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## From Breakthrough to Business

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# Genome Surgery and xReader

## Martin Schiller, Life Sciences Professor

Each week a group of students gather in life sciences professor Martin Schiller's bioinformatics lab to discuss what they have been reading in scientific journals.

It was here, in a nondescript room with brown leather couches, where the idea for a new approach to genome surgery was first discussed. From this exchange, Schiller and his team developed a novel idea combining two technologies with bioinformatics tools to remove disease-causing DNA from cells.

The discovery could lead to a new way to treat HIV/AIDS.

UNLV recently submitted a patent application for this idea to the U.S. Patent Office, a development of huge impact to Schiller.

"Unless someone else submitted an application for the exact thing before we did, we may own a big advancement in medicine at UNLV," says Schiller, explaining his discovery with a short lesson on the way some viruses interact with DNA.

"When a person is infected with some pathogenic viruses, such as HIV, the virus inserts its DNA and becomes part of the DNA of the infected cells," he says, explaining that patients receiving drug therapy may get well temporarily, but the DNA of the virus remains behind. Later, it can become reactivated, and the patient relapses.

"Latency is when you have the virus in your genome, but it isn't actively producing infective virus," says Schiller, who came to UNLV in 2009 from the University of Connecticut School of Medicine. "This is the reason you can't cure someone of AIDS. You can lower the viral levels for a functional cure as long as the person stays on a cocktail of drugs the rest of their lives. But as soon as you take them off the drugs, the virus explodes and mutates. At that point, the drugs no longer work."

Schiller notes that a technology exists allowing researchers to specifically target and cut out a region of DNA – which, he reasoned, could be employed to fight latent

HIV infection. But there is another pertinent technology that emanates from HIV itself – it is a protein that can actually travel across cellular membranes; scientists have learned how to harness the protein to deliver a change to the interior of a cell.

"What we did is combine these two technologies," says Schiller, "while taking advantage of our bioinformatics expertise."

By "bioinformatics," he is referring to his laboratory's tremendous amount of biological information on the human genome with its 23,000 genes and resulting proteins. His lab is known for its comprehensive database on short contiguous peptide sequences that are known to have a function in at least one protein. Schiller credits an undergraduate student in his lab, Horacio Guerra, with using this vast database and the Los Alamos HIV sequence database to help identify the right region to target in the HIV cells.

Schiller's team analyzed thousands of different HIV sequences and determined parts in the HIV genome where a mutational change is very rare, indicating that these are critical genomic elements of HIV (and good sites to target for intervention). Then, in the laboratory, they designed a protein to enter the cells of a person with a latent HIV infec-

tion, and snip out those parts of the genome, effectively killing it.

In humans, blood stream injection would be used to deliver this discovery. Because it has a portion of a protein from HIV itself, it would move across cell membranes.

Still, Schiller acknowledges that much additional work is needed before this technology will be approved for use in humans. He notes that there are four stages of development to bring this product to market: The first stage is to show that the protein works in a test tube, which has been successfully accomplished in his lab.

The second stage is to grow active HIV cultures in the lab, and when this protein is added, it should cure the infection in a dish of cells. Schiller notes that Christy Strong, a postdoctoral fellow in the lab, is currently helping to shape this portion of the research. The third and fourth steps are animal and human trials, respectively.

Although confident of the viability of this discovery, Schiller is aware of the difficulty in bringing a new drug or technology to market.

"Only 1 in 500 of these types of applications ever lead to a drug," he says. "This one could fail along the way. Right now, it's a promising strategy, and we have some sound



Life sciences professor Martin Schiller and his team have designed a protein to enter the cells of a person with a latent HIV infection and snip out critical parts of the HIV genome.

indication that it has a chance of working.

"We have the hope that if this is successful with the HIV virus, with adaptations to the system, it could work on almost anything – cancer, immunological diseases, and more. There's no reason that this strategy can't become a commonplace treatment for any disease."

