Abstractions

LAST AUTHOR

The genetic changes underlying the evolution of language in humans remain mysterious. *FOXP2* is the only gene to be linked so far to inherited speech and language dysfunction — prompting researchers to probe its evolutionary significance. On page 213, Daniel Geschwind of the University of California, Los Angeles, and his colleagues express the human and chimpanzee versions of *FOXP2* in human brain cells to compare their activities. Geschwind talks to *Nature* about what they found.

How did this work come about?

My lab is interested in understanding what makes humans human. We study the genetic basis of language both in health and in diseases such as autism and neurodegeneration. In this study, we tried to combine a hypothesis-driven study to learn more about the specific functions of a known gene with discovery-based science that might help to identify an evolutionary context for its function.

Did the work shed light on the differences between chimpanzees and humans?

Yes. We found that not only *FOXP2*, but also some targets of the FOXP2 protein, may be co-evolving in humans. We first introduced the human and chimpanzee versions of *FOXP2* in cell culture and looked at which genes were turned on as a result, then we compared the patterns of gene expression with those normally seen in adult brain tissue from humans and chimpanzees. We found that a significant proportion of FOXP2's targets that were different between chimpanzees and humans in cell culture were also different between the chimpanzee and human brain.

So, is there much doubt that *FOXP2* is central to language evolution?

The high correlation between FOXP2 targets and the differences observed between chimpanzee and human brains does suggest an important role. FOXP2 is probably part of a larger regulatory network. For example, FOXP2 also regulates another gene involved in language and autism, *CNTNAP2*. Our work also raises the possibility that FOXP2 regulates the development of some key motor and physical structures that are important for speech — such as the larynx and pharynx.

Is mixing hypothesis-based and discovery-based science typical in this field?

Neuroscience is traditionally a hypothesis-driven field. By combining hypothesis testing with discovery-based methods, we can more quickly make progress in understanding what is happening at multiple levels — from molecules to cells to circuits and to behaviour. ■

MAKING THE PAPER

Richard Mathies

Tracking the structural evolution of chemical reactions.

Fluorescent tags have become a staple of biological experiments since their prototype — the green fluorescent protein (GFP) of the jellyfish *Aequorea victoria* — was cloned in 1992. The protein glows green when it is excited by blue light, the result of the transfer of a proton between two amino acids. Richard Mathies and his colleagues at the University of California, Berkeley, have now teased apart the changes in GFP's atomic structure that allow this proton transfer to occur.

Mathies, a chemist, is interested in reaction dynamics, especially those involving photo-excitation. He has long been trying to visualize the structural changes that molecules undergo during chemical reactions as result of atomic motions that occur in the time range from tens of femtoseconds (10^{-15} seconds) to a picosecond (10^{-12} seconds). "This was no-man's-land for structural techniques," he says. In 1997, during a sabbatical at the University of Leiden in the Netherlands, he realized that he could adapt Raman spectroscopy — a laser-based technique that detects the frequencies of atomic vibrations in molecules — to collect high-resolution vibrational spectra on the femtosecond timescale. "I was so excited I sent faxes to the lab in the middle of the night trying to get my students fired up and working on it," he says.

Mathies first applied the technique, dubbed femtosecond-stimulated Raman spectroscopy, to the photoreaction of the visual pigment rhodopsin. During this process — which normally occurs in the retina of the eye — rhodopsin's excited state lasts for only 50 femtoseconds, too short a time for the researchers to monitor the evolution of the excited state, even with the new technique. "Nevertheless, we gained a lot of information about the first step in the visual process," says Mathies. Then graduate student Renee Frontiera suggested trying the technique with GFP, which remains in its excited state for 5–10 picoseconds.

A talented new postdoc, Chong Fang, took up the project and developed a system of multiple lasers with the appropriate wavelength ranges — a process that took several years. The group got their first taste of success when they used the system "to obtain really good signal-to-noise vibrational spectra of GFP every 25 femtoseconds," says Mathies.

By analysing hundreds of these spectra, they reconstructed the structural alterations that occur in the excited GFP molecule as it undergoes proton exchange (see page 200). "If you are trying to drive from one place to another, the simplest way, in theory, is to follow a straight line from A to B," says Mathies. "But, as we know from driving in any city, the reality is not that simple — you might first have to go through a tunnel, then up a ramp and then onto the freeway. The same thing happens with GFP. The proton is not simply handed from one amino acid to another. The molecule undergoes a series of skeletal changes that eventually align the atoms in just the right way for proton transfer."

Although the findings provide a detailed description of excited-state proton transfer — a widespread chemical reaction — the work paves the way for even more detailed studies. "The lasers used in this study were put together years ago, limiting us to 25–50 femtosecond resolution," Mathies says. "With up-to-date lasers, we could get down to 10 femtoseconds. That would be unprecedented." ■

FROM THE BLOGOSPHERE

In an exclusive interview on The Great Beyond, *Nature* reporter Geoff Brumfiel explores Romanian hopes to launch a balloon to the Moon. Bogdan Sburlea, project manager of the non-profit Aeronautics and Cosmonautics Romanian Association (ARCA), talks about plans to test-launch 'Helen', ARCA's proof-of-concept rocket for its bid for the Google Lunar X PRIZE. The contest will award millions of dollars in prize money to privately funded teams that successfully land and manoeuver a robot on the Moon, and send data and images back to Earth, before 31 December 2014.

Sburlea describes why the test vehicle will not actually make it into orbit: "We need to check the launch from the water, the usage of [the] world's largest solar balloon, not to mention the stabilization method and the strange position of the stages. We've got enough things to test; reaching orbit is not an objective for this launch."

You can check out the full interview, along with a short video of Helen's flight plan, set to music, at http://go.nature.com/zi4j2s. ■

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