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.

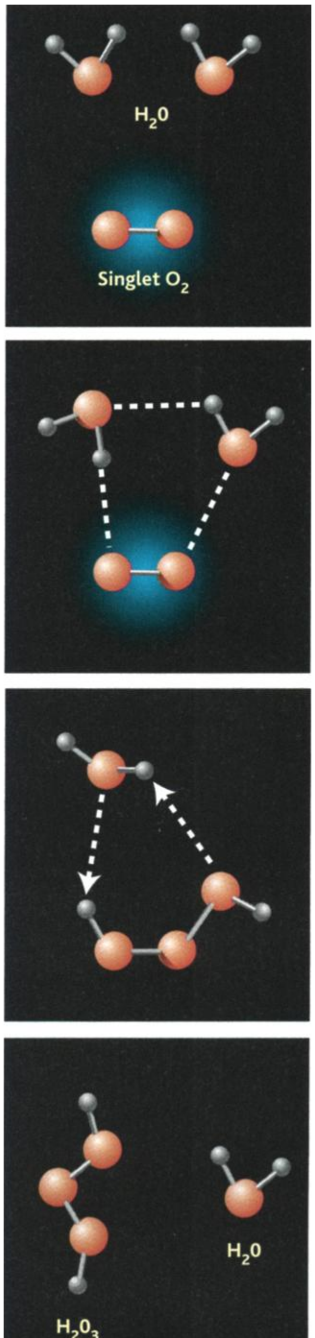
Now, it looks as if these plucky night watchmen may also dabble in chemical warfare. On page 1806, a team of California researchers reports that antibodies create highly reactive chemicals that cells can use to cleanse themselves and poison invaders. More surprising still, they seem to make them by burning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



Action. A water molecule catalyzes a reaction between singlet oxygen and another water molecule to form H_2O_3.

ILLUSTRATION: C. SLAYDEN

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 water 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