But if advancing a strategy that might cure disease were not enough, Schiller has also managed to develop another completely different form of intellectual property with great commercialization potential.

He has invented a new type of reading accelerator, called xReader, for which the university has filed another patent application.

The purpose of the tool is to make it easier to read complicated documents, including scien-

tific or legal journal articles that contain jargon.

"These types of documents often contain words that are difficult to understand. With this program, as you're reading, and you don't know a word, you point to it and a definition pops up along with relevant images."

This would be useful for myriad circumstances, but particularly valuable for someone who has been recently diagnosed with a disease and wants to learn more about it from actual medical or research journals, Schiller says.

"The xReader will enable you to better understand the jargon in order to make more informed medical decisions."

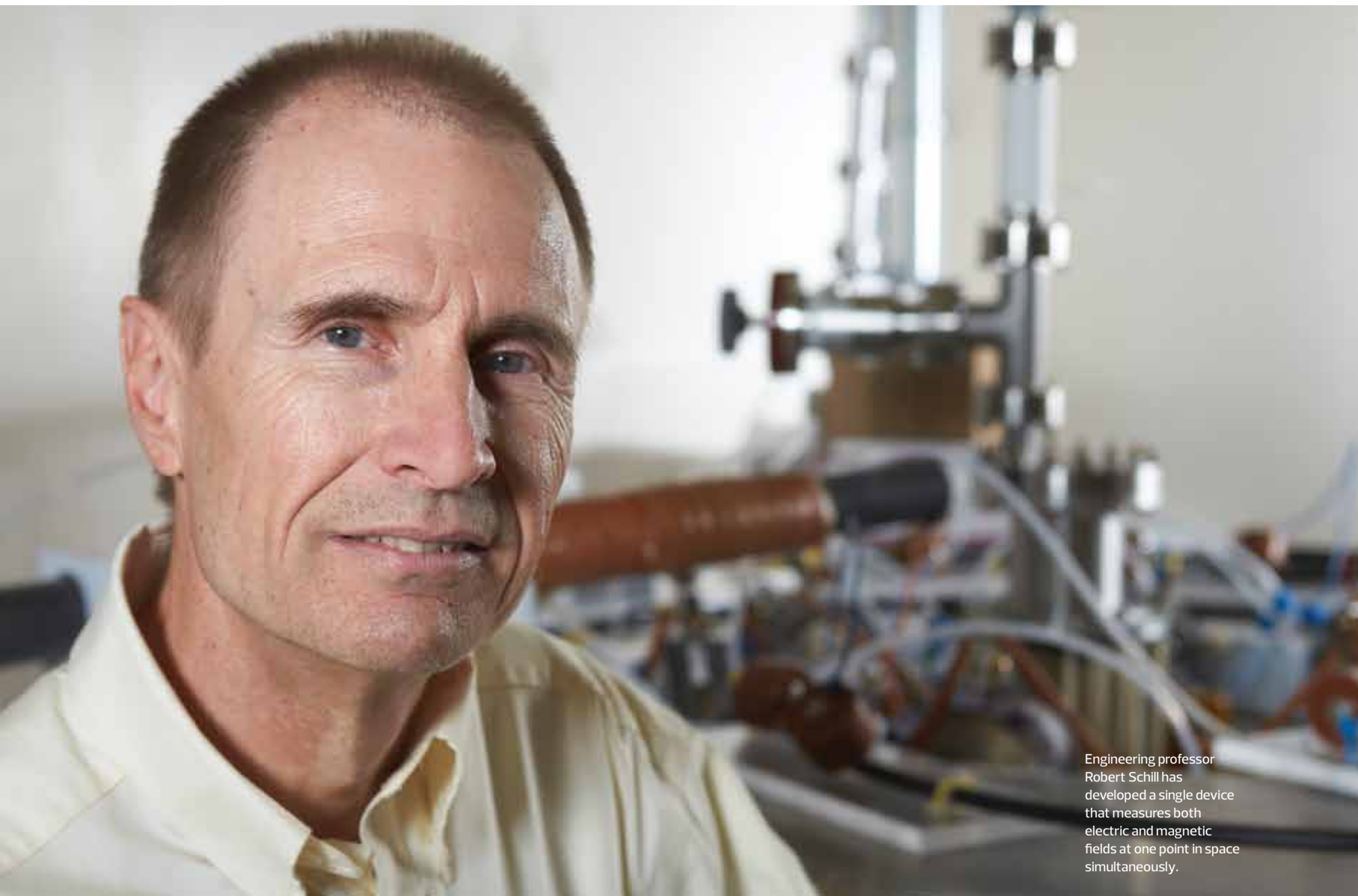
Schiller thought of the invention when he was working with the huge amount of

