THE BETTER WORLD REPORT 2009

Innovations from Academic Research That Positively Impact Global Health

2009 Edition
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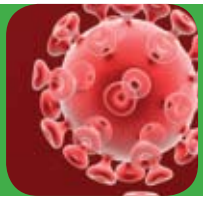

Innovations from Academic Research That Positively Impact Global Health

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The Better World Project

The Association of University Technology Managers launched the Better World Project in 2005 to promote public understanding of how academic research and technology transfer have changed our way of life and made the world a better place. The project draws from more than a decade's worth of case studies and news from AUTM members—the professionals who make academic technology transfer happen.

This fourth edition of the project focuses on global health—innovations that make a positive impact on the health of communities around the world.

Materials and Support

The Better World Project materials are available in print and electronic formats. Visit The Better World Project Web site or contact AUTM headquarters for details.

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The Association of University Technology Managers

AUTM is a nonprofit professional association with a mission to advance the field of technology transfer and enhance the ability to bring academic and nonprofit research to people around the world. AUTM's 3,500 members represent intellectual property managers from more than 350 universities, research institutions, teaching hospitals and government agencies as well as hundreds of companies involved with managing and licensing innovations derived from academic and nonprofit research.

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The Better World Report is a testament to the efforts of institutions' technology transfer offices, their directors and staffs, who gathered and submitted these stories and more. These contributions tell the story of how institutions are doing their part to improve the world we live in not only through education but through innovation, and it is the return on innovation that we bring to light in this report.

Editors and Staff

The stories in the 2009 *Better World Report* were researched and written by Pamela C. Baker, Barbara Donohue, Ralph Fuller, Mary Jane Roberts Henderson, Charlotte Huff, Ashley Mastrandrea, David Perilstein, Lisa Richter, Julie Ritzer Ross, and Susan Weiss. The Better World Report was produced by The Sherwood Group, Inc., an association management firm serving science, technology and health care specialty fields. AUTM's management staff and the communications department at The Sherwood Group, Inc. provide strategic, editorial and design support for The Better World Project.

Better World Report Committee

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Forward

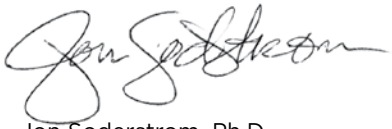
Welcome to a Better World

The 2009 AUTM *Better World Repor*t is the fourth in our series of reports making up the Better World Project. This report illustrates the real impact of technology transfer—bringing the results of research into use for the benefit of the general public, our institutions and the communities we serve.

The stories in this year's report illustrate that academic technology transfer can and does contribute to a positive affect on global health. Those of us in the profession already know that moving academic research into use requires partnering at a number of levels in the public and private sectors. I'm proud that these stories in particular show the creative thinking involved in moving innovations into underserved communities.

The overall message of the stories comprising the 2009 *Better World Report* is that the world is changing—in a good way. Brilliant minds are at work developing technologies that go beyond the profitable, and directly benefit communities that were once beyond our reach.

The members of AUTM facilitate the movement of research into broad use through the relationships they help establish. The 2009 *Better World Repor*t highlights only a few of these collaborative successes.



Jon Soderstrom, Ph.D.
AUTM President 2008

Preface

What It Takes to Change the World

By Christopher D. Earl, Ph.D.

In the field of global health it takes two types of people to change the world: systems utopians and technical utopians. Systems utopians say, "If only we could get all the processes to work—getting today's medicines to those in need, or improving health care delivery— then we could dramatically improve the treatment of developing world diseases." Technical utopians, on the other hand, say, "If we could only invent the right gadget (or drug, or vaccine, or diagnostic), we could leapfrog today's obstacles and revolutionize treatment for these diseases."

Of course, both visions are right. Most of us who are scientists, having spent our lives trying to create or fund improvements in medicine through biotechnology innovation, fall into the latter group, though we share profound respect for the essential role of those who ensure that innovations reach their intended recipients and achieve their intended goals.

The 2009 Better World Report celebrates successes, and lessons learned, by a host of inspired technical utopians: researchers, inventors, developers, engineers. Their creativity has changed the ways that problems are addressed in just about every type of setting, improving the lives of countless people and communities. Such progress proves that technology, applied in appropriate and affordable ways, can transform lives and livelihoods in some of the most difficult and desperate settings in the developing world.

But we still have a long way to go. There are tremendous opportunities to solve medical problems in developing countries that have yet to be pursued. Indeed, the progress that has been made in improving delivery of today's medicines through programs such as the Global Fund, WHO, and the distribution of HIV/AIDS drugs through U.S. President's Emergency Plan for AIDS Relief (PEPFAR) only accentuates the inadequacy of treatments for malaria, tuberculosis, diarrheal diseases, systemic worm infections and trypanosomal parasites such as African sleeping sickness. In many cases these treatments are decades old. Some are inadequate, toxic or treacherous to administer. In other cases pathogen resistance is rendering today's treatments ineffective.

We know there's no reason, in theory, that we can't prevent and treat those diseases. Since the invention of recombinant DNA technology in 1973 there has been a revolution in the science of drug and vaccine discovery, and stunning breakthroughs in genomics and biochemistry that give us the tools to understand and harness the molecular mechanisms that underlie human disease. These advances have borne fruit in the important biotech-based drugs and biologics that have been introduced by the biotechnology and pharmaceutical industries over the past thirty years.

These biopharma successes in developing new preventions, treatments and detection methods for infectious diseases such as HIV/AIDS and drug-resistant gram-positive bacteria, and proliferative diseases such as cancer, mean that there's no reason to think that neglected diseases of the developing world wouldn't yield to a comparable all-out effort. In our work at BIO Ventures for Global Health (BVGH) we've endeavored to show how biotech advances can create breakthroughs in treating neglected tropical diseases. For example, in our 2007 report, Closing the Global Health Innovation Gap, we showed that many of the molecular targets and compound libraries that have been used to create new drugs for developed world diseases are readily transferable and applicable to discovering new therapeutics for developing world diseases.

The problem, of course, is that biopharmaceutical R&D is an expensive and financially risky undertaking, and the millions of patients who might be helped have little purchasing power. So the "innovation gap" is driven by a funding gap, where the investment in R&D for neglected tropical diseases is a fraction of what's needed. Overcoming this gap will require further increases in funding for product-related R&D, where the Bill & Melinda Gates Foundation has shown tremendous leadership and what can be accomplished with focused, sustained sponsorship. In addition, the most powerful incentives for investment in innovation is to design, legislate and fund incentives for the purchase and distribution of novel medicines in ways that will reward risk-takers for their efforts.

The work presented here is an important contribution to the process of breaking down barriers that hinder global health R&D. For donors, policy-makers, investors and CEOs to be willing to devote their initiative and dollars to developing-world solutions, they have to believe that these efforts will bear fruit—that these problems aren't insuperable. These case studies prove that we are experiencing an era of unprecedented opportunity for technical utopians—inventors of the better mousetraps for global development and global health—and that their work deserves the resources that will allow them to transform the lives of millions in need.

As Bill Gates has said, "I believe that if you show people the problems and you show them the solutions they will be moved to act." These stories, by showing us real, practical solutions, should inspire visionaries—whether they focus on novel technology or systemic improvements—to tackle the major challenges of improving the lives of millions around the globe.

Dr. Christopher D. Earl is President and CEO of BIO Ventures for Global Health (BVGH), a not-for-profit organization whose mission is to harness the resources of the biotechnology industry to create new medicines for infectious diseases of the developing world. BVGH breaks down barriers that hinder industry initiatives in global health product development. The organization fosters collaboration among stakeholders in industry, philanthropy, academia, and government, and catalyzes industry investment through the creation of new market-based incentives. Dr. Earl previously served as Managing Director of the Perseus-Soros BioPharmaceutical Fund, LP, a leading investor in later-stage life science companies, where he managed investments in biopharmaceutical companies and served as a director on portfolio company boards. Dr. Earl received a BA in Biology from the University of Pennsylvania, and a PhD in Cellular and Developmental Biology from Harvard University. For further information on BIO Ventures for Global Health, please visit www.bvgh.org.

Strengthening Health Care Systems in Africa Provides Practical Assistance and Profound Personal Growth

Yale University

Stella is a nurse anesthetist in Liberia, a country where women have limited social status and operating rooms have little in the way of infection control. Both have been elevated with the help of the Yale-Clinton Foundation Fellowship in International Healthcare Management, a program in which Western health care managers work side-by-side with hospital employees in developing nations to improve the quality of health care.

The premise of the fellowship, a joint effort between the Yale School of Public Health and the Clinton Foundation, is that, without strong health care systems, reducing the rates of mortality and AIDS transmission in struggling nations will be largely impossible. By tapping the knowledge and expertise of health care providers from the United States and other developed countries, the partnership seeks to improve—or, in some cases, introduce—standards of care in the hospitals of Africa and other struggling nations.

"These countries have resources, what they don't have are systems," says Elizabeth Bradley, Ph.D., associate professor and director of Global Health Initiatives at the Yale School of Public Health, who co-directs the program with Mae Podesta, country director for the Clinton HIV/AIDS Initiative in Liberia.

To strengthen those systems, the fellowship program has sent senior health care managers and post-graduate students with experience in hospital administration and public health to share their education and know-how with health care workers in both Liberia and Ethiopia. Their job is to import the best practices in hospital management from the Western World to their African counterparts, while providing leadership training to ensure improvements can be measured and sustained.

"The idea is not to do for them, but to give them the expertise they need to function on their own and to teach them how to build capacity within their groups," says Bradley.

The program, which received 180 applications for its first 25 fellowship positions, has been successful at recruiting highly qualified health care workers from around the world. Each has a master's level degree in hospital administration or public health and, as a group, they average 10 years of work experience in both the private and public sectors.

In 2006, the first group of 25 fellows was sent to Ethiopia to work in 12 public hospitals and health bureaus, and nearly half of them stayed on for another year. A second wave of five fellows was stationed in the much smaller country of Liberia beginning in early 2007.

Once abroad, the fellowship teams implement a strategically designed educational experience that offers both classroom instruction on topics such as human resource and financial management, procurement and infection control, along with on-the-job training.

"With just didactic learning, employees may learn how to do a spreadsheet, but they don't get the practical experience," says Bradley. "We put a real-time mentor right in their workspace with them."

A 'Blueprint for Hospital Management,' developed by the Yale-Clinton Fellowship teams, guides the fellows in establishing management structures. Every quarter, fellows measure their progress on each of the Blueprint's goals, including eight critical functions and 125 standards—from an organizational chart to a payroll system to privacy curtains and bed nets to organized pharmacy supplies.

Making Progress with New Standards and Systems

By the end of the program's first year in Ethiopia, it was evident that the intensive education and mentoring in the field had paid off. The fellows reported significant improvement on 40 of the program's 70 standards.

"Tremendous headway has been made," says Bradley. "Clinical outcomes are being established, structural changes have been made and a patient satisfaction tool is in place. Patient registration is smoother, wait time is down and cleanliness has improved."

What's more, a whole new class of African executive health care managers has emerged: at half the country's 100 hospitals, newly appointed chief executive officers have assumed responsibility for the institutions, including monitoring the quality of health care offered on a going-forward basis.

"The addition of chief executive officers was a major step forward," says Bradley. "We convinced Ethiopia's Ministry of Health that CEOs were needed for each hospital, instead of being run by a physician who didn't want to manage a hospital."

Of those 50 executive managers, 26 have completed the Yale educational program and are being paid at a high level of civil service pay.

"These CEOs have become quite good at lobbying," says Bradley. "We watched them go from shy and mumbling to putting together PowerPoint presentations and being able to stand up and lead."

A Life-Altering Experience for All Involved

The new hospital CEOs aren't the only ones who have evolved in profound ways. For the fellows who left homes in the United States, Spain and the Philippines to spend a year or more abroad in a developing nation, the program is much like a stint in the Peace Corps.

"It's just exceptional what happens to both our health care workers and the employees they mentor," says Bradley.

Arriving in Liberia, which is just emerging from years of civil war, fellows found the country's hospitals lacked basic systems that Westerners take for granted—from running water on patient floors to an on-site incinerator for hazardous waste to a complete list of employees' names.

"It can be quite shell-shocking," says Bradley. "The fellows can look agog at the conditions, which can be quite frustrating."

As their work continues, the fellows experience lots of ups and downs, and admittedly, a few points where they think nothing will ever change, says Bradley, who has spent considerable time abroad as well.

"It's difficult, but in the end it's an unbelievable experience, very fulfilling," she says.

That's no doubt due to the fact that, over time, the fellows are able to affect the future of care provided to millions of Africans, many of whom face dire health circumstances. On a personal level, there is no discounting the impact of living and working among the Liberians and Ethiopians, who often express profound gratitude for the fellows' guidance.

"The people are so warm and so thankful," says Bradley. "Our fellows become a part of their families."

For the African health care workers, the fellowship program can be nothing short of dramatic.

"The workers say the experience gives them hope and makes them feel good about themselves," says Bradley. "They believe they'll all be in a better place as a result."

In Stella's case, organizational changes in the operating room have given her and other surgical nurses an opportunity to shine. New operating room protocols to help reduce post-surgical infection rates – that need to be enforced by nurses – have changed the dynamics between male surgeons and female nurses.

"Here is a group of women who are in the position of telling male surgeons what to do now," says Bradley. "It has been empowering for them."

