

Solutions *

SHARKLET TECHNOLOGIES DRAWS ON NATURE TO PREVENT INFECTIONS



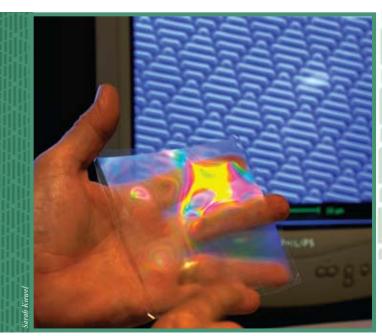
By AARON HOOVER

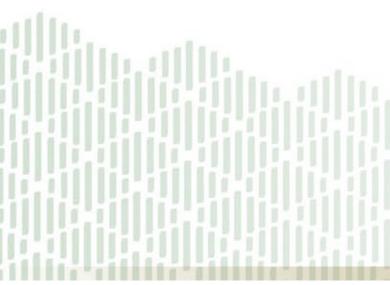
odern medicine has defeated a lot of bogeymen, but it remains locked in a war of attrition with an age-old nemesis: infection. Nationwide, hospital care workers confront about 1.7 million healthcare-related infections annually — and lose about 99,000 patients to them, according to the Centers for Disease Control and Prevention. That's more than double the fatalities tied to auto wrecks every year.

What's worse, medicine's main weapons are flawed or weakening. Disinfectants are impossible to apply everywhere, inevitably leaving spots for bacteria to grow. Chemical controls, such as coated implants, can have dangerous side effects or harm the environment. Antibiotics, onetime miracle cures, are losing their punch to genetically resistant bacteria.

But common menaces such as *Staphylococcus aureus*, as well as more dangerous cousins such as "flesh eating" methicillin-resistant *staph* — commonly known by the initials *MRSA* — may soon face a new barrier.

Ironically, it is inspired by a fearsome flesh eater of its own kind: the shark.





Sharklet is gearing up to sell what it calls "engineered surfaces" that, laboratory tests show, ward off not only staph and Escherichia coli but also the more dangerous MRSA, Vancomycin-resistant enterococcus and Pseudomonas aeruginosa.

Conventional controls aim to kill bacteria. Tapping the discoveries of a University of Florida materials science and engineering researcher, UF biotechnology spin-off Sharklet Technologies has a radically different approach. The Alachua-based company seeks to discourage bacteria from colonizing surfaces in hospitals and medical devices using a microscopic pattern modeled on the skin of the ocean's most notorious predator.

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"We believe we will have hygienic surface covers on the market this year," says Sharklet Technologies CEO Joe Bagan. "We're working on different medical devices to put our pattern on, and it's going to be a little longer for those. Maybe a couple of years."

HULLS TO HEALTH CARE

The latest weapon in the war on bacteria didn't spring from a medical laboratory. Instead, it is rooted in materials science and engineering Professor Tony Brennan's efforts to solve a seemingly unrelated problem: how to keep algae from coating the hulls of submarines and ships.

Some people are lucky enough to have great ideas. For Brennan, it was more a matter of asking a great question.

Brennan remembers the day well. He was visiting the U.S. naval base at Pearl Harbor in Oahu in 2002 as part of his Navy-sponsored research. Convinced he could stop tiny algal spores from attaching by using rows of microscopic channels, he had eagerly awaited a look at experimental samples previously submerged in the harbor. But the results were abysmal, with the samples coming out of the water festooned with algae.

He and a handful of colleagues were watching an algaecoated nuclear submarine leave port when the question popped into his head.

"The submarine looked like a big whale lumbering out of the harbor," Brennan says. "I asked, 'Do whales foul?' And everyone said, 'yeah, whales are heavily fouled.' So I started asking the question, 'which marine and freshwater animals don't foul?'"

He couldn't get the question answered to his satisfaction that day. But follow-up research revealed that of all big marine animals, sharks remain most glisteningly smooth.