bioinformatics data he and his team had collected for their research on genome surgery.

"I was thinking about ways in which we could use the large data warehouse that we built," he says.

This invention is further along in the commercialization process than the genome surgery discovery, Schiller notes. Earlier this year, the Schiller lab launched Taecan LLC, a new startup company to advance the xReader in the marketplace. It will commercialize the xReader technology, which is in the final stages of review by the U.S. Patent and Trademark Office. Soon, the company will be releasing several new mobile apps and browser plug-ins for personal computers.

– SHANE BEVELL



Engineering professor Robert Schill has developed a single device that measures both electric and magnetic fields at one point in space simultaneously.

## EM Dot™ Robert Schill, Engineering Professor

**A**t first glance, it wouldn't appear that the Post-it note, the Kevlar vest, and the Electro Magnetic (EM) Dot™ would have much in common.

But dig a little deeper and you'd find that they are all revolutionary inventions originally intended for some other purpose.

For instance, the glue on Post-it notes, which was once deemed capable of sticking nothing together reliably, was viewed as ideal for attaching bookmarks in church hymns. Before Kevlar became synonymous with body armor, it was a material designed

for racing tires.

And now comes the EM Dot, a novel electric and magnetic sensor that will soon have some innovative – and undoubtedly unexpected – applications.

The EM Dot was developed by UNLV electrical and computer engineering professor Bob Schill and his research associate, Marc Popek, in 2005 to aid in their experiments with pulsed power in the Energy Materials Interaction Technology Initiative of Nevada (EMITION) Center, located in the Science and Engineering Building at UNLV.

Schill had previously acquired the Ne-

vada Shocker Pulse Power Machine, a one million-volt, 100,000-to-200,000-ampere device that helped the researchers study the interaction of pulsed power and materials. But the team was stymied by a lack of the right kind of field diagnostics for the machine. What existed at the time were two separate field sensors: one was the B dot, used to measure magnetic fields, and the other was the D dot, which is used to measure electric fields.

"When you transition from the measurement of radio waves, which have very long wavelengths, to micro waves, which are

much shorter, the dots' construction, calibration, and relative location must be carefully considered for accurate and valid measurement," Schill says. "The existing sensors were too large and expensive for the work we were doing. So, we came up with the idea for the EM Dot out of pure necessity."

Their breakthrough in electric and magnetic field sensor technology combines the B and D dots into one sensor, creating a device resembling a wishbone that's slightly smaller than a regular paperclip.

"This single device measures both the electric and magnetic fields at one point in space simultaneously," Schill says.

It was patented in 2009, and in 2013 the technology was licensed to Kyma Technologies, Inc., a leading supplier of advanced semiconductors, sensor technologies, and other materials solutions that promote safety and energy efficiency.

Though Kyma has kept their plans for the EM Dot mostly under wraps to maintain their competitive business edge, Schill sees various potential applications for the device.