Being a catalyst for change—and equipping health care workers with the skills they need to go forward on their own – is all part of the plan for the Yale-Clinton Foundation Fellowship program.

"Our exit strategy for this program was to put ourselves out of business and move on to another country," says Bradley.

"Clinical outcomes are being established, structural changes have been made and a patient satisfaction tool is in place. Patient registration is smoother, wait time is down and cleanliness has improved."

— *Elizabeth Bradley, Ph.D., Global Health Initiatives Yale School of Public Health*

Berkeley-Darfur Stoves Improve Women's Safety and Feed Refugees

University of California, Berkeley
Lawrence Berkeley National Laboratory
Engineers Without Borders

The humanitarian crisis in the Darfur region of western Sudan has displaced nearly 2.3 million people. While many of these individuals live within the safe confines of refugee camps, they are not always out of harm's way.

Women must venture outside camps to collect firewood to cook for their families. The sudden and drastic increase of people relying on the camps' surrounding land has taken a toll on the environment. Deforestation has left the area surrounding camps barren, and the lack of firewood causes more than 50 percent of families to miss one or more meals a week. As women spend more time outside of the camps in search of wood (a typical trip can last up to seven hours), they put themselves at risk of being raped or subjected to genital mutilation by the Janjaweed militia.

When Dr. Ashok Gadgil, Senior Scientist and Group Leader for the Environmental Energy Technologies Division at Lawrence Berkeley National Laboratory, was contacted by an officer of the United States Agency for International Development (USAID) to help refugees in Darfur, he knew little about the daily lives of refugees and wondered how a group of scientists could help better their lives.

The initial USAID proposal was to develop a compactor to turn sun-dried kitchen waste into a fuel source. On his first trip to Darfur, Gadgil concluded that there was not enough kitchen waste to provide an adequate fuel source for cooking fires. He did note that refugees cooked over three-stone fires, which transfer just five percent of heat to food. This inefficient cooking method inspired Gadgil to develop a field test in Darfur to study the efficiency of various cooking stove designs.

Researchers assessed the factors of cooking in Darfur. They worked closely with women, taking note of what they liked and didn't like about each stove in the trial. Other factors they considered included the size and shape of the pots used, how the stove was manned and the cooking environment—either outdoors, in close proximity to neighbors, or inside refugees' small shelters.

The team also took note of the types of food cooked. One of the staple foods of Darfur is assida, a bread that is cooked in a pot and must be continuously stirred. As the assida cooks, it becomes viscous and requires the cook to use the leverage of the pot to stir—stability is crucial to ensure the pot and stove do not tip over. Mulah is a sauce served with the assida. Cooks must fry onions, a cooking technique that requires a higher heat output from the fire than other techniques such as boiling water.

Back in the United States, Gadgil and students at the University of California, Berkeley designed a stove that would address the specific needs of refugees in Darfur. The resulting Berkeley-Darfur Stove is four times more efficient than a three-stone fire and features customized engineering to benefit the refugees.

A tapered wind collar increases fuel-efficiency in the gusty Darfur environment and allows for multiple size pots. Wooden handles allow for the stove to be handled while hot. Metal tabs accommodate a flat plate to bake bread. Internal ridges create the optimum space between the stove and pot for maximum fuel efficiency. Feet provide stability, and optional rods can be pounded into the earth for more stability. Nonaligned air openings between the outer stove and inner firebox prevent too much airflow, and a small firebox opening prevents cooks from using more fuel wood than necessary.

Berkeley-Darfur Stoves use 25 percent of the fuel used in three-stone fires. The stoves have more combustion efficiency (how well energy is converted into heat) and better heat transfer (how heat gets to the pot).

The design also minimizes the changes required of the refugees. It allows them to prepare the same kinds of food as before in the same amount of time, something not guaranteed by other options such as solar stoves.

With the design in place, the next step was to devise a plan to produce and distribute the stoves. The Berkeley group partnered with the San Francisco Professionals Chapter of Engineers Without Borders to develop a manufacturing system with Darfur's infrastructure in mind. Led by Ken Chow, this group of engineers revisited the stove design to make it simpler to build by reducing the number of parts and streamlining the assembly without compromising the design of the stove.

The Berkeley-Darfur Stove is metal, instead of clay, because metal provided better quality control when producing mass quantities. Sheet metal is stamped and cut to the exact dimensions shown to provide the most efficiency.

These flat kits are shipped to Darfur and assembled by local workers. In cooperation with CHF International, a pilot production facility has been set up in Darfur. The facility currently produces between 200 and 500 stoves per month, not nearly enough to provide for the estimated 400,000 stoves needed. The facility is currently working to increase production by increasing days of operation and adding a second shift. The project hopes to open more facilities in the future.

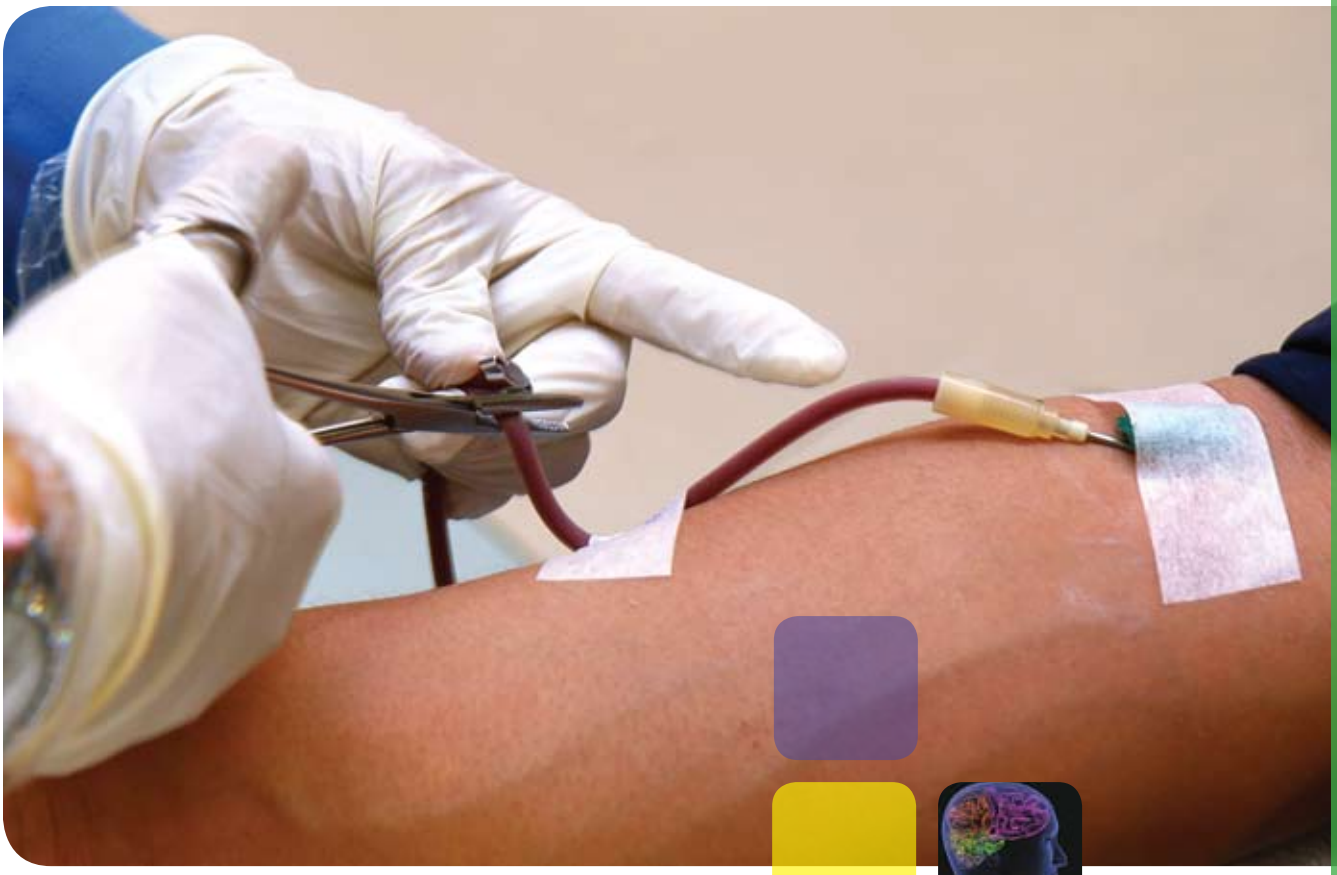
The manufacturing sites will create new jobs in Darfur, just one of the economic benefits of the Darfur Stoves Project. Families who use the stove will save $250 a year on firewood. Women will spend less time looking for firewood and will be able to pursue entrepreneurial activities such as weaving mats. An influx of money to the Darfur economy will improve the living conditions of refugees.

Each stove costs $25. Since this is an outrageous amount for refugees to pay, international non-governmental agencies underwrite the stoves. Amy Callis, Executive Director of the Darfur Stoves Project, works with organizations such as The Hunger Site to distribute the stoves and provide training to ensure the most efficient cooking.

There has already been a high demand for the stoves. During a three-week trial, 50 stoves were distributed and assessed. After the study, the stoves were offered for sale, and each one was bought.

This successful program could not have been possible without the collaboration of experts from various fields—Gadgil and his scientific team, Chow and his engineers and Callis' networking and communication skills. The project was executed almost entirely by volunteers. Each had their own specialty and none worked exclusively.

"We're doing what we can to relieve them from suffering, but the humanitarian crisis is extreme," said Chow. "The stoves will improve the situation but will not be an answer to the crisis." For more information visit www.darfurstoves.org.



Biomarkers and Blood Test Breathe New Life into Diagnosis and Treatment of Mental Illness

University of Cambridge

Early detection and proper care is a common message used by health care organizations in their efforts to educate people and governments throughout the world about winning the war against certain cancers and other chronic diseases.

But does this message offer the same real hope of change for individuals and caregivers who live with the chronic and disabling affects of schizophrenia and other mental and neurological disorders? Early detection and proper care is less than assured. This is especially true when general practitioners and psychiatrists must rely on a century-old, highly subjective and time consuming verbal diagnosis that hopefully will help them identify the exact psychosis that is causing the delusions, hallucinations, disorganized thinking and other psychotic symptoms. This process often delays treatment and extends the suffering of millions throughout the world. Consider the facts just for schizophrenia:

- About 24 million people worldwide suffer from this treatable disorder
- Treatment is more effective in the initial stages of the disease
- More than 50 percent of persons with this disorder are not receiving appropriate care

"Our diagnostic blood test represents new hope for the millions of individuals throughout the world with schizophrenia..."

— *Sabine Bahn, M.D., Ph.D., Cambridge Centre for Neuropsychiatric Research*

Existing diagnosis and treatments are failing too many people who suffer from schizophrenia and other mental and neurological disorders, as well as contributing to runaway global health care costs.

Bit in early 2009, Rules-Based Medicine Inc. (RBM), the leading multiplexed biomarker testing laboratory based in Austin, Texas, plans to sell worldwide a reliable and objective blood test for the diagnosis of schizophrenia. This diagnostic blood test, which relies on RBM's comprehensive protein biomarker assay and technology platform, is based in large part on proprietary biomarkers that are a signature for schizophrenia.

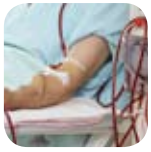
The identity of these biomarkers are the result of 12 years of ground-breaking research by Sabine Bahn, M.D., Ph.D., MRCPsych, of the Cambridge Centre for Neuropsychiatric Research (CCNR) at the Institute of Biotechnology, University of Cambridge in the United Kingdom. Aided by funding from Stanley Medical Research Institute, the National Alliance for Research on Schizophrenia and Depression and University/ Higher Education Innovation Fund, Bahn and her team of researchers tested spinal fluid and analyzed post-mortem tissues of schizophrenic brains in their quest for a scientific approach that can enable more appropriate and timely therapeutic intervention.

A psychiatrist by training, Bahn cofounded Psynova Neurotech in 2005 to develop and commercialize novel biomarkers—genes or proteins in tissues, blood and body fluids—that can distinguish schizophrenia from Alzheimer's disease, bipolar disorder, manic depression or dementia. The founding intellectual property of her ground-breaking work is licensed on an exclusive worldwide basis by Psynova from Cambridge Enterprise Limited, the University of Cambridge's technology transfer company.

The last piece to fall in place came in June 2008 when Psynova and RBM agreed to partner in the validation, regulatory approval and manufacture of a diagnostic blood test.

This first blood test for the diagnosis of schizophrenia is a scientific tool that can help general practitioners and psychiatrists diagnose patients much sooner, say Bahn and RBM's Chief Executive Officer, Craig Benson, both of whom have witnessed first hand the suffering of a family member with a mental disorder. It also offers the potential to identify disease subtypes, develop proper treatment options, monitor patient responses and discover novel drug approaches.

"Our diagnostic blood test represents new hope for the millions of individuals throughout the world with schizophrenia," says Bahn, "not only for early detection and proper care but more personalized treatments that would make the trial and error approach they now know obsolete."



Researchers Invent an Intelligent System for Hemodialysis and Hemofiltration

Cincinnati Children's Hospital

Patients waiting for a kidney transplant usually depend on dialysis to stay healthy until an organ donor can be found. They spend hours in a hospital or dialysis center several days a week so the machine can clean the toxins from their blood because their own kidneys can no longer do the job. Medical personnel carefully monitor and adjust the equipment throughout the process because even a small error could be very dangerous.

