down vital organs. The work suggests that neutralizing this protein would halt the disease in some people, but researchers acknowledge that a human trial is still years away.

Sepsis arises as a complication of pneumonia, appendicitis, burns, infections, trauma, or other factors. Cell damage, either by microbial toxins or injury, sets off the immune reaction that leads to severe sepsis. As the body lurches into a self-defense mode, it mass-produces inflammatory proteins, such as tumor necrosis factor alpha (TNF-alpha) and high-mobility group box 1 (HMGB1).

Some patients die when their blood pressure crashes and organs fail, a combination of phenomena known as septic shock. This inflammatory spiral is orchestrated by TNF-alpha, says Kevin J. Tracey, a neurosurgeon at North Shore–Long Island Jewish Research Institute in Manhasset, N.Y.

However, many people who die from severe sepsis have few signs of inflammation in their tissues, autopsy data show. Tracey suspected that HMGB1 is the major culprit in such patients. In earlier work, he and his team had found that HMBG1 undermines the linings of body cavities, such as the abdomen, making them leaky. The chemical imbalance that results probably leads to organ failure, he says.

Tracey and his colleagues recently tested two anti-HMGB1 agents in mice with severe sepsis. The researchers had induced the condition by perforating the large intestines of 36 mice. Twenty-four hours later, they gave half the animals antibodies against HMGB1, and the other mice received unrelated antibodies. After 2 weeks, 13 of the mice getting anti-HMGB1 treatment had survived, compared with only 5 of the others. Giving an HMGB1-inhibiting drug called A-box achieved similar results in another batch of mice, the researchers report in the Jan. 6 *Proceedings of the National Academy of Sciences*.

In severe sepsis, dying cells release compounds that attract immune cells called macrophages, which then produce HMGB1. Anti-HMGB1 antibodies act by surrounding HMGB1 molecules, keeping them from binding to healthy cells. The A-box compound works by stalling HMGB1 production in macrophages.

The new study "underscores the potential of HMGB1 as a therapeutic target in the future treatment of sepsis," says Mark Perrella, a pulmonologist at Harvard Medical School and Brigham and Women's Hospital in Boston. But Perrella notes that sepsis is an unpredictable disease. While HMGB1 is apparently the problem in some patients, death occurs in others because anti-inflammatory proteins compromise immunity and leave a person vulnerable to further infection. Eventually, doctors might use genetic profiling to choose the best anti-sepsis therapy, Perrella says.

Doctors might also determine a patient's immune status by measuring HMGB1 concentrations in the blood, Tracey notes. —N. SEPPA

Gene Screen

Ultrasensitive nanowires catch mutations

In the nanoworld, the division between wet biology and dry electronics can disappear. As a demonstration, researchers have devised a nanowire sensor that binds to DNA molecules and produces an electrical signal almost instantaneously. Such direct detection of DNA could enable physicians to use a single drop of blood to swiftly screen patients for myriad genetic disorders.

The sensor, developed by chemist Charles Lieber of Harvard University and Jong-in Hahm, now of the Pennsylvania State University in State College, consists of a silicon wire several microns long and 20 nanometers wide. That's the width of a common cold virus. The small-scale system detects a genetic mutation that underlies cystic fibrosis, a lung-clogging disorder that affects about 30,000 people in the United States.

To detect the mutation, the researchers placed the wires on a silicon surface and fixed an electrode to each of the wires' ends. They then coated the wires with receptors harboring fragments of DNA that are complementary to the normal sequence of the gene implicated in cystic fibrosis.

When a sample containing DNA passed over the nanowire, the relevant DNA bound to the receptor and the nanowire's conductivity increased. Normal DNA formed tight bonds with the receptor DNA, boosting the nanowire's conductivity dramatically. Mutant DNA, on the other hand, bound to the receptor only loosely, resulting in a much smaller increase in conductivity. Lieber and Hahm describe their results in the Jan. 14 *Nano Letters*.

Not only can the nanowires respond to a gene within seconds, but they also generate measurable signals from just a few DNA molecules, says Hahm.

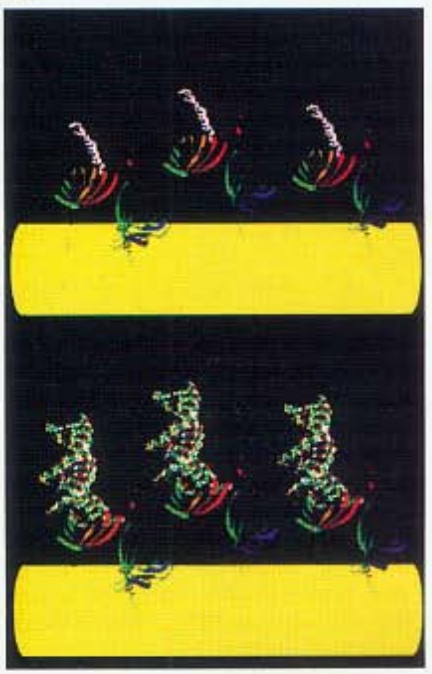
Existing genetic-screening technologies are more cumbersome. To obtain a strong signal, clinicians have to extract DNA from cells, produce many copies of it, label it with fluorescent tags, and then measure the fluorescence after it binds to detectors. The new nanowire skirts those time-consuming steps.

"What's also great about this technique is its versatility," says Hahm. In the cystic fibrosis demonstration, the nanowires detected a particular gene mutation that accounts for 70 percent of the disease's cases. Scientists have identified hundreds of additional mutations in this same gene that appear to underlie the remaining 30 percent of cases. With the new biosensor method, researchers could pack a chip with hundreds of wires—each tailored to a specific mutation—and hook them up to arrays of electrodes so that their individual signals could be read out. Such a device could detect all the cystic fibrosis mutations simultaneously from a single blood sample.

Because the nanowires are so tiny, researchers could eventually pack millions of them onto a chip and rapidly test a blood sample for all the known genetic mutations in the human genome. The sensor could do this at a fraction of the cost of current genetic screens, says Hahm.

"What's exciting here is that the researchers expanded the capability of the nanowires to detect DNA," says Yi Cui, a chemist at the University of California, Berkeley. The same silicon nanowires used to make these DNA sensors have been used by Lieber's team to make nanoscale transistors for computing devices.

Compared with complex computer circuitry, Lieber says, the DNA sensors "are probably one of the most realistic near-term applications of nanoscience." —A. GOHO



ELECTRIC MATCH When receptors on a silicon nanowire (top) bind to DNA, the resulting complex (bottom) increases the wire's conductivity.

LIEBER

W. FEIMER/NASA