Brennan spent much of his career engineering new biomaterials for dental implants. He asked a colleague at the Florida Institute of Technology, Geoffrey Swain, to take an impression of a shark skin using a common silicone material. Like an impression for an ordinary tooth crown, it provided a negative imprint — in this case, a small, but visible pattern of rounded-off, diamond like, scales. (Many people believe sharks don't have scales. In fact, the creatures' scales are very small. They are known as placoid scales, or dermal denticles.)

Each scale was made up of seven tiny ribs. Brennan used a special tool, an optical profilometer, to measure the scales' corresponding roughness. To his surprise, the ribs' widthto-height ratios closely matched one of his mathematical The patterns on sharks' tiny scales closely matched one of Brennan's mathematical models for roughness — one that he had estimated would discourage algae spores from settling.

20 a.m.

20 a.m.

20 um

DAY 0

DAY 2

DAY 7

DAY 14

DAY 21

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At the time, Brennan believed the spores would have a negative reaction to surface roughness features measured in a handful of microns. The shark scale ribs were far bigger. So he shrunk the sharkskin rib pattern by a factor of 20, separating each rib by two to five microns. Tapping a process similar to the one used to make computer chips, he next fabricated thousands of these tiny "riblet" patterns on plastic.

He plunged the plastic into algae-laced seawater, waited an hour and pulled it out.

"The first time we tested it," Brennan

says, "we had an 85-percent reduction in the settlement of green algae."

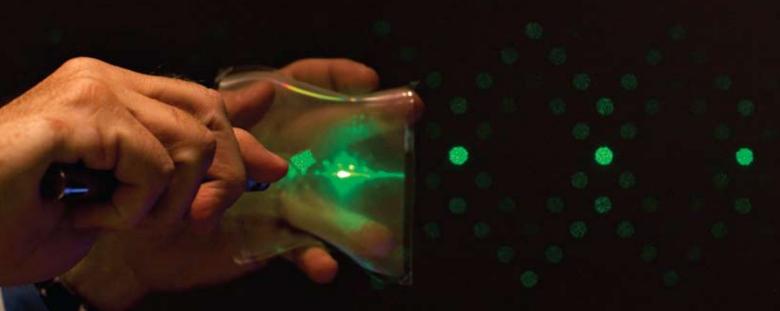
"HOLY SMOKES!"

It was just one small test with just one type of fouling organism, but the results were exciting. That's because algae and its ilk are major problems not only for the Navy but for all shippers. Fouled vessels have more drag as they move through water, slowing them and cutting into their fuel efficiency. The Navy estimates fouled hulls use 15 to 30 percent more fuel than clean ones, raising its fuel bill by tens of millions of dollars. BACTERIAL COLONIES GROW STEADILY ON A SMOOTH SURFACE OVER A PERIOD OF THREE WEEKS, WHEREAS THEY SEEM TO STRUGGLE TO GET ESTABLISHED ON THE SHARKLET PATTERN.

Shark skin

Following in the footsteps of shipbuilders since antiquity, the Navy and commercial shipping lines have fought the problem with copper-based paint. But pollution and cost concerns spurred the Navy to look for more environmentally friendly, less expensive solutions.

With the Office of Naval Research's continued sponsorship, Brennan set about confirming and expanding his results while also seeking to understand the underlying mechanism. He applied for his first patent in 2004. Several years and at least \$1 million later — the Florida High Technology Corridor Council has also been a supporter — Brennan has confirmed that his pattern resists not only green algae but also some varieties of barnacles. He has received two patents,



SHARKLET TECHNOLOGIES HAS CLEARED ALL THE MAJOR HURDLES IN AN EFFORT TO TEST ADHESIVE-BACKED VERSIONS OF THE PATTERN ON COMMON HOSPITAL SURFACES AT A LARGE CALIFORNIA HOSPITAL.

has applications for several more patents under consideration and continues to work toward testing the pattern on real-life ship hulls.