As John J. Bissler, M.D., a nephrologist at Cincinnati Children's Hospital, cared for patients in the intensive care unit, he became frustrated by the limitations of the monitoring equipment. He recognized the need for a system that accurately monitored, measured and regulated dialysis and filtration treatments. He envisioned a system that would automatically adjust dialysis or filtration when it recognized a problem instead of simply beeping. In 1988, he began assembling a team of doctors and engineers to develop an intelligent hemodialysis and hemofiltration system.

Traditional dialysis equipment works by diffusion across a membrane. On one side of the membrane is the patient's blood; on the other side is a fluid composed of sterile water and dialysate that supplies needed salts. Moving from an area of high concentration to an area of low concentration, toxins in the blood diffuse across the membrane and are washed out, while the fluids and salts diffuse into the blood. Dialysis requires frequent adjustments by personnel who must monitor the fluid removed from the patient on a regular basis. This activity leads to a significant increase in nursing care and raises the cost of the therapy. There are an estimated 1.5 million dialysis patients worldwide.

The machine Bissler invented works by hemodialysis, filtration or both. Taking advantage of new, stronger materials, his machine can force blood through a membrane that acts like a colander, straining toxins from the blood as the filters in the kidney do. The system then replaces fluids and salts and returns the blood to the body. This hemofiltration technology uses highly accurate scales, pumps, filters and pressure transducers to remove a desired amount of fluid from the blood at a desired rate. "Fluid balance is critical," Bissler explains. "Even a small error can be very dangerous. We were looking for stunningly accurate filtration. Tracking weight as the measure solved the problem. What we invented was a way to control the volumes so it is safe."

The whole system is computer-controlled, using sophisticated software. It notices changes and assesses what's wrong. If the pump is going too fast or too slow, the computer automatically adjusts the rate of flow. If the filter is going bad, the computer gives a warning and tells you how much time you have to fix it. The machine also pays attention 100 percent of the time, reducing the need for medical supervision and the possibility of human error.

"What sets this new device apart is the level of accuracy attained, allowing for safe and effective treatment, combined with the ease of use and portability," says Bissler. "While this technology is critical for the intensive care unit patient, it also offers new therapeutic promise for families with children affected by renal failure. It represents a major leap forward in the area of home care, and an opportunity for these patients to lead more normal lives." In the near future, many of the 250,000 American children and adults currently on dialysis may no longer have to go to a hospital or physician's office to receive treatment but can get it at home—at lower cost and with greater safety.

Working through the Cincinnati Children's Hopsital Office of Intellectual Property, Bissler licensed the technology to British Technology Group (BTG), a world leader in the commercialization of new health care technologies. Through sublicense agreements with Gambro and Fresenius, the technology has found commercial outlets, which comprise the majority of the worldwide hemofiltration market.

Livestock Feed Supplement Developed at Cornell Helps Reduce Phosphate Pollution

Cornell University, Phytex, LLC

In the 1990s, while he was working on his Ph.D. in animal science, Xingen Lei learned that phosphorus pollution from livestock is a huge problem. When he came to Cornell University, Ithaca, N.Y., as a professor in the Department of Animal Science, his first project was to develop an enzyme that could be used as a feed supplement to alleviate this problem. His research resulted in OptiPhos, a feed supplement that can reduce phosphorus pollution from pigs and poultry by as much as 50 percent.

Necessary Nutrient

As animals grow, they need phosphorus for bone and muscle development, and to help them use the energy in their diet. Much of the phosphorus in a typical corn-soy-based diet for livestock occurs as phytic acid. Livestock with simple stomachs, such as pigs and chickens, cannot digest the phytic acid, so it is excreted.

Pigs, chickens and other simple-stomach livestock animals need to receive supplementary phosphorus in the form of inorganic phosphates, which their digestive systems easily absorb. For pigs, the cost of this phosphate supplementation is currently $2 to $4 per animal during its growth cycle, the third most costly component of the animal's feed. Inorganic phosphate is obtained from mines and is a non-renewable resource. The depletion of this resource has resulted in an increase in price per ton of phosphate from $200 or $300 to $1,000 in recent years.

Even though animals need the phosphate supplements, the phosphorous they excrete causes phosphorous pollution, taking a toll on the environment. While pig and chicken manure can be used to fertilize crops, the high level of phosphorus in the manure limits how much manure can be spread on a field. In livestock-raising areas, water runoff from farms washes much excreted phosphorus into neighboring waterways, lakes and ponds. This promotes eutrophication—excessive growth of aquatic plants that deplete the oxygen concentration in the water, often killing fish and other organisms.

Fortunately, through research in the U.S. and abroad, phytase enzymes are now available as feed supplements to help animals break down the phytic acid in their feed into usable phosphate. "Phytases are a group of enzymes," says Lei. There are different versions, but they all do the same job: breaking down the phytic acid. "It's like cars. There are different models, different engines, different colors, but they all do the same thing—get you from here to there."

Phytase Developments

The first phytase supplements, developed in Europe in the early 1990s, showed promise but did not act effectively in the conditions present in an animal's stomach. To be effective, a phytase supplement needs to do its work in the presence of stomach acid and digestive enzymes. And the phytase needs to work fast. Food doesn't stay in the animal's stomach for very long; an hour to an hour and a half in pigs, and less in poultry, is all the time the phytase has to do its job.

Lei and his students found a strain of E. coli bacteria that produces a phytase enzyme resistant to the digestive enzymes and acid in the stomach. Also, it works quickly enough to convert a significant amount of phytic acid to useful phosphate while food is in an animal's stomach.

After isolating the gene responsible for making phytase, Lei expressed it in yeast to produce the phytase in quantity, and improved the enzyme's stability. Then, he published a paper based on animal studies of the enzyme's performance.

Partnership

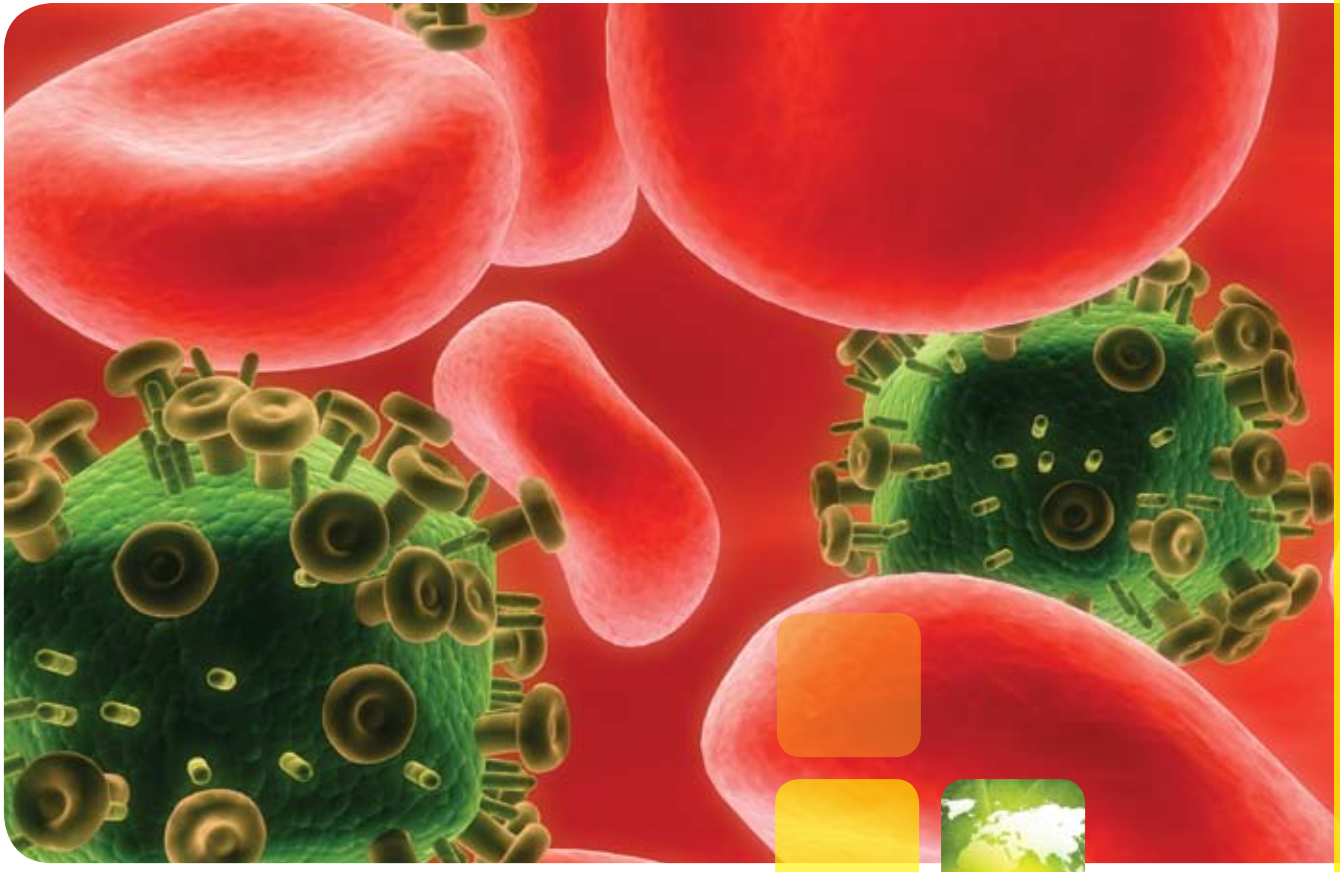
Lei's work attracted the attention of Frank Ruch, president of Protein Scientific, Inc., a Portland, Maine, company specializing in nutritional products for humans and animals. Protein Scientific and JBS United, a Sheridan, Ind. animal feed company, formed a joint venture, Phytex LLC, to license the technology from Cornell and further develop it. In 2001 Cornell granted Phytex an exclusive license for the development and production of the phytase enzyme.

Phytex performed further development of the enzyme and transferred it to large-scale production. The company has also worked with academic laboratories in the U.S. and abroad to improve the yield. In 2005, Phytex completed a 3-year Food and Drug Administration approval process for OptiPhos. Meanwhile, "the cost of the enzyme went down, and the cost of phosphate went up," says Ruch. It became cost effective to substitute animal feed with more and more phytase enzyme in place of inorganic phosphate, enabling farmers to raise pigs on a diet with very little inorganic phosphate supplementation.

The OptiPhos technology transfer program has involved patents in three main areas, says Alice Li, a senior technology commercialization and liaison officer at the Cornell Center for Technology Enterprise and Commercialization. One family of patents covers bacteria phytase enzyme. Another covers improved versions of bacteria phytase that have been developed. Other patents cover methods of phytase production.

Continuing research includes applications in the poultry industry with turkeys, chickens, and ducks, as well as work with swine to investigate substitution of greater amounts of enzyme for more and more of the inorganic phosphate supplements. Additional work at Cornell has included improving the enzyme's resistance to the heat and moisture encountered during the pelleting process.

Within the phytase research programs, Lei has had "the opportunity to teach students that technology can make a real impact—research is not just about writing papers," he says. And he has been pleased with the experience of working with commercialization partner, Phytex. "There is a great role for university professors and industry to work together as a team."



Once-a-Day HIV Meds Improve Quality of Life and Hold Promise for Developing Countries

Emory University

Not so long ago, HIV sufferers took 10 to 15 pills a day and still the outcome was often bleak. Today, more than 80 percent of HIV patients take at least one of the drugs developed by Emory scientists in a single tablet, once a day. Although it's not a cure, the treatment restores life as it lowers the daily drug regimen burden, diminishes side effects, relieves disease symptoms, and adds longevity.

Emory professors Raymond Schinazi, Ph.D., Dennis Liotta, Ph.D., and researcher Woo-Baeg Choi discovered an unusual molecule, FTC (emtricitabine, sold alone as Emtriva®, with the "Em" suggesting Emory) and a chemically similar compound, 3TC (lamivudine, sold alone as Epivir®). Both drugs are in the nucleoside reverse transcriptase inhibitors class, which means they work against the enzyme that copies HIV RNA into new viral DNA.

"They are what we call DNA chain terminators," explains Liotta. "Think of viral DNA as a line of rail boxcars, the drugs destroy the hitch so no more cars are added. The virus accepts the compounds and mistakes them for normal nucleotides, but they lack a function group necessary to copy the RNA to DNA."

Typically, HIV sufferers take a three-drug combination, with Emtriva being one of the three. "Special credit goes to the scientists at Gilead," says Liotta. "They are the unsung heroes that developed a compression technique to fit a full day's dosage of all three drugs in a single tablet, and it's not a 'horse' pill."

"That's the thing, thousands of people make contributions to the ultimate success of this drug," says Liotta.

Indeed, many people have persevered at getting the drugs to patients around the globe. Gilead and Bristol-Myers Squibb gained FDA approval in 2006 for the first once-a-day, single tablet regimen for adults with HIV called Atripla®. Atripla contains three drugs—efavirenz (Sustiva®), emtricitabine (Emtriva®), and tenofovir disoproxil fumarate (Viread®), combined in one tablet and hence can be used as a stand-alone therapy in patients. Atripla reduces pill burden and simplifies dosing schedules, which not only makes things easier and more tolerable for patients, but also greatly eases storage, transport and distribution of the drug to places with less than ideal conditions. "Gilead did a tremendous amount of work in stability studies to increase the shelf stability of the drugs in hot, humid climates and poor storage conditions typical in third world countries," says Liotta.

