

erates new DNA.

PARP acts by removing ADP-ribose from a small molecule called NAD<sup>+</sup> and then adding it to the target proteins. To see whether tankyrase displays a similar catalytic behavior, Smith and de Lange did test tube studies in which they mixed the enzyme with NAD<sup>+</sup> and TRF1. They found that tankyrase adds ADP-ribose both to itself and to TRF1. Typically, TRF1 exists bound to DNA, but when tankyrase is present, "TRF1 comes off the DNA," says Smith.

De Lange cautions that they still need to demonstrate that what they see in their test tube studies occurs in living cells. But she and her colleagues suspect that TRF1 normally sits on the telomere, thereby inhibiting telomerase activity. During, or perhaps after, DNA replication, tankyrase modifies TRF1 such that it leaves the telomere, enabling telomerase to replace DNA lost during replication in blood cells, germ cells, or tumors. "It looks like [tankyrase] could be an important component in a regulatory or signaling pathway," says Tom Cech, a biochemist at the University of Colorado, Boulder.

Tankyrase is the second protein linked to DNA repair that has now been found to be associated with the telomeres; the first was a protein called Ku that binds to broken DNA. That suggests that DNA repair and telomere synthesis may have some common components. But until researchers pin down tankyrase's exact function, it's "too early to tell whether [the enzyme] is a good target for drug discovery," says telomere expert Calvin Harley of Geron Corp. in Menlo Park, California. Nevertheless, he says his company is thinking about procuring rights to pursue this possibility—Rockefeller University has filed a patent application on tankyrase—in hope of finding ways to extend the lifespan of cells.

—ELIZABETH PENNISI

## NEUROSCIENCE

### fMRI Provides New View of Monkey Brains

**LOS ANGELES**—Neuroscientists who want to map brain activity in monkeys have many options that aren't available with human subjects. But a favorite method for studying human brains, functional magnetic resonance imaging (fMRI), which delivers pictures of brain activity by measuring increases in local blood flow, has not been well suited to monkey studies until now. Aided by a specially designed magnet, Nikos Logothetis of the Max Planck Institute for Biological Cybernetics in Tübingen, Germany, has made high-resolution fMRI images of the brains of both anesthetized and awake monkeys.

Those who saw his presentation here last week at the 28th annual meeting of the Soci-

ety for Neuroscience say the work is a marked advance over the only other published fMRI images of monkey brains, reported last summer by two teams (*Science*, 10 July, p. 149). Some researchers worried that the several-millimeter resolution of those images was not good enough to see some of the structures in monkey brains, which are much smaller than those of humans. And because those experiments, like all other fMRI studies done on monkeys until now, used a horizontal magnet designed for supine human patients, the animals had to crouch in an awkward position that promised to make it hard to perform the choice-based tasks on which many brain activation experiments are based. Also the monkeys were awake because previous work had failed to obtain fMRI images on the anesthetized monkeys used for many other types of neurophysiological studies.

Logothetis, however, produced images from anesthetized animals with a resolution of less than a millimeter, close to the theoretical limits of the technique, which detects magnetic signals from oxygenated blood, says fMRI expert Robert Turner of University College London. Indeed, he calls the work "a technical tour de force." In the specialized setup, Logothetis also got crisp images from awake monkeys sitting in the position to which they were accustomed and performing choice tasks. The results will convince many researchers of the usefulness of monkey fMRI, says neuroscientist Leslie Ungerleider of the National Institute of Mental Health. "I thought it would be 10 years before imaging in the monkey reached this level of sophistication," she adds.

Such images have been eagerly awaited because neuroscientists want to compare fMRI images of monkey brain activity to data gathered by sticking electrodes directly into monkey's brains and use that information to infer more about the neuronal activity that underlies human fMRI brain images. They also would like to use fMRI to identify new areas of activity in monkey's brains that they can then study with electrodes. And being able to study anesthetized animals is a plus, because sensory stimulation of unconscious animals is a widely used method for mapping areas of brain activity.

To develop his system, Logothetis turned to Bruker Medical Instruments in Ettlingen, Germany, to design a vertical, monkey-sized magnet with a field three times stronger than those of the magnets commonly used

on humans, a change that improves spatial resolution. He also refused to accept reports that fMRI wouldn't work on anesthetized animals. Researchers had blamed earlier failures on effects the anesthesia might be having on blood flow response to brain activity, but Logothetis felt that shouldn't be the case if the monkey were monitored as carefully as a human patient.

Consequently, he hired a professional anesthesiologist who anesthetized the animals while keeping parameters such as pulse, blood gases, blood pressure, and blood volume "absolutely within the normal range." He then tested his method by recording fMRI images of the anesthetized monkeys viewing visual images, such as moving patterns, and got high-resolution images of activation in the monkeys' visual cortex.

Logothetis notes that his team's results remain just a demonstration that the technique works and have not yet answered any research questions about brain function. In that respect, monkey fMRI has some catching up to do. Japanese researchers have for several years been studying brain activation in monkeys with positron emission tomography (PET), which uses radioactive tracers to detect blood flow changes. For example, using a dedicated monkey PET scanner at



**Seeing is believing.** A monkey's visual cortex responds to a moving image.

Hamamatsu Photonics in Hamakita, Japan, Hirotsuka Onoe's team at the Tokyo Metropolitan Institute for Neuroscience last year discovered a new site of color processing in the monkey visual system. PET in monkeys has better resolution than it does in humans, says Ichiro Fujita of Osaka University, who has been doing monkey PET studies at Hamamatsu. That's because monkeys can be scanned repeatedly, while the risks of the radioactive exposure limit human subjects to a few scans. This forces researchers to average the data from several different subjects, reducing the image quality.

But even monkey PET cannot match the temporal and spatial resolution of fMRI, says Akichika Mikami of Kyoto University, who also does PET studies on monkeys. He predicts PET will be eclipsed by fMRI, except in specialized niches such as using radioactive neurochemicals to visualize their receptors in the brain, which is not possible with fMRI. Turner agrees and expects a rapid research boom in monkey fMRI: "I've been taking bets on how many presentations there will be at next year's meeting," he says. "I'm going to put money on there being more than fifty."

—MARCIA BARINAGA