One possible application he has researched focuses on leak detection in underground pipes. He used PVC piping to mimic water transportation systems in order to find out how the EM Dot could be used by water districts to pinpoint compro-

mised integrity of underground pipes. By using an antenna inside the pipe at a fixed position to send a pulse through the pipe, Schill is able to receive readings with the EM Dot at a fixed location external to the pipe to detect and locate leaks.

This method – as opposed to using a remote, submersible device propelled in the pipe system that detects leaks based on sound waves – has its benefits. It allows for continuous monitoring over fixed locations based on radio wave signals without acoustic noise signatures that are generated when a shower is turned on or toilet is flushed.

While he has so far tested the technology on PVC piping only, Schill predicts that this system would provide similar results in metal and concrete pipes, particularly those used in areas with hard water, such as Nevada. There is also potential to detect pipe degradation with continuous monitoring, especially in metal pipes, which would allow for preventive maintenance.

Since developing the EM Dot, Schill has used it to conduct experiments for other ongoing projects, including one started in 2010 that will have military and/or law enforcement applications. He calls it "the detonator defeat system," and it has the potential to disarm detonators of explosive devices without actual physical contact. The

system uses a coil that, when placed near an improvised detonator, heats it up to the point of controlling or confounding the mechanism that detonates the blast. The university filed a patent application on the technology this year.

The device could be invaluable in locating and "defeating" improvised explosive devices (IEDs) that caused so many horrendous injuries and fatalities among military personnel in Iraq and other countries.

What makes Schill's system unique is its non-specificity to devices and its ability to impact various materials.

"The difficult thing with improvised detonators," Schill says, "is that you essentially have a black box, and you don't know what's in it. You don't know what has been used to build the detonator, and each possibility – tungsten, platinum, copper, etc. – has its own fingerprint. Moreover, one does not know *a priori* the connecting circuitry to activate the detonator. We've conducted numerous experiments with different materials and connecting circuit loading effects, and we found similarities in results, pointing to the device's ability to perform in all scenarios."

In its current state, the coil is relatively small, and it requires an individual or a robot to place it so close to a detonator that its exact location must be known. As he continues work on the system, Schill hopes to extend its size to cover wider areas, eliminating the need to know a detonator's location, and to implement a detection system that would allow for potential disarmament of underground mines on the battlefield.

In addition to inventing several technologies, Schill has also founded and directed the EMITION Center and performed countless hours of research. Since 2005, his center has been home to ground-breaking work on initiatives that he hopes will one day enable UNLV to become more competitive in conducting research in novel areas that are beneficial and pertinent to the state and the nation.

– SHANNON SPOLLEN



R. MARSH STARKS

# C. diff Prevention

## Ernesto Abel-Santos, Chemistry Professor

Imagine the following scenario: You go to the hospital for bronchitis or another ailment. You are prescribed an antibiotic and start feeling better, but you suddenly get severe abdominal pain and uncontrollable diarrhea. You go back to the doctor and learn that you now have a different, secondary infection. The doctor takes you off the bronchitis medication and gives you a new antibiotic that targets the secondary infection. You start feeling relief from the diarrhea, but the bronchitis returns. Now the doctor stops the second medication to start treating the bronchitis again.

This vicious cycle continues and can eventually become very serious, even deadly.

The secondary infection in the above scenario is from the bacterium *Clostridium difficile* (C. diff). In the United States alone, there are approximately 500,000 cases and 20,000 deaths each year as a result of it. Illness from C. diff typically occurs after use of antibiotics and often affects patients who have suppressed immune systems, many of whom have been in a hospital, nursing home, surgery center, or similar facility where C. diff is present.

However, all hope isn't lost for those who are exposed to this infection. UNLV biochemistry professor Ernesto Abel-Santos and his team of students believe they have found a potential solution.

The university shares their belief in the value of the treatment and has pursued a patent for his discovery through the U.S. Patent and Trademark Office. He also has co-founded Abel Therapeutics LLC to develop a new drug for preventing C. diff. Additionally, he has worked with College of Business entrepreneurship students, who developed a business plan for his company. The team won second place at the Southern Nevada Business Plan Competition.