Atripla is marketed jointly by Gilead and Bristol-Myers Squibb in United States, Canada and Europe, but in much of the developing world, marketing and distribution is handled by Merck & Co., Inc.

In addition, Gilead established partnerships with 10 Indian companies to produce and distribute quality, low-cost generic versions of Gilead's HIV medications in 95 developing countries. Other industry collaborations include local manufacturing and distribution by South Africa's Aspen Pharmacare and a manufacturing collaboration in the Bahamas with PharmaChem Technologies and the Grand Bahama Port Authority.

Meanwhile, Gilead is hard at work clearing the political and regulatory paths in developing world countries. "If you work with import waivers you might get products into a country one month, but not the next," explains Clifford Samuel, senior director of International Access Operations at Gilead. "We prefer to take the high road and pursue full regulatory approval in each country so that patients have sustainable access to the antivirals they need on an uninterrupted schedule."

This is no easy task as the regulatory process varies greatly by country and not all governments are motivated by humanitarian concerns. Nonetheless, Samuel and his team continue to push their way through the various regulatory challenges in Africa, Eastern Europe, China, Southeast Asia, Latin America and the Caribbean.

While these highly coordinated efforts seem brilliant in their simplicity, the history of FTC, like other new discoveries, is a bit more convoluted.

FTC was licensed by Emory in 1996 to Triangle Pharmaceuticals, a biotech company founded by Schinazi and others in 1995. In 2003, Gilead acquired Triangle for $482 million and in the same year, Emtriva was approved by the FDA. In 2002, Shire and GlaxoSmithKline jointly licensed Emory's patents related to 3TC, now used in at least 5 products. In 2005, Gilead Sciences and Royalty Pharma signed a deal with Emory to buy its royalty interest for FTC for $525 million. Gilead obtained approval for Truvada®, a fixed-dose combination of Emtriva and Viread in 2004.

Today's combined efforts of Emory, Gilead, Merck and Bristol-Myers have saved millions of lives worldwide.

Although these results are very gratifying, this is far from the end of the story. Emory researchers are expanding their search for more lifesaving drugs. The new Emory Institute for Drug Discovery will open either late fall or early winter of 2009. Within its walls, scientists will attack several diseases with an unfailing determination to stop their trek across human lives. "We may not make a fortune, but we will make a difference," smiles Liotta. Indeed, sir, you already have.

"Think of viral DNA as a line of rail boxcars, the drugs destroy the hitch so no more cars are added."

— Dennis Liotta, Ph.D., Emory University

Using Very Small Chips to Meet Very Big Goals

Harvard University

Of all the initiatives targeted at improving the health of the world's neediest citizens, a small nonprofit company called Diagnostics-For-All (DFA) has some of the biggest goals.

"Our success as a company," says Executive Director James J. Barber, Ph.D., "will be measured in how broadly we can make a difference in how health care is delivered in the developing world...in how many lives we can touch with our capabilities."

But improving health care in, for example, Africa, where 60 percent of the population lives in rural areas underserved by hospitals, is a colossal challenge that begs the question: Where, exactly, do you begin to make a difference?

For DFA co-founder George Whitesides, Ph.D., the answer is simple: with a diagnosis.

Introducing the Paper Lab-on-a-Chip

As a result of his groundbreaking work in microfluidics—which involves the manipulation of fluids that are geometrically constrained within a small space—Whitesides realized that he could create "simple" solutions for point-of-care diagnostics for use in resource-poor settings.

His invention, created in his Harvard University lab called The Whitesides Group, is a paper-based microfluidic chip the size of a fingernail. It works like a miniature, portable laboratory capable of testing a tiny sample of bodily fluid such as blood or urine for proteins or other enzymes that indicate health or disease.

Using a patent-pending technology, The Whitesides Group patterns the paper with water-averse polymers, forming a series of channels that guide a fluid sample to a specific location on the chip that is pre-treated with a reagent. When the reagent is exposed to the fluid sample, it results in a color change that can be read and translated into a diagnosis.

By using paper instead of glass, plastic or silicone commonly used in microfluidic devices, Whitesides and his team have created the perfect portable lab-on-a-chip. Inexpensive to produce—manufacturing costs could be as low as one cent per chip—and easy to transport, the paper-based testing device requires no equipment or power sources and once used, it can be incinerated. What's more, its user-friendly design will require minimal training for public health workers in the field.

First Application: Health Monitoring for AIDS and TB Patients

DFA's first paper diagnostic chip will test for liver function, a simple test that could save thousands, if not millions of lives in the developing world.

The high incidence of AIDS in places like Africa has brought about another epidemic: tuberculosis (TB). According to the World Health Organization, the rate of TB has quadrupled in many countries since 1990. In Africa, where those weakened by HIV/AIDS are susceptible to the infection, more than 500,000 succumb to TB each year.

Although the infectious disease can be cured with proper treatment within six months, the antiretroviral drugs prescribed for both TB and AIDS can have serious side affects. According to DFA, about five percent of patients in the developing world receiving treatment for TB or AIDS—nearly one million people—die of drug-related liver complications due to lack of access to the necessary health monitoring.

"These drugs are very toxic and put patients at high risk of developing liver failure," says Hayat Sindi, Ph.D., DFA co-founder. "In the U.S., patients undergoing similar treatment would be tested for liver failure once or twice a week. In countries like Africa, if patients are lucky enough to live near a lab, it can take weeks for a result. By then, it may be too late to stop or alter the course of treatment to recover damage done to the liver."

Inventor and Co-founder George Whitesides

Microfluidics is just one of the many frontiers explored by Whitesides and his highly technical team of scientists working in the The Whitesides Group laboratory.

In his nearly 50-year career, the Harvard chemistry professor has contributed groundbreaking research in such diverse areas as nuclear magnetic resonance spectroscopy, materials and surface science, and nanotechnology. He has also explored biophysics, the origin of life, cell-surface biochemistry and science for developing economies. A highly accomplished and award-winning scientist, he has received both the National Medial of Science and the American Chemical Society's Priestly Medal.

"Maybe every 50 or 100 years or so, someone comes along who can not only dabble in a broad range of sciences, but who can make significant contributions in those fields," Barber says. "George is one of those people, a completely remarkable man in terms of influence."

He is also, colleagues say, blessed with practicality and a burning desire to help. He strategically structured DFA as a not-for-profit entity in order to maintain a focus on serving the developing world first.

"Dr. Whitesides' work developing the diagnostic-on-a-chip was driven by a desire to produce diagnostic devices that could reach people in need," says Barber.

Citing its commitment to acting with flexibility and speed to improve global health, Harvard University, through its Office of Technology Development, agreed to give DFA the option to exclusively license the diagnostic technology royalty-free for not-for-profit purposes.

A Laboratory Full of Rising Stars

As an educator at the Massachusetts Institute of Technology (MIT) and now at Harvard, Whitesides has mentored countless up-and-coming scientists, researchers and entrepreneurs. Two of those students, Hayat Sindi and Jim Barber, are central players in the formation of DFA (other principals include Carmichael Roberts, Ph.D., co-founder and board member, and Isaac T. Kohlberg, Harvard's Senior Associate Provost and Chief Technology Development Officer).

Hayat Sindi

Sindi, of Saudi Arabia, came to Harvard as a visiting scholar specifically to work with Whitesides. She found in him both a mentor and a kindred spirit.

"From the time I was a young girl, I knew I wanted to make a difference in the universe," Sindi says. "I really admired scientists, and I knew I wanted to dedicate my time and education to helping others."

Whitesides encouraged Sindi, the first woman in the Persian Gulf area to hold a doctorate in biotechnology, to enroll in a Harvard Business School course on commercializing science. She formed a multidisciplinary team that not only wrote a business plan for DFA, but also worked tirelessly to compete in both the 2008 MIT $100,000 Entrepreneurship Competition and Harvard Business School's 12th Annual Business Plan Contest. In an unprecedented sweep, DFA took top honors at both competitions, marking the first time MIT would award its grand prize to a not-for-profit team.

"By formulating a business plan for a nonprofit company, the group was pushing to change the opinion in the marketplace that it isn't all about making money...it's also about saving people's lives," says Sindi.

In addition to helping to capitalize the new company, the MIT prize is also a harbinger of success: in its 19 years, the competition has helped create nearly 100 companies with an aggregate market capitalization of $10 billion.

Jim Barber

DFA executive director Jim Barber knows a thing or two about building value in emerging markets. After completing a doctorate in organic chemistry under Whitesides in 1980, he went on to a successful career in specialty chemicals and materials, most recently as president and CEO of Metabolix Inc., which he shepherded from a research boutique to a leader in biodegradable plastics. When that company went public in 2007, Barber seized the opportunity to once again work with his mentor.

"I had become very interested in public health and wanted to put my time and energy into that realm," he says. "DFA is the perfect marriage of a broadly applicable technology with great social need."

"Our success as a company will be measured in how broadly we can make a difference in how health care is delivered in the developing world…in how many lives we can touch with our capabilities."

— James J. Barber, Ph.D., Diagnostics-For-All

The Future of Diagnostics-For-All

While its fundraising efforts are ongoing, Barber says DFA hopes to have a working prototype of the liver function test by the end of 2009 and to be conducting field studies with the paper diagnostic by 2011. In the meantime, the company is connecting with public health groups and other organizations to establish distribution networks across the developing world, from Africa to Asia and Latin America.

From there, say DFA's co-founders, the sky is the limit on the type of tests that can be embedded on the paper chip.

"We are developing a test that is broadly useful in different settings, in different geographies, in different social contexts," says Barber.

The list of possibilities includes tests for kidney function, electrolyte levels and malaria as well as specialized applications for emergency responders, pediatric care and environmental testing.

Straightforward and simple, each assay meets DFA's central criteria: to make a difference by providing a much-needed on-the-spot diagnosis.

"Diagnosis is critical," says Barber. "It allows care to be delivered."

Green Power of Centia Moves Biofuel Energy Closer to Reality

North Carolina State University

The cry for alternative fuels echoes around the world. It doesn't really matter whether individual cries are in mourning the toll of global warming, or in fear of the ever-diminishing supply of fossil fuels, or both. In any case, the plaintive chorus calls for immediate relief. Now, that relief may be at hand with North Carolina State University's recent breakthrough in biofuel production, which converts vegetable oil and animal fat—even cooking grease and algae—into jet fuel, biogasoline and biodiesel using a 100 percent green process at a much reduced cost. The technology is called Centia™, a name that means "green power" in Latin.

It is not that biofuel is a new idea, but low energy yields and costly raw materials called feedstock, i.e. plants and animal fat, the most common of which is corn, have made its reality more of a dream.

"In renewable energy, we want to stay away from crop oils so that we do not compete with the food supply," explains William L. Roberts, Ph.D., Professor and Centia co-inventor, Department of Mechanical and Aerospace Engineering at N.C. State University. Indeed, grocery store chains and warehouse stores saw rising prices and even purchase limitations this year as efforts to produce biofuels began to pressure the food supply.

The first order of the day, then, for Roberts and his fellow inventors was to find a way to effectively and efficiently use feedstocks that were too low in quality for human consumption. By doing so, millions of people around the globe could then afford food staples such as flour, corn meal and vegetable oil.

However, food supply was not the only thing dwindling in the wake of biofuel production. "Rain forests were being destroyed to make way for palm oil and other plantations," says Roberts. While the renewable energy industry is launching many new jobs, a "green" technology is not truly green if its use or production wreaks havoc on the environment in any way. In essence, current biofuel efforts were selling out the long-term in favor of the short-term, even if by accident.

There was also a problem with tying the industry too closely to a handful of feedstocks. "Seventy percent of the final price of biofuel comes from the cost of feedstocks so you don't want the process tied to one feedstock which in turn is vulnerable to market swing and unduly high costs," says Roberts. Ultimately, it is the free fatty acid in the feedstock that is needed to create biofuel; the higher the content, the more expensive the raw material.

Thus feedstocks became a central issue in the research. Roberts worked alongside H. Henry Lamb, Ph.D., professor in the Department of Chemical and Biomolecular Engineering; Larry F. Stikeleather, Ph.D., professor in the Department of Biological and Agricultural Engineering; and, Timothy L. Turner, Doctoral Student in the Department of Mechanical and Aerospace Engineering to resolve this and other obstacles typical of biofuel production.

Remarkably, the Centia process can use low-quality feedstocks of virtually any origin and in any combination. "We can use any starting material including crop oils—virgin or waste—animal fats, even lipids from algae," says Roberts.

Another huge obstacle to creating biofuel was the low energy content. Simply put, previous biofuels simply did not have enough oomph to power existing machines. Usually, costly modifications to machinery were necessary to make biofuel useable at all. "We set out to mimic the fuel we were attempting to replace so we worked backwards from there, almost a reverse engineering," laughs Roberts.

After two months of theoretical work followed by 18 months of proof of concept work, the N.C. State team was successful in rendering the right mix of physical and chemical properties to produce a biofuel the true equivalent of a fossil fuel.

"We achieved the two extremes, lowest quality feedstock to produce the highest quality fuel," beams Roberts.

