cluster of proteins that works by priming other proteins for degradation and is key to the cell-division process of mitosis. "We looked for how the proteins in the APC complex talked to each other, how they attached to each other and which proteins in APC attached to Id2," says Iavarone.

With the help of a cancer-biology group at New York University (NYU) that had expertise in looking at biochemical processes triggered by APC, Lasorella and Iavarone found that when APC links up with Id2, the complex then degrades the protein. But when mutations that prevented binding to APC were introduced in Id2, the protein became resistant to degradation and accumulated inside the cells at very high levels.

Meanwhile, a paper from a group at Harvard Medical School assigned a new function to APC in mature neurons, the ability to prevent axon growth. But the paper didn't explain the exact mechanisms. With a hunch that Id2 might play a role, Lasorella and Iavarone collaborated with the Harvard group. They showed that the mutated 'super Id2' protein allows axons to grow in different types of neurons, even in the presence of the myelin components that normally coat nerves and prevent them from regenerating after injury.

"This was a very exciting journey," says Iavarone. "We moved from finding Id2 as a target of the APC to showing there are APC–Id2 complexes in neurons, and we discovered how all of this happens." The path taken by these researchers, from looking at a protein complex associated with cell division to finding out how the same complex can affect axonal growth, shows how simple problems in molecular biology can turn into long, unexpected trips. ■

# KEY CONTRIBUTOR

During the past ten years, Shuya Fukai, an associate professor at the Tokyo Institute of Technology, Japan, has developed techniques to help other scientists better determine three-dimensional protein structures, particularly for protein–RNA complexes. He began this work as a graduate student at the University of Tokyo, working with Osamu Nureki. This work, followed by continuing collaboration, produced clear snapshots of a three-step chemical reaction (see page 419). According to Nureki, Fukai's expertise in crystallography, combined with his skills in biochemistry and molecular biology, made solving these structures possible.

Fukai plays down his role. "When someone meets a problem in crystallography, I give advice to help solve it, or, in more difficult cases, try to solve it myself," he says. "In this paper, as first author Tomoyuki Numata is a good crystallographer, minimum advice was mostly sufficient."

Nureki demurs, saying that Fukai was instrumental not just in resolving the initial structures, but also in validating them using electron density maps, improving on the initial picture quality. These efforts paid off. "The three crystals correspond to the three reaction stages," Fukai says. "That's an unexpected success." ■