"There are really only two drugs that treat the *Clostridium difficile* infection," says Abel-Santos, who came to UNLV in 2006 from the Albert Einstein College of Medicine in New York City. "So after the second relapse, you

are basically out of pharmacological options. Other options are not pleasant and include a colectomy, which involves cutting out the infected intestine, or fecal transplantation, which replenishes the good bacteria in your intestinal tract."

The problem is that while antibiotics kill the bacteria that are causing bronchitis or other infections, they also kill the good bacteria in your body, and that is when C. diff introduces itself.

What Abel-Santos discovered is a compound that basically functions the same way the good intestinal bacteria does: It keeps the C. diff spores from germinating, acting as a surrogate for gut bacteria and thereby preventing infection.

Abel-Santos' path to this discovery emanated from his research in the area of bacterial spores, anthrax being the most famous. He became interested in bacterial spores after the Sept. 11 terror attacks when letters containing anthrax spores were mailed to several news media offices and two U.S. Senators, killing five people and infecting 17 others.

*Clostridium difficile* is another bacteria that forms spores. "The problem with these types of bacteria is that when you try to kill

them, instead of dying, they form a very resistant structure," he says.

The resistant spores stay in the environment or body for a long time and, under the right conditions, can germinate, producing toxins and infecting those who are vulnerable.

Abel-Santos studies that germination process. "We want to understand how a dormant spore can detect its environment. It has to be able to figure out when it is sitting on a desk contaminating a surface and differentiate that from when it is inside your body."

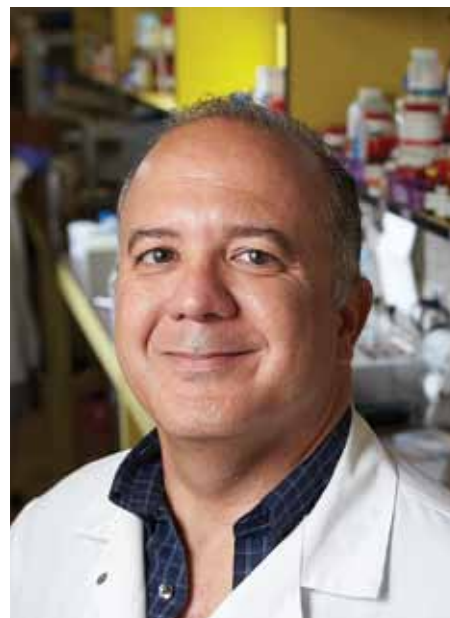
He explains that bacterial spores use signals from the environment to germinate – typically substances found inside the body, such as amino acids and sugars. So Abel-Santos and his team made molecules to mimic the signals that the bacteria use to trigger germination. Once they were able to make compounds that mimic these types of biomolecules, they were then able to make compounds that inhibit them. These inhibitors are then able to block the spore from germinating. If the spore germination is blocked, then the spore passes through the body without producing toxins.

So far, the compound has proven successful in animal models, though his studies continue. Eventually, the team will plan for testing of the compound's effect on humans, though much work is necessary before that phase of the research is pursued.

Someday, Abel-Santos says, his discovery could be prescribed as a prophylactic measure for those likely to be troubled by C. diff, as the drug is designed to prevent infection rather than treat it.

"The idea is that patients will be given the anti-germinant at the same time as other antibiotics, so that even if they are infected with the spore, this compound will keep the spore from germinating," he says. "If they don't germinate, they don't produce toxins. And once you finish the antibiotic treatment, your gut bacteria are going to come back, which will allow you to stop the anti-germinant treatment."

– SHANE BEVELL



Chemistry professor Ernesto Abel-Santos has discovered a compound that keeps C. diff spores from germinating.

R. MARSH STARKS