The process consists of a first stage hydrolysis reaction, where fats and oils are converted into free fatty acids. In a second stage, a carbon dioxide molecule is removed from these free fatty acids, yielding a long, straight chain hydrocarbon. These long straight chain molecules are then isomerized, cracked, and/or aromatized, yielding a wide range of molecular sizes and structures. The final recipe of iso-alkanes, aromatics, and cycloalkanes can be adjusted to yield the desired octane number. "The high temperature, high-pressure catalytic process changes the structure as needed to mimic diesel, gas or jet fuel," says Roberts.

These fuels are consumable in any conventional gasoline engine without modification, a major plus in reducing the overall costs associated with converting to alternative energy use.

Since no petroleum-derived products are added to the process, Centia is 100 percent green. There is no soot or particulate matter associated with fuel from fats so the fuel created by the new process also burns cleaner.

What remains to be solved is scalability, i.e. moving from the teaspoon to the gallon level. N.C. State has licensed the technology to Arizona-based Diversified Energy Corporation to push the technology into the commercial space.

Diversified Energy Corporation specializes in transitioning alternative and renewal energy technologies into viable commercial products. Currently, Centia is one of four technologies in the company's portfolio. "It's still at benchmark scale in nature, but it's sexy, and we're doing the necessary R&D now to have it commercially ready by 2013," says Jeff Hassannia, vice president of business development at Diversified.

The key advantages of fuel products rendered from the Centia process, according to Hassannia, are:

1. No external hydrogen is used which means no fossil fuels are needed to produce the biofuel.
2. The jet fuel made in this process contains the necessary aromatics so there is no damage to engine seals and valves.
3. Diversified Energy incorporates a glycerol burner (another technology in its portfolio) into the process to increase the energy conversion efficiency.

N.C. State made 2008 its "Year of Energy" to highlight its commitment to energy conservation and the development of alternative and renewable energy sources. The university was recently selected by the National Science Foundation to lead a national research center tasked with revolutionizing the nation's power grid. This Engineering Research Center for Future Renewable Electric Energy Delivery and Management (FREEDM) will be headquartered on N.C. State's Centennial Campus and will be supported by an initial five-year, $18.5 million grant.

N.C. State's Office of Technology Transfer is hopeful that Centia will prove to be an important contributor to America's quest for energy independence and will prove crucial to bridging the gap between fossil fuels and the new generation of clean and renewable energy sources.

Milton Mutchnick, M.D.

Therapeutic Developed in United States Benefits Many in Asia

Wayne State University

For a scientist with an idea that might make a difference to people's lives, the path from illuminating insight to world-changing reality can be dramatic and satisfying. Or it can be filled with financial obstacles, poor execution, and disappointing results.

Since Wayne State University gastroenterologist Milton Mutchnick, M.D., first proposed using the hormone-like peptide thymosin alpha 1 to combat Hepatitis B in the mid-1980s, the drug has seen both outstanding success and somber letdown. Overseas, thymosin has become an important tool for fighting Hepatitis B, cancers and infections. Within the United States, its promise remains in doubt decades later.

Mutchnick, now Chief of Gastroenterology at Wayne State's School of Medicine, is a liver specialist who thinks the liver is a "really ugly-looking organ." But, he adds, "I have a great love for it. I find it fascinating. Among its functions, it secretes bile to help the body digest food. It filters toxins from the blood and metabolizes drugs. It has roles in blood formation and antibody creation. And it can regenerate itself."

Following his hepatology residency at Yale University, Mutchnick undertook a year of training in immunology at the University of Michigan – good preparation for an early focus on Hepatitis B and Hepatitis C.

"We file patent applications in many countries, with royalties from successful therapeutic products put back into research..."

— Fred Reinhart

Both are infectious viruses that invade the liver. Some people's immune systems are able to clear their infections naturally. But for many, the diseases become chronic, lurking silently for decades, eventually inflaming the organ and causing the potentially fatal scarring of cirrhosis, possible liver failure or liver cancer. The B virus can be acquired through a number of routes, from sexual contact to infected drug needles. But the most common cause is being born to an infected mother.

It's estimated that in the United States there are two million Hepatitis B patients and four million Hepatitis C patients. Outside the U.S., the proportions are reversed: 350 million with Hepatitis B and 150 million with Hepatitis C. The B virus is epidemic in Asia, and it's estimated that 10 percent of China's population carries the infection. More than half of liver cancer cases worldwide occur in China.

Bringing Balance to the Immune System

A vaccine that can prevent infection with the B Virus has been available since 1982, but when Mutchnick was beginning his career in the 1970s, he notes, it was a disease without an effective therapy. Although there are seven drugs now approved for B Virus treatment, including interferon, a sure-fire cure for Hepatitis B still doesn't exist (treatment begun early in the disease's course seems to be most effective).

Mutchnick's concept of using thymosin began with a visiting lecturer's talk on immune modulators in the mid-1970s. Allan Goldstein, Ph.D., suggested that a deficiency of the hormone thymosin alpha 1, produced by the thymus gland, was a factor in certain immunodeficiency diseases.

"I suspected that the issue wasn't that the B virus attacked the liver cells," Mutchnick says. "Apparently, once it invades the cells, it lives there without injuring them. The problem is that the host's immune system goes after the virus and kills the liver cell along with it.

"My thought was that perhaps thymosin doesn't enhance or suppress the immune system but modulates it. I pursued this theory in lab research and found that, in the absence of thymosin, the immune system killed the cells, and that, when thymosin was added, it didn't. In 1986, I was able to treat 10 patients – with promising results."

The next steps were patents and further studies. "Thymosin showed good results and had few side effects," says Fred Reinhart, who joined Wayne State's Technology Transfer Office some years after Thymosin's emergence. "We definitely get excited about a therapeutic that seems to be effective. We filed patents both in the U.S. and in a number of foreign countries."

Differing Results, Expanded Uses

The rights were licensed to two pharmaceutical companies for clinical trials. Rights in the United States and Europe went to a small biotechnology company. Rights to test and sell the drug outside the U.S. and Europe were licensed to SciClone Pharmaceuticals International, which focuses on drug distribution overseas.

In the U.S. tests, thymosin alpha 1 was given the brand name Thymalfasin and taken to multi-center trials in 1992. But there were problems – among them, funding difficulties, questions about protocols and too few patients involved. Results were positive – but too limited for definitive conclusions. Thymalfasin use went nowhere.

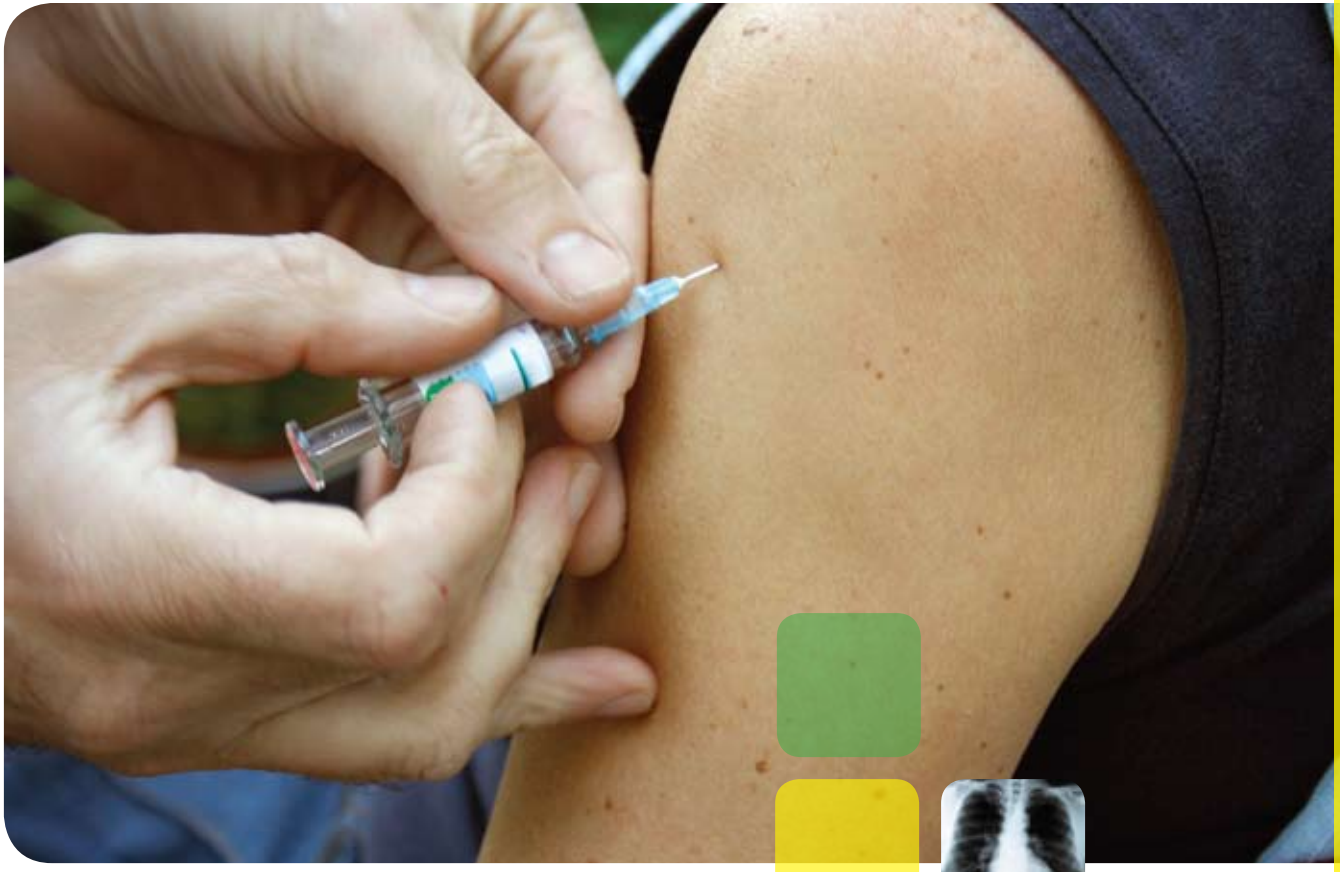
On a parallel track, under the brand name Zadaxin™, SciClone began trials throughout Asia and received its first approval from China in 1995. It began sales there in 1996. Other approvals followed. Today, Zadaxin is approved for use in 36 countries, from Argentina to Vietnam. Eventually, SciClone acquired the rights for Europe and, after that, the United States.

"Zadaxin's original approval in China was for monotherapy treatment of Hepatitis B," notes Randy McBeath, SciClone's Vice President of Marketing. "That began in 1996 and continues today. Since then, Zadaxin's value as an immunity enhancer has been built upon. Today it's also used in China to treat liver cancer and problems of post-surgical infection."

He adds: "Some Asian countries use it to fight Hepatitis C. In Italy, it is employed as an adjuvant drug with both flu and B Virus vaccinations – it lessens the risk of patients with compromised immunity systems developing the virus."

SciClone has continued to seek Zadaxin applications within the U.S. and Europe. In late 2008 the company received FDA approval to begin Phase III trials of Zadaxin's use for treating malignant melanoma – like liver cancer, a disease in which in which patients' immune systems play key roles, McBeath notes.

As for Mutchnick, he's moved on. "I'm out of the thymosin game," he says. And despite thymosin's heavy utilization in China, Wayne State University receives minimal royalties for Mutchnick's thymosin work. "We file patent applications in many countries, with royalties from successful therapeutic products put back into research," Reinhart says, "but in this case we didn't get a patent in China. We're very happy that research out of our university is helping people. I just wish we had filed in China."



TB: Designing the Perfect Vaccine

Oregon Health & Science University,
The Portland VA Medical Center,
Doernbecher Children's Hospital, and
Aeras Global TB Vaccine Foundation

At least from a bacterial survival standpoint, tuberculosis is the perfectly designed bug. Mycobacterium tuberculosis infiltrates the cell and then lurks within, identifiable by skin test, but not causing any symptoms.

"People estimate that one-third of the world has at least been exposed to tuberculosis," says David Lewinsohn, M.D., Ph.D., associate professor in pulmonary and critical care medicine at Oregon Health & Science University and Portland VA Medical Center. "We think that many of them are latently infected. So they have the bacteria and the bacteria is kind of there, but not causing any trouble. And 90-plus percent of the time that works just fine—people don't get sick."

When the disease does become active, though, tuberculosis can inflict significant harm—to the infected individual and others. Symptoms include chest pain, hemoptysis (coughing up blood), fever and weight loss. Someone with active disease, who goes untreated, can unknowingly infect 10 to 15 people annually by coughing, sneezing, or even talking, according to the World Health Organization (WHO).

In 2006 alone, 9.2 million people worldwide became ill and 1.7 million people died, according to WHO data. And some regions of the developing world have been particularly devastated by the bacterial infection. Five countries in Africa and Asia—India, China, Indonesia, South Africa and Nigeria—rank among the top five countries worldwide, in their total number of tuberculosis cases. The highest rate of new cases occurs in Africa, with nearly 350 cases per 100,000 population. Residents in Africa also suffer from the highest mortality rate compared with other regions of the world.

While medications typically can treat the disease, multi-drug resistant (MDR) strains are of increasing concern. An estimated 0.5 million cases of MDR tuberculosis worldwide were identified in 2007 alone and vaccine protection remains limited at best. The Bacille Calmette-Guerin (BCG) vaccine provides limited protection, particularly among adults, who are most likely to transmit the infectious bacteria. The vaccine isn't typically recommended in the United States because it can interfere with skin testing and because TB is primarily controlled by active surveillance and drug treatment.

