

Illegal immigration. Neurons in a forebrain from a 20-week-old human fetus travel from telencephalon structures (yellow) to the dorsal thalamus.

Neuroscience, might explain some of the differences, he says, as well as allow researchers to study which molecules are key to building a human brain.

Developmental neurobiologist Pasko Rakic of Yale University, who conducted the research with grad student Kresimir Letinic, calls the neurons' route an "illegal immigration." Normally, cells from the telencephalon, the part of the developing nervous system that grows into the most sophisticated parts of the brain—those that do the heavy lifting when it comes to problem solving, social interactions, and memory—don't mingle with cells from the diencephalon, which gives rise to less advanced structures such as the hypothalamus and optic nerves. No other neuroanatomists have ever reported that neurons can breach the theoretical wall between the two regions; when Letinic and Rakic looked at fetal monkey and mouse brains, they saw, as expected, no crossover from one region to the other. But when the team stained and studied slices from fetal human brains, obtained from aborted tissue that had been donated to a brain bank, they found a stream of cells migrating from the telencephalon to the diencephalon.

These wayward neurons land in the thalamus, a relay station that distributes information to the cerebral cortex. Although the diencephalon still builds most of the thalamus, the second wave of telencephalon cells specifically boosts the parts of the thalamus that feed into the frontal lobes and other cortical areas that are responsible for higher-level cognition. This includes passing along both sensory information and internally generated information, such as emotional responses processed in the hypothalamus. "The frontal cortex doesn't operate without interaction with [this part

of] the thalamus," says neuroscientist Edward G. Jones of the University of California, Davis. The new report implies that "along with the expansion in cortex goes a new elaboration in the thalamus that helps promote [the cortex's] activity," Jones says.

To try to identify how the thalamus summons telencephalon cells, the researchers turned to fetal neurons in lab culture. They found that the human thalamus sends "come hither" signals that human telencephalon cells eagerly respond to, scooting toward the thalamus in a dish. Mouse telencephalon cells, in contrast, are repelled by the mouse thalamus. The Yale team hasn't yet identified the molecules that direct the neuronal migration. But if the researchers can decipher those molecular messages, the findings might help further explain how the human brain came to tip the interspecies scales.

—LAURA HELMUTH

SCIENCE POLICY

Group Raises Hackles As Well as Funds

A Republican legislator has created the first political action committee (PAC) to support preresearch candidates for Congress. But some researchers and lobbyists are worried that the group's plan to back only Republicans could divide the community by forcing scientists to choose sides.

Representative Vern Ehlers (R-MI), a nuclear physicist who chairs the Science Committee's environment, technology, and standards subcommittee, heads the new group, called SciPAC. In a 10 August letter to potential donors, he complains that the U.S. scientific community "has not taken the steps necessary to support elected officials who have supported science." The stated goal of the committee is to "increase the influence of supporters of science, engineering, and technology in Washington."

But Ehlers makes clear that he's only talking about one side of the aisle. "As a Republican, I'm obviously not going to contribute to Democratic candidates," he told *Science*. Indeed, his letter takes an indirect swipe at the opposition, noting that "since Republicans took over Congress a mere 6 years ago, the federal investment in research and development has increased nearly \$20 billion." Thomas Jones,

SciPAC vice chair and public policy director for the American Association of Engineering Societies, puts it more bluntly: "Republicans are good for science."

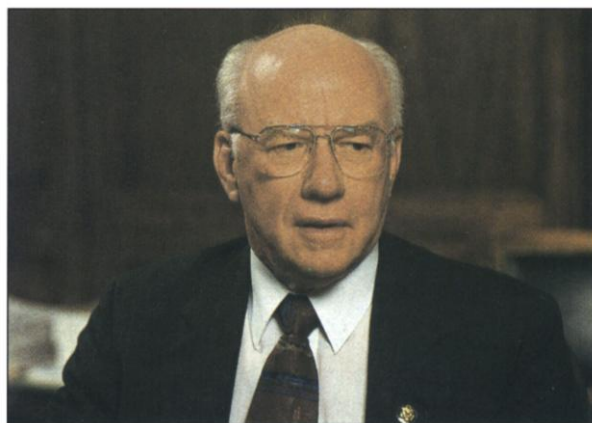
Science advocates have long complained that their community lacks the political muscle of other interest groups. And political action committees, which disburse funds to candidates, are a traditional way to win recognition and support. But the fact that Democrats need not apply for SciPAC funding troubles some old hands.