Meanwhile, the research has also expanded in a vastly different direction. One of the fouling organisms that Brennan sought to discourage was the tubeworm. Tubeworms need bacteria to settle. So, in the spring of 2005, he asked an undergraduate at work in his laboratory to grow some bacteria on the SharkletTM pattern.

A few weeks later, Mathew Blackburn reported back: He couldn't do it. The *E. coli* bacteria would not attach. Brennan assigned two graduate students to work with Blackburn, but the team could coax the *E. coli* to grow only up to the side of the pattern.

It wasn't until Brennan read Blackburn's final report that the idea dawned on him: Perhaps the pattern could do more than ward off organisms that go after ships. Maybe it could discourage those bad bacteria that target people.

"He thought he was failing, and when I got his report and looked at it, it was like, 'Holy smokes!" Brennan says. "This could be very interesting."

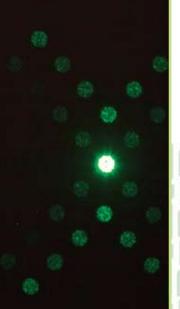
HOSPITAL HELP

Marine fouling organisms and bacteria are very different life forms. But the two also share important similarities, Brennan says. Both can move, and both put down adhesive pads when they first stick to a surface. Green algae and many bacteria also seem to appreciate company. They take hold singly or in small groups, then seek to establish large colonies.

Like other life forms, Brennan says, bacteria and fouling organisms seek the path of least resistance. He believes the Sharklet pattern discourages colonization because it requires too much energy to put down roots. The consequence: The organisms decide to keep house hunting. With enough surface protected, the theory goes, they die or become less of a threat.

Whatever the mechanism, the Sharklet pattern works — in laboratory tests, at least.

The Navy's interests were confined to fouling, so Brennan turned to UF's extensive medical resources to pursue the medical applications.





In 2007, he founded Sharklet Technologies, based at UF's Sid Martin Biotechnology Development Incubator. There, Brennan chairs the company's scientific advisory board.

Brennan's and the company's tests reveal that the pattern is remarkably effective at delaying colonization from *staph, Pseudomonas aeruginosa, E. coli* and other pathogens. Bagan, Sharklet Technologies' CEO, says the independent infectious disease laboratory also found a "statistically significant" difference in the survival of *MRSA* and VRE bacteria in short time trials.

Sharklet Technologies' time-lapse images tell the tale graphically.

Bacterial colonies grow steadily on a smooth surface over a period of three weeks, whereas they seem to struggle to get established on the Sharklet pattern. By day 21, bacterial films turn 77 percent of the smooth surface bright red versus 35 percent of the Sharklet pattern.

As promising as the results have been, the pattern has yet to be tested in a real medical setting. But that's about to change.

Bagan says Sharklet Technologies has cleared all the major hurdles in an effort to test adhesive-backed versions of the pattern on common hospital surfaces at a large California hospital. Technicians, he says, have already determined the surfaces most likely to contain large bacterial colonies. Known as "high-touch" surfaces, they include nursing call buttons, bed rail control panels and touch-screen cardiac monitor screens. The company plans to apply the adhesive-backed Sharklet pattern to these surfaces and then monitor them for colonization.

Down the road, Sharklet Technologies also hopes to cover and test medical devices and instruments. Bagan says that because the pattern is not a chemical coating and does not introduce any new substances, it probably will not require clinical trials, but some safety trials may be needed.

Whatever the hurdles, the market is huge. The CDC estimates that 32 percent of all healthcare-related infections are tied to urinary tract infections, often stemming from urinary catheters. If the Sharklet pattern could make catheters safer, that alone would have a huge impact.

Brennan, for his part, is eager to gauge his invention's appeal.

"I am anxious to see this thing put out there because once you put it on the market, you really get a test," he says. "The market will determine viability."

Tony Brennan