The best solution, in short, is a better vaccine, one that mimics the immune system's natural ability to wall off the life-threatening bacterium. Solving that immune system riddle has become a driving passion for Lewinsohn and his research partner and wife, Deborah Lewinsohn, M.D., a pediatric infectious disease specialist and OHSU associate professor at Dorenbecher Children's Hospital.

"We think the TB is kind of hidden within this [cellular] structure," David Lewinsohn says. "The TB is not dead—it's there. And the immune system has got it contained. ...If we really understood how the human immune-response contained tuberculosis, then that would be our model for a better vaccine."

Fighting TB—Progress to Date

Along with the inherent cellular complexity, researchers describe a number of other hurdles involved with designing a tuberculosis vaccine. Since the disease develops slowly, it's difficult to assess the relative effectiveness of any given vaccine prototype. Plus, triggering a broad population-wide immune response is complicated by the natural variability in individuals' immune responses. "What your immune system will recognize is determined by your genetic makeup," says John Fulkerson, Ph.D., head of vaccine discovery at Aeras Global TB Vaccine Foundation, (Areas) a not-for- profit organization.

In tackling this issue, the Lewinsohns have applied more than 15 years in infectious disease research, with a particular interest in immune responses. David Lewinsohn's work related to tuberculosis dates back more than a decade. Deborah Lewinsohn, who initially focused more on HIV, started working more closely on tuberculosis once the pair joined the Oregon Health & Science University (OHSU) in the late 1990s.

Traditionally, tuberculosis researchers have been particularly focused on one component of the immune system, CD4 T-cells, which are believed to play a crucial role in keeping active tuberculosis at bay. (The depletion of CD4 T-cells in those infected with HIV, for example, makes them more vulnerable to developing tuberculosis.) But the Lewinsohns have become increasingly intrigued by another immune system component, the CD8 T-cells, which they also believe to be influential. They describe those cells as uniquely designed to locate foreign-seeming antigens hiding within a cell.

In 2004, the Lewinsohns received $4.6 million to further study the antigens, or proteins, believed to be influential in the onset of active tuberculosis. The substantial five-year contract was one of 14 contracts, totaling more than $73 million, awarded by the National Institute of Allergy and Infectious Diseases as part of its Large-Scale Antibody and T Cell Epitope Discovery Program. The program's goal is to stimulate breakthroughs in the understanding of epitopes—small portions of antigens—that can lead to vaccine breakthroughs against infectious diseases, including bioterrorism targets.

With the infusion of funding, the Lewinsohns have been delving further into identifying differences in antigens and epitopes between people with active tuberculosis and those with latent, or inactive, tuberculosis. Their goal: to identify specific cellular markers that the CD8 T-cells must recognize in order to swing into action against the lurking tuberculosis bacterium within.

Identifying Vaccine Components

By 2006, the Lewinsohns had identified a dozen antigens that showed sufficient promise, leading OHSU to file a provisional patent application. The following year, in late 2007, OHSU granted to Aeras an exclusive license to develop and market OHSU's antigen based vaccine for human vaccination against TB. "From the initial discussions with Aeras, which occurred at the 2007 AUTM Annual Meeting, they were excited about the opportunity to in-license and work on these antigens," says Andrew Watson, Ph.D., Licensing Associate in OHSU's office of Technology & Research Collaborations. "The licensing of OHSU's technology was an important step towards the development of a broad-based vaccine containing multiple epitopes," says Rita Khanna, Ph.D., J.D., General Counsel at Aeras. Aeras, which is funded by the Bill & Melinda Gates Foundation, the Dutch government and others, was founded in 2003 with the goal of developing a more effective TB vaccine by the middle of the next decade. "OHSU is pleased to be a partner in helping achieve this objective and meeting the global need for low-cost or at-cost vaccines, especially in the developing world," says Watson.

Along with addressing a vital public health need, the market incentives are substantial. The potential payoff, depending upon the type of tuberculosis vaccine developed, ranges from $450 million to nearly $1 billion annually, according to a 2006 analysis by BIO Ventures for Global Health, a Washington, D.C.-based nonprofit organization.

Aeras, based in Rockville, Md., has numerous vaccine development resources including partner clinical trial sites and a manufacturing plant. "We are functionally modeled like a pharma or a biotech, even though we are a non-profit," Fulkerson says. "Aeras can conduct more of the required vaccine development activities in-house than most big companies can."

Aeras is pursuing a number of vaccine strategies, some of which are already in Phase I and II clinical

trials. Aeras officials also have started working with the 12 antigens they've licensed from OHSU. In the coming years, Aeras will evaluate vaccine constructs encoding the identified antigens in rodent models and then in non-human primates on the most promising candidates prior to initiating trials in humans. "Aeras is excited about using OHSU's antigens for developing an effective vaccine against TB," says Khanna.

Moving Forward

Collaboration is key to making the project succeed. Aeras' scientists and the Lewinsohns continue to work in partnership on the development of vaccine candidates involving these antigens. In addition, Aeras will continue to track the Lewinsohns' progress as they identify other intriguing antigens in the future. In discussing the significance of the Lewinsohns' research, Fulkerson circles back to their ability to isolate specific epitopes, or pieces of antigens. Fulkerson believes that identification of those epitopes—specifically the ones that help trigger an immune response in individuals of diverse genetic backgrounds—may open the door to a broader-spectrum vaccine, one that could contain a dozen or possibly more epitopes.

"What this will allow is the capacity to design a vaccine that contains, instead of a large antigen or several large antigens, one that will instead use portions of many different antigens that you know are recognized by people of many different backgrounds," Fulkerson says. "And by doing this you can make a vaccine that will drive a strong immune response in people of any genetic makeup. I think their approach to antigen discovery is absolutely spectacular. Some of the most interesting results we've seen have come out of the Lewinsohns' work."

OHSU sees the relationship with Aeras as a promising opportunity for continued growth in the future. "Our hope is that as new antigens and/or antigenic epitopes are identified by the Lewinsohns, Aeras will continue to be an exceptional development partner," says Watson.

Scanning for Survival: Portable Head Scanner Makes Time-Critical Injury Diagnosis Possible

Baylor College of Medicine,
Baylor University,
Drexel University,
University of Pennsylvania

About 25 years ago, Alok Sharma, M.D., watched an episode of the "Star Trek" science fiction television series that featured a USS Enterprise crew member having his injured head examined with a hand-held device. Sharma thought this concept was interesting, but not something that would ever evolve beyond the science fiction realm. But Sharma was wrong: He was recently involved in a trial of such equipment at Lokmanya Tilak Medical General Hospital (Sion Hospital) in Mumbai, India, where he serves as chief neurosurgeon.

Known as the Infrascanner™, the device tested by Sharma and his team detects intracranial hematomas—blood clots on the brain's surface that result from traumatic brain injury. Computer-aided tomography (CAT) scanners are viewed as state-of-the-art technology for diagnosing brain hematomas, yet many hospitals—particularly in developing countries—do not have this equipment in place. Other facilities have only a limited number of units, and, in turn, delayed diagnosis of some patients. However, time is of the essence in intracranial hematoma cases, as outcomes have been found to be significantly better if treatment begins within one hour after head trauma has occurred. Left undetected or detected too late, intracranial hematomas can expand, compressing the brain and resulting in death. Even if death does not occur, brain function can be compromised by an intracranial hematoma of any size.

Wanted: Non-Invasive Diagnosis

Development of the Infrascanner™ began as a collaborative effort by Britton Chance, Ph.D., Sc.D. (Cantab.), M.D. (Hon), a professor emeritus of biophysics, physical chemistry and radiologic physics at the University of Pennsylvania, and Claudia S. Robertson, M.D., a leading neurosurgeon in the Department of Neurology at Baylor College of Medicine, Houston. Robertson was seeking a non-invasive means of identifying brain hematomas. Based on his own extensive research, Chance proposed that beaming near-infrared light at the brain via a hand-held instrument, and subsequently analyzing the light reflected back at the device, could indeed reveal the presence of intracranial hematomas.

"Dr. Chance had a number of workable patents, and Dr. Robertson was the neurologist with the right application," says Stewart Davis, assistant director of Baylor Licensing Group, Baylor College of Medicine's technology transfer arm.

Robertson and her colleagues conducted clinical trials of the device over a period of several months, utilizing it on more than 300 patients. Their study indicated that it could facilitate the detection of hematomas in and around the brain by measuring the differential absorption of near infrared light in brain tissue and/or the three layers of membranes between the brain and the spinal cord.

Scratching an Entrepreneurial Itch

In 2002, Chance was approached by Baruch Ben Dor, Sc.D., a medical optics specialist and acquaintance who had worked as a CEO and was anxious to start a company of his own. Ben Dor spent several learning about Chance's technologies to determine which of the professor's intellectual properties he might develop into a commercial product. "I chose the brain scanner because I saw it as the most mature option in terms of its ability to get to market, and also because it had strong potential to address the

need for a cost-effective, efficient means of closing the neurological window in brain injury cases—particularly in environments where a CAT scan isn't even an option," Ben Dor explains. He adds that the latter include not only health care facilities, but ambulances and battlefields, among others.

As Chance had formally retired from University of Pennsylvania when the device was developed and tested, he and Robertson licensed the technology to InfraScan, the Philadelphia-based company Ben Dor had formed, solely through Baylor Licensing Group. "It seemed like an extremely good fit given Dr. Ben Dor's area of expertise and the potential for multiple commercial applications," notes Davis.

Then came Ben Dor's first obstacle: raising capital for his venture. He wrote a business plan in 2003, but failed to generate the necessary monies. Undeterred, he reviewed the feedback he had received and followed critics' suggestions that he improve the plan and increase the size of his team. To handle the former, he called upon two business students at the University of Pennsylvania's Wharton School, Sandeep Naik and Samonnoi Banerjee. Naik and Banerjee entered the plan in the 2004 Wharton Business Plan competition and won the $20,000 prize. "They got the money, and I got an excellent business plan along with credibility for investors," Ben Dor says.

Meanwhile, to develop the technology further, Ben Dor partnered with Banu Onaral, Ph.D., director of the School of Biomedical Engineering, Science & Health Systems at Drexel University, and her colleagues. Onaral specializes in biomedical signal processing and imaging.

Funded in part by a Phase I Small Business Innovation Research (SBIR) grant from the U.S. Navy, the group embarked on several modifications to the device. Most importantly, Ben Dor explains, the original unit "was scientific, rather than medical," and required the use of "knobs and dials" to manually measure light reflection. "We developed a prototype that runs proprietary software," he continues. "The software does the measuring and automatically adjusts measurements according to an algorithm we devised."

The Infrascanner™ unit itself comprises a sensor and an off-the-shelf, hand-held personal digital assistant (PDA) that runs the proprietary software and operates on the Windows Mobile platform. Like the device developed in Chance's laboratory, the device relies on the differential light absorption of the injured versus the non-injured part of the brain. A healthy, normal brain displays light absorption that is symmetrical in the right and left hemispheres. However, when there is internal bleeding, the higher concentration of hemoglobin present results in a greater absorbance of light and commensurate reduction in the reflected component. This difference is detected by the unit's sensor component, which is placed symmetrically on the skull lobes.

By using the principle of diffused optical tomography, the Infrascanner™, via the proprietary software, converts the differential optical data into interpretable results. Communication between the sensor and PDA components occurs via the Bluetooth™ wireless protocol.

"Dr. Chance had a number of workable patents, and Dr. Robertson was the neurologist with the right application..."