"The science community needs to be much more involved in the political process, and I have no problem with people raising money for candidates," says physicist Neal Lane, a former science adviser to U.S. President Bill Clinton and former head of the National Science Foundation (NSF). "But the science budget has bipartisan support, and no party can claim [full] credit." Lane warns that "making science into a partisan fight would not be good for science or for the community."

PACs created by politicians are typically designed to help just one party, says Jones, adding that Ehlers's role is to support the House Republican leadership. "And giving money to Democrats could jeopardize that leadership." More important than the question of partisanship, Jones argues, is the need to shore up support for science as the federal surplus disappears.

To succeed, however, Ehlers must convince scientists to write checks to a general fund that he controls. Direct contributions from researchers have helped elect some members, notably Representative Rush Holt (D-NJ), a physicist who has actively courted the scientific community. But a specific science-focused political action committee has never been tried.

Touted as "America's Voice for Science in Washington" on its Web site (www.scipaconline.org), SciPAC's financial goals are modest. "We're not going to raise a million dollars," Jones says. But he hopes



PACman. Representative Vernon Ehlers has created the first preresearch political action committee, for Republicans only.

that the committee will come up with enough funds to help at least a few struggling candidates "to buy a few more ads and give them an extra boost."

SciPAC was registered on 7 August and has a post office box in the building adjacent to NSF's headquarters in suburban northern Virginia, just outside Washington, D.C. Its first contribution, for \$250, came from Vinton Cerf, who helped create the Internet.

—ANDREW LAWLER

BIOCHEMISTRY

Body's Secret Weapon: Burning Water?

In the immune system's war against the world, antibodies have long been cast as semicombatants. They might spot invaders and even tie them up for a while. But when push comes to shove, they holler for big-gun immune cells such as macrophages to move in for the kill.

Now, it looks as if these plucky night watchmen may also dabble in chemical warfare. On page 1806, a team of California researchers reports that antibodies create highly reactive chemicals that cells can use to cleanse themselves and poison invaders. More surprising still, they seem to make them by burning water.

"These are important, interesting, and intriguing results," says Chris Foote, a biochemist at the University of California, Los Angeles. Foote says the data clearly show that antibodies generate reactive compounds. He cautions that it's less certain that they are oxidizing—or burning—water to do it. But, he concedes, "I don't have a better explanation."

Chemistry, particularly lethal chemistry, hasn't traditionally been considered part of antibodies' repertoire. "Over the last 100 years, chemists have come to peace with a theory that antibodies don't do anything. The killing is left to others," says Richard Lerner, a chemist who heads the Scripps Research Institute in La Jolla, California, and helped lead the team. "Now, it looks like the sheriff is the executioner as well, or at least contributes to the act."

Lerner, fellow Scripps chemist Paul Wentworth, and colleagues came upon the antibodies' expanded role largely by accident. While studying fine points of how antibodies function as catalysts, they found that the antibodies in their experiments were generating the reactive compound hydrogen peroxide (H_2O_2). "We thought something was peculiar with the experiment," Lerner says. They tested 100 other antibodies, and the result was the same each time. The group published the perplexing finding last year in the *Proceedings of the National*

Academy of Sciences, but it still had no real leads as to what was creating the H_2O_2 .