— Stewart Davis, Baylor College of Medicine, Baylor Licensing Group

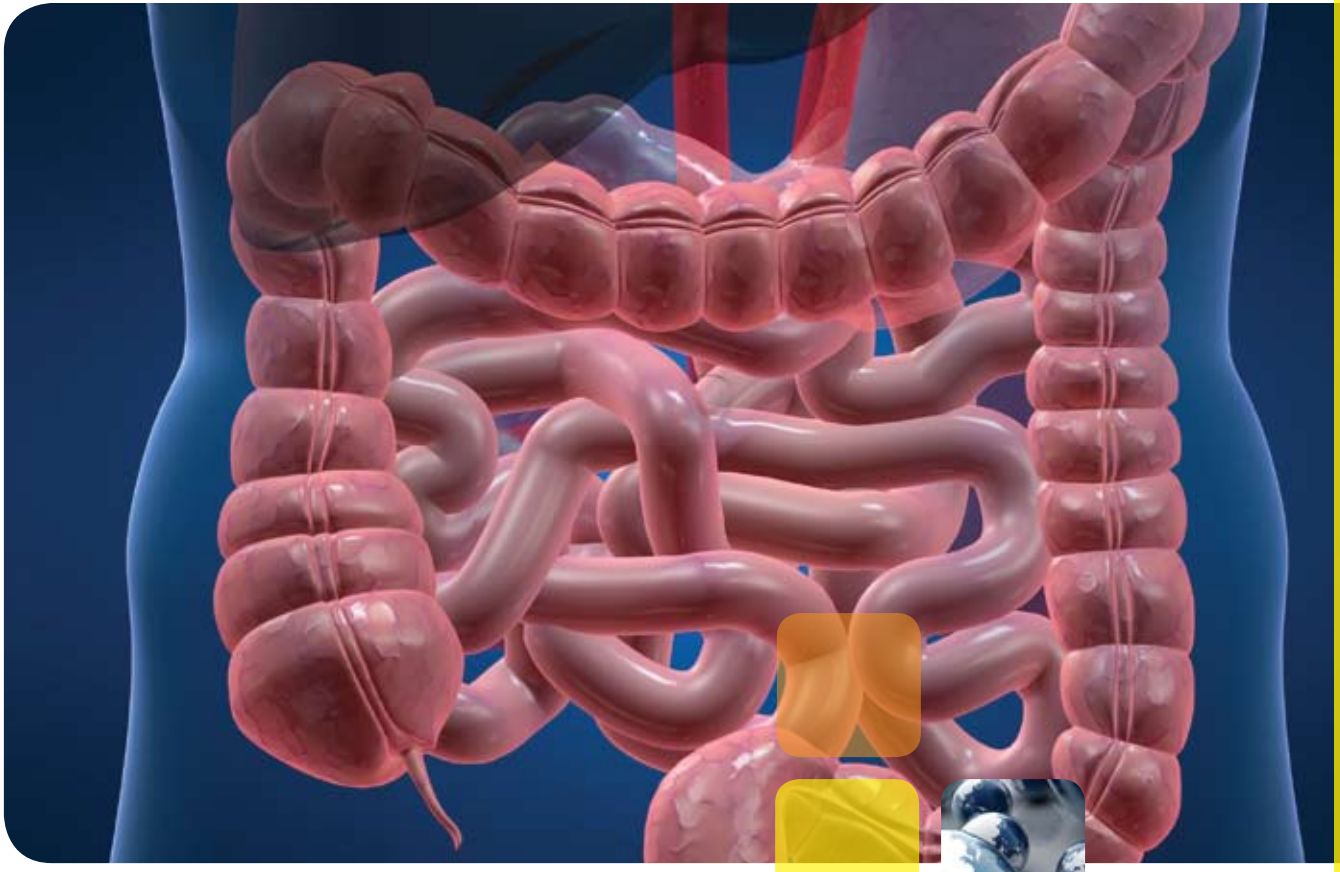
Three months after Naik and Banerjee won the business plan competition in April 2004, InfraScan incorporated and before the summer was over, the team received a $50,000 pilot investment from BioAdvance, the biotechnology greenhouse of Southeastern Pennsylvania, to fund the conduction of due diligence on InfraScan's business plan.

In January 2005, BioAdvance awarded InfraScan, Inc. an additional $450,000. The U.S. Navy and Army have also recognized the relevance of deploying Infrascanner™ technology in combat operations, providing $1.1 million in grants. InfraScan has since received several other grants, including $100,000 from a U.S. Army SBIR and $150,000 from the National Institutes of Health (NIH), and has secured additional investments from Ben Franklin Technology Partners of Southeastern Pennsylvania and the Philadelphia Industrial Development Corp.

A number of studies of the Infrascanner™ have since been conducted. A pilot human clinical study conducted on 305 patients at the Baylor College of Medicine demonstrated high sensitivity for detecting bleeding in the brain and for rapidly identifying the onset of delayed hematomas. Equally positive outcomes have been revealed in a subsequent 400-patient multi-hospital study, as well as a limited study by the U.S. Army and a trial of the device by Sharma at Lokmanya Tilak Medical General Hospital.

In late 2008, InfraScan received the CE Mark, or European marketing clearance, for the device, certifying that it meets European Union health, safety and environmental requirements. The company has since signed its first distributors in the United Kingdom, Spain, Israel, India and Africa. Ben Dor is now awaiting FDA clearance to market the device in the U.S.

"Meanwhile, we are leveraging the fact that we can sell the device not just in Europe, but in undeveloped countries, where other scanning methods are not readily available," Ben Dor concludes. "The market need and the benefits are clear."



3-D Virtual Colonoscopies—Changing Attitudes, Reducing Colorectal Cancer

Stony Brook University

Colorectal cancer is a leading cause of cancer-related deaths worldwide and claims about 677,000 men and women annually, according to the World Health Organization. This cancer burden can be decreased if cases are detected and treated early. Unfortunately, most individuals over 50 avoid the unpleasant and invasive tests that can screen for colorectal cancer or precancerous growths—until now.

A new 3-D Virtual Colonoscopy, also known as computed tomography (CT) colonography, is changing the way people view colorectal screening. It is expected to become more commonly used than a conventional optical colonoscopy thanks to its non-invasive nature. The procedure takes less than 15 minutes and typically requires the patient to drink a contrast solution, which eliminates the need for a harsh purgative prior to the scanning. The patient, without being sedated and after a small tube is inserted in the rectum to inflate the colon with CO_2, lays on his/her back and stomach while a CT scan takes pictures of the abdomen and pelvis in several seconds.

This fast, safe and cost effective procedure is based on patented diagnostic 3-D imaging software, techniques and a computer system developed by a Stony Brook University research team led by its inventor, Arie E. Kaufman, a Distinguished Professor and Chairman of the Department of Computer Science who pioneered the field of "volumetric representation." Unlike an ordinary 2-D computer image, a 3-D volumetric representation is a stack of 2-D images laid on top of each other forming a continuous 3-D space. Development of volumetric representation, which was funded by the National Science Foundation, has led to a number of advances in software for graphics display and graphics acceleration hardware.

In the case of the 3-D Virtual Colonoscopy, approved for use in the United States by the Food and Drug Administration, this innovative computer graphics technology puts the CT images together into a high quality 3-D computerized image of the colon so a physician can see 100 percent of its surface vs. the estimated 77 percent with a conventional colonoscopy.

After the exam a radiologist can actually "fly through" the patient's virtual colon, from beginning to end, and around all folds, thoroughly searching for polyps that are as small as a few millimeters. By contrast, a conventional colonoscopy using a fiber optic endoscope is invasive and expensive, and requires a day of preparation involving laxatives and usually a day for the procedure since the patient must be sedated. A conventional colonoscopy also carries the risk of perforation of the colon wall and even a small risk of death.

To date, more than 100 potentially lifesaving 3-D Virtual Colonoscopy systems have been used in the United States to screen thousands of patients. In 2008, both Siemens Healthcare of Germany and GE Healthcare of General Electric Company signed non-exclusive licenses for the portfolio of innovations developed by Kaufman and his team.

"By offering the capability to screen lots of people quickly, easily, inexpensively and noninvasively, the virtual colonoscopy can change the way people throughout the world view colorectal screening and start to save thousands of lives worldwide through early detection and treatment," says Kaufman.

Working for a Good Clause: Canadian University Negotiates Global Access Licensing Deal for a Drug Reformulation That Could Save Thousands of Lives

University of British Columbia

Whenever Mommy and Daddy start talking about work, 6-year-old John Paul Wasan is quick to quip, "Oh, no! Not that science thing again!"

But the tedious dinner conversation that Ellen and Kishor Wasan's son is so eager to change is actually about an exciting discovery—the reformulation of a drug called amphotericin B (Amp B) that could save the lives of many little boys—as well as men, women and children around the world. And its journey is filled with all the elements of a good children's story—unsung heroes, Lady Luck and kinship working together to stand up for the underdog and fend off evil intruders.

Only in this tale, the "bad guy" is *Leishmania donovani,* an insidious parasite that invades white blood cells, infiltrates vital organs and can ultimately lead to severe infection and death. And the good guys are the researchers, university staff and students, and licensee of the technology that are working together to ensure that, if the promising new "science thing" that the Wasans are working on pans out, it could impact patients dealing with systemic fungal infections and the more than 350 million people from 88 countries—most of whom are in the developing world—affected by a deadly parasitic disease that causes visceral leishmaniasis.

The Perfect Storm

The story starts, in part, with a small band of idealistic students at the University of British Columbia (UBC) in Vancouver, Canada. In 2005, they formed a chapter of the Universities Allied for Essential Medicines (UAEM), an organization that works with student and faculty groups across the U.S., Europe and Canada to construct new approaches to developing and delivering public health goods.

This fledgling group of approximately 20 students, many of whom were doing graduate work in life sciences and medicine, started its charge by approaching the University-Industry Liaison Office (UILO) at UBC to discuss ways to enhance global access to the university's technologies.

Their timing was impeccable, according to Ian Bell, a technology transfer manager at UBC's UILO, because, as it so happened, the conditions were ripe for developing global access principles—guidelines for how the university provides global access to its technologies—and, eventually putting them into practice with a licensing deal that included a global access clause for Amp B.

"The licensing deal for Amp B was the result of a perfect storm in a way," recalls Bell. "Just as this group was forming on campus, we had an associate director, Barbara Campbell, who was more than willing to champion the cause."

Another stroke of luck, says Bell, was that the university had recently appointed a new president and vice chancellor—one with a keen interest in social justice—Stephen J. Toope, Ph.D., a former international law professor, with a strong human rights and humanities background.

"He was very open and receptive to the ideas," recalls Bell. "It meant that we could undergo a philosophical paradigm shift. We realized that while we couldn't sacrifice deals or shun traditional commercial avenues, we could still look at ways to go beyond that."

Campbell began work with the students to get the go ahead from the president's office before leaving for a new post as associate director of Industry Liaison and Innovation at Dalhousie University in Halifax, Nova Scotia, Canada. After about a year of writing and consultation with industry and university administration, UBC became the first Canadian university to formally adopt global access principles.

(A copy of "Principles for Global Access to UBC Technologies" is available on UBC's Web site at http://www.uilo.ubc.ca/global.asp.)

Family Fortunes

Meanwhile, serendipity was at work in UBC's lab. Kishor and his team had stumbled across something that they had thought was impossible: that Amp B, which he had been working with for more than two decades, could be reformulated from its current intravenous form to one that could be administered orally. This breakthrough would make the drug much more practical for treating two conditions: systemic fungal infections—which often afflict immunosuppressed individuals such as cancer and AIDS patients—and leishmaniasis—which is mostly prevalent in India, Bangladesh, Nepal, Sudan and Brazil, but has cropped up in Mexico and the southern United States in the unsanitary conditions in the aftermath of hurricanes.

"Amp B is the gold standard," says Kishor, "but it can only be given as an injection which is impractical for many people, such as those who live in remote villages. It also has some toxicity issues that means it must be monitored carefully. Since I had been involved in developing the parenteral drug during my graduate work, I was sure an oral form was impossible. ...It sounds like it would be simple, but the science is actually quite complex."

With so much time invested in the drug throughout his career, Kishor was ready to concentrate on other projects. But then, a set of experiments in the Wasan lab using Amp B as a negative control resulted in the discovery of a new way to mix the drug with a lipid—and that put an oral formulation within reach.

The lab data looked so promising, says Kishor, that he knew he had to go back to work on Amp B. However, he needed a formulation specialist on board. That's when Lady Luck stepped in again, only this time in the form of his wife, Ellen, who possesses just the right expertise. (Ellen Wasan, Ph.D., is an adjunct professor on the faculty of pharmaceutical sciences at UBC and on the faculty at the British Columbia Institute of Technology in Vancouver.)

"My wife says, 'Oh no! You aren't dragging me into another one of your projects, are you?'" laughs Kishor. "I'm a pharmacist by training and I had the animal models I needed, but what I didn't have was someone to bounce ideas off of about the best formulations. And there she was, right next to me."

Under the Right Conditions

With the promising results in hand, Kishor contacted the UILO, which was able to negotiate its first tangible licensing deal using the newly developed global access principles.

"Originally, we were all thinking along the traditional commercial path," recalls Bell. "Our initial consultations led us to believe there might be hesitancy from industry in agreeing to these global access principles."

But Amp B was different. Because it was already approved by the FDA and in use in its intravenous form, it was a lower risk technology. But, more importantly, it could be used to treat two conditions each in a separate market, and, thus it was an easier sell. As it turns out, however, it was not difficult to find a licensing company at all, in fact, in yet another twist of fate, the licensing company found UBC.

"I'm slightly embarrassed to say that it was one of our shareholders who introduced us to this opportunity," admits Andrew Rae, president and chief executive officer of iCo Therapeutics, a Vancouver-based reprofiling company focused on redosing or reformulating drugs with clinical history for new and expanded indications. "He had heard about this technology and asked us to go out to the university and have a chat," Rae continues.

That chat eventually resulted in iCo acquiring the worldwide exclusive rights to iCo-009, iCo's oral formulation of Amp B, in May 2008.

In return for the worldwide right to develop and sell the oral formulation in the developed world as a treatment for blood-borne fungal infections, iCo Therapeutics agreed to ensure the availability and accessibility of a suitable formulation to countries in the developing world to treat leishmaniasis.

"This is basically a win-win," says Rae. "The fact that the product really only requires a candy-wrapper lipid and has been tested and approved makes it lower risk and fits our business model. Plus, it is suitable for two noncompeting markets."

Further, says Rae, because one of those markets is the developing world, additional funding for the reformulation may be available from what he calls the super philanthropies, some of which are targeting neglected diseases. But it's not all about money, says Rae, the true value of the product lies in its potential to impact society, and the good will that results.

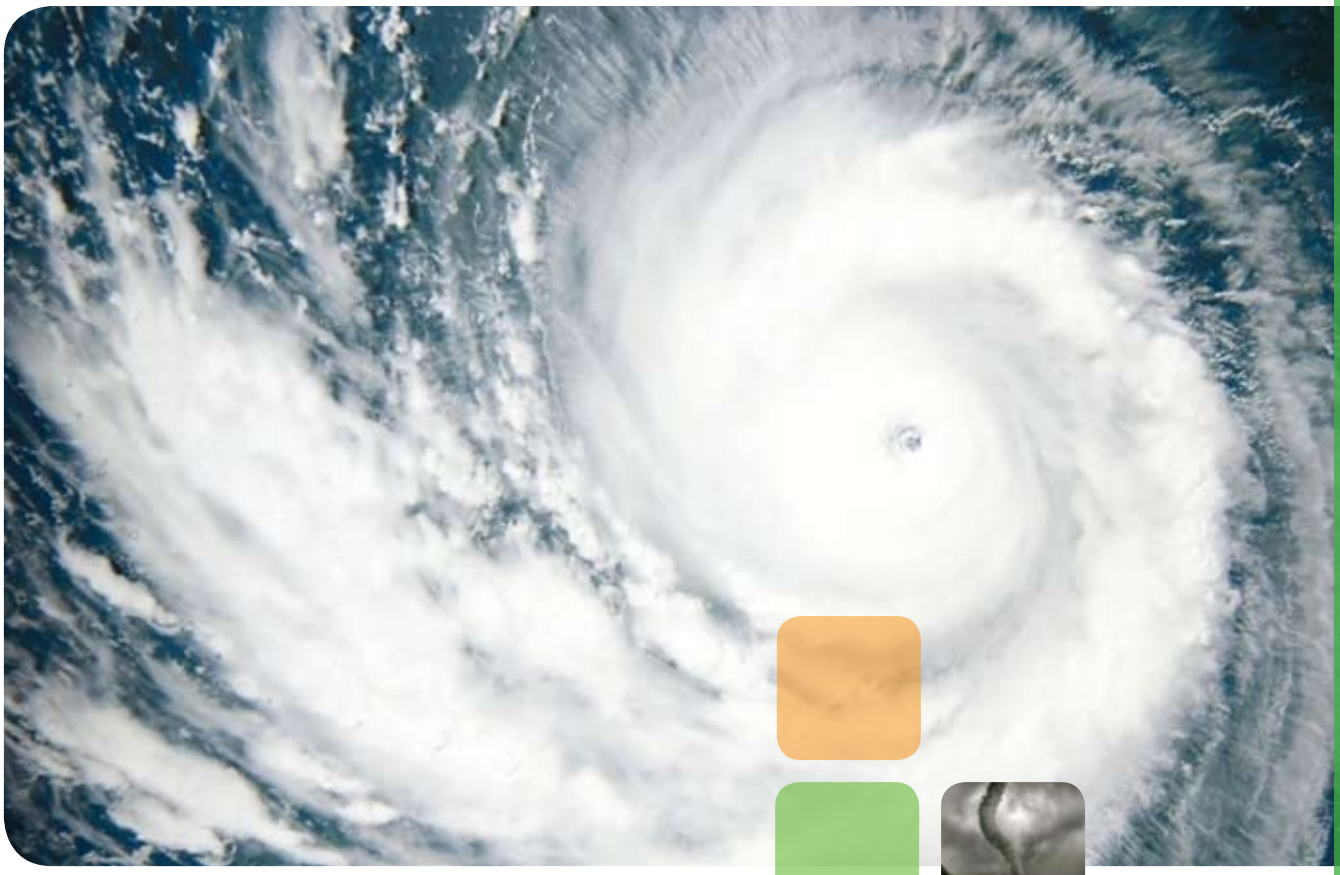
"There is a natural inclination in the health care industry to do well," says Rae. "As health care providers, we are proud to see products improve the quality of life."

A Chance of a Lifetime

And no one is prouder than Kishor, who is quick to point out that Amp B still has a ways to go before actually going to market. (The reformulation is currently undergoing preclinical testing in animal models, where it is showing a greater than 99 percent eradication of leishmaniasis.) However, it is possible to advance the formulation to market on an accelerated development schedule, given the existing safety data on Amp B. Still, Kishor says, he can't help but dream of a day when he can visit his parents' birthplace, India, and help his physician uncle actually administer the drug to some of the many people infected with the parasite in that country.

"I know I have been lucky," says Kishor. "It's such a unique situation that I fell into almost by mistake. But I am embracing the moment because this is such a wonderful opportunity to make a difference."

For now, says Kishor, that's enough to make his story have a happy ending. And maybe, just maybe, give millions of other people a chance to live out their happily ever-afters.



With Extreme Weather Prediction, Time Saves Lives

University College London

On the Tropical Storm Tracker map at University College London's TropicalStormRisk.com, the weather disturbances show up as colored lines—from green for tropical depressions through blue, two yellows, orange and red, to purple for Category 5 hurricanes, cyclones and typhoons.

Tropical depressions, tropical storms, hurricanes, typhoons, cyclones, European windstorms: They're all variations of big wind disturbances and they're all the focus of scientists at Tropical Storm Risk (TSR) and EuroTempest, Ltd., ventures developed from work by Professor Mark Saunders and his fellow climate researchers at the university's Aon Benfield UCL Hazard Research Centre.

Using sophisticated computer models, the University College London (UCL) team works to assess storms' strength, where they will go, when they will get there – and what damage they're likely to cause. While Tropical Storm Risk tracks extreme weather events worldwide, EuroTempest focuses on the destructive wind storms that often sweep onto the European continent off the north Atlantic.

Advance Warning

"Time saves lives," says Michael Arnott, Senior Business Manager at University College London's Technology Transfer Office. "For specific weather events, these ventures can predict extreme weather behavior up to five days in advance. This can warn people to evacuate and it can alert governments and relief organizations to mobilize medical and food supplies.

"Even when there are shelters, people need to know to go to them."

A case in point: Storm Tracker warnings about Cyclone Sidr, which drove off the Indian Ocean onto the coast of Bangladesh in November of 2007. Sidr was the most powerful storm to affect Bangladesh since a cyclone in 1991 killed 140,000 people.

Sidr left millions homeless but TSR warnings helped the Bangladeshi government plan mass evacuations and keep casualties at around 3,500, a fact praised by Bangladeshi officials. "The UCL tropical storm tracker played a crucial role the day before Sidr struck," one noted. "The UCL warnings helped save thousands of lives," another added.

It's an ongoing service. Since 2004, TSR has worked in partnership with ReutersAlertNet, a humanitarian news site that distributes real-time TSR alerts for active extreme weather events worldwide.

Modeling is Critical

To arrive at their forecasts, the UCL computer models process input data through proprietary storm assessment and prediction models, correlating factors as diverse as ocean surface temperatures, wind speeds, atmospheric pressures, the intensity of the North Atlantic Oscillation and the variability of the El Niño phenomenon in the Pacific. The basis of the work is weather data drawn from National Oceanic and Atmospheric (NOAA) satellites.

"The value lies in what you do with the data," notes Saunders. "The modeling is critical. We've developed systems that can forecast the intensity of the coming hurricane season, display the path of tropical storms as they develop and move, and anticipate the likelihood of damage they may cause before and after they make landfall."

Tropical Storm Risk is the older of the two projects, an outgrowth of British government-funded research on cyclones in the late-1990s. The Web site, TropicalStormRisk.com was launched in 2000. In 2007, the site received more than 1.6 million hits.

A Commercial Application

The modeling capabilities have an economic role as well as a humanitarian one: In 2008, UCL spun off EuroTempest, Ltd., as a commercial arm for subscribers focusing on windstorms affecting the European continent. The venture has attracted several high-profile insurance clients.

The winds in question are the powerful storms that sweep in off the North Atlantic rather than the hurricanes, typhoons and cyclones that affect the tropics. Services range from five-day warnings of impending significant storms to predictions of aggregate losses that will result from them.

"In Europe," Arnott says, "the greatest insurance losses are due to wind storms. Because the continent is so densely populated, even a mild storm can cause millions of dollars in damages. And, since weather zones vary enormously throughout Europe, the forecasts need to be as localized as possible. If we have an understanding of a client's assets, we can develop a vulnerability curve that predicts its risk from a given event.

"Recently," he adds, "a company was being told to raise a huge amount of funding to cover losses following a big windstorm. We were able to advise – accurately – that only a tenth of that amount needed to be tied up. This capability can mean significant savings for the companies and more rapidly settled claims and repaired property for their customers."

Tropical Storm Risk remains based within University College London. But UCL began licensing TSR services to subscribers in 2008, and anticipates the possibility of incorporating the program in the future. Saunders serves as the lead scientist for Tropical Storm Risk and technical director for EuroTempest.

Awards and Capabilities

The Tropical Storm Tracker has proved so useful to insurers that it has won two British insurance industry awards – for "Innovation of the Year" in 2004 and for "Risk Management" in 2006. A statistical analysis published in *Nature* in 2005 concluded that buyers and sellers of reinsurance could improve their returns by more than 30 percent over a period of years by using Tropical Storm Risk forecasts. This model also successfully predicted the active U.S. hurricane season in 2008.

"There are a lot of people forecasting these days," Arnott notes. "What's critical is how far out you can forecast and how accurately you can predict the damage likely to be experienced. TSR consistently has an advantage in lead time. We can usually give an extra day's notice over other systems."

Long-range forecasting, on the other hand, is more art than science—often difficult to predict with precision. When the group releases its forecasts well ahead of the season, it's not the end of the story. They continue to update them on a monthly basis.

The team provides seasonal forecasts for three regions—the North Atlantic (hurricanes), the Northwest Pacific (typhoons) and the Southwest Pacific and Southeast Indian Oceans (cyclones). Although hurricanes attract the attention in the United States, China, Japan and the Philippines actually experience more typhoons than the U.S. does hurricanes.

"This is very satisfying work," Saunders says. "It's particularly pleasing to have researched and developed a product which has helped to save many lives."

Rapid Diagnostic Tests Could Benefit Millions in the Developing World

University of Cambridge

Chlamydia trachomatis ***is an enormous global public health problem—infecting more than 90 million annually in both the developed and developing world.***

As the most prevalent bacterial pathogen causing sexually transmitted disease (STD), chlamydia frequently causes Pelvic Inflammatory Disease (PID) and its long-term consequences, which include chronic pain, ectopic pregnancy and infertility. It also can cause sterility in woman and it is the main cause of blindness in babies in the developing world. The World Health Organization (WHO) recognizes it as a major cause of disability in affected communities in Africa, the Middle East, Central and Southeast Asia.

The infection is difficult to diagnose, with around 70 percent of female carriers and 50 percent of male carriers showing no symptoms. But if detected early, the disease is very easy to treat with one antibiotic pill.

"Now, we would like to successfully implement a two-tiered pricing policy to provide the tests to the developing world at near to manufacturing cost, and work with distributors as well as non-government organizations so the FirstBurst test is applied in settings where the more than 90 million people annually infected by chlamydia can be diagnosed and treated early."

— Helen Lee, Ph.D., University of Cambridge

Can chlamydia be detected early and thus treated? Researchers at the University of Cambridge in the United Kingdom and various funding partners—Wellcome Trust, WHO and National Institutes of Health—believe that it can through rapid diagnostic tests for the chlamydia infection.

Almost 10 years ago a group of industry scientists who worked at a multinational diagnostic company set up the Diagnostics Development Unit at the University of Cambridge. Led by Helen Lee, Ph.D., Associate Professor of Medical Biotechnology, the team's goal was to develop innovative, simple, rapid and inexpensive but high performance tests for the detection of infectious agents in developing countries.

The company "Diagnostics for the Real World" was established in 2002, acquiring rights to the founding technology from Cambridge Enterprise, the University's technology transfer office. The first product to emerge from their research is called FirstBurst, a "dipstick" test that gives results in half an hour. The speed of the diagnostic test enables health care providers to treat patients immediately instead of having them return to a clinic after two or three weeks. It is ideal for use in the developing world as well as in clinical settings in the developed world. FirstBurst received the CE mark from European Union authorities and is scheduled to be presented to the U.S. Food and Drug Administration for approval.

The antibody-based dipstick relies on a patented sensitive visual amplification detection technology platform called the Signal Amplified System (SAS), which provides a strong visual signal that chlamydia is present. Inexpensive, robust and stable, the device is easy to use and non-invasive because it uses self-collected vaginal swabs for women and the first few milliliters of urine for men. Field development work and trials in the Philippines and the United Kingdom proved it to be a more effective than any of the rapid tests currently available when compared to the "gold standard" nucleic acid-based test.

Lee and her colleagues still hold true to their altruistic goal: to develop innovative, simple, rapid and inexpensive tests for the detection of infectious agents in developing countries. They are exploring ways to develop tests that use their patented technology platforms for the detection of hepatitis B virus (HBV), human immunodeficiency virus (HIV) and hepatitis C virus (HCV).

Today, the team also runs Diagnostics for the Real World, a California-based spin-out company that provides a business structure to deliver the much needed diagnostic tests to resource-limited settings in both the developed and developing world. The company is on sound footing because Cambridge Enterprise, the University of Cambridge technology transfer company, and Wellcome Trust, the United Kingdom's largest non-governmental source of funds for biomedical research, collaborated to establish the intellectual property ownership that led to the formation of the spinout in 2002.

"As our corporate shareholders, they have supported us throughout the years, from the development of our platform technologies, to the launch of our first