The big puzzle was where the energy to make the H_2O_2 was coming from. Initially, Lerner says, the researchers thought the reaction was burning the protein itself, but they found that far too much H_2O_2 was produced for that to be the case. Then, they hit upon the notion that much of the energy could be coming from molecules of singlet oxygen, an energetic and highly reactive form of O_2 produced when a source of energy, such as ultraviolet (UV) light, breaks water molecules apart and energizes the oxygen. Singlet oxygen can then react with more water to create H_2O_2 . By tagging water molecules with a heavy isotope of oxygen, Lerner's team confirmed that the oxygen that wound up in H_2O_2 had indeed come from water—evidence that singlet oxygen could be fueling the reaction.

For the reaction to occur, however, extra electrons need to be coming from somewhere else. So the Scripps team set off to find their source. After a battery of tests eliminated the obvious candidate, ions in the solution, the Scripps researchers teamed up with reaction modeling expert William Goddard III of the California Institute of Technology in Pasadena and his student Xin Xu. They suggested that a water molecule could combine with a singlet oxygen to produce a highly reactive compound, H_2O_3 , which eventually reacts to produce H_2O_2 (see diagram).

Because of energy barriers, the initial reaction of water and singlet oxygen probably would never take place on its own. But Xu and Goddard calculated that if the reaction started with at least *two* water molecules, one of them would act as a catalyst, driving the reaction forward.

Getting that precise arrangement of wa-

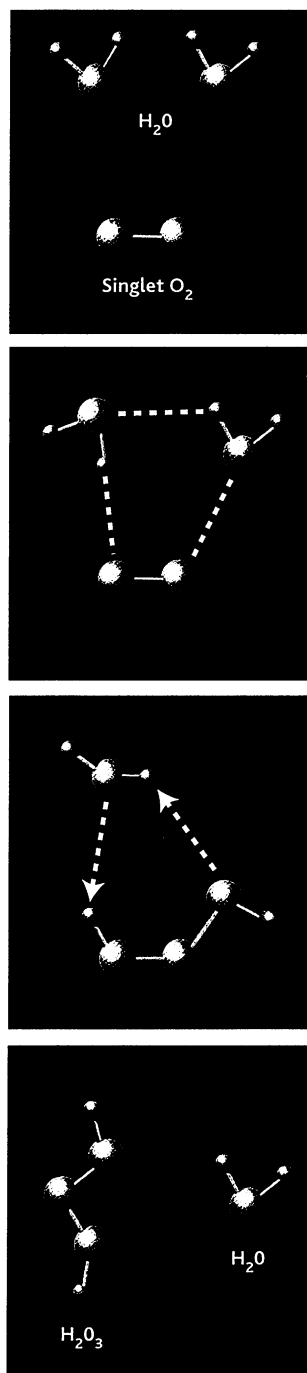
ter molecules and singlet oxygen to come together isn't easy. But perhaps the antibody was holding the actors in place so the reaction could take place. To find out, Wentworth and Lerner turned to Ian Wilson, an x-ray crystallographer at Scripps.

Using high-resolution x-ray techniques, Wilson made three-dimensional maps of the atomic structures of four different antibodies. Scrutinizing the regions that all antibodies share in common, Wilson's group identified three close-together sites that could bind oxygen molecules, as well as neighboring sites capable of holding water molecules in the right places. The antibodies also harbored a nearby unit of tyrosine amino acid, a likely spot where photons of UV light could be absorbed to generate singlet oxygen.

Although Foote agrees that such evidence is suggestive that antibodies promote reactions between water molecules and singlet oxygen, he's not yet convinced that's what is happening. One problem, he says, is that UV light—the presumed source of energy for generating singlet oxygen—is absorbed by the top layers of the skin and doesn't penetrate the blood vessels, where antibodies do most of their work. Still, he says, the idea is provocative and worth following up.

In a final series of tests, Wentworth, Lerner, and their colleagues found that the toxic compounds generated by antibodies were capable of killing bacteria without the need for immune cells such as macrophages. Wentworth doubts these poisons play much of a role in immune defenses today. But in early organisms, he says, the ability to brew them may have offered a significant evolutionary advantage—a remnant of which their remote descendants have inherited.

—ROBERT F. SERVICE



Action. A water molecule catalyzes a reaction between singlet oxygen and another water molecule to form H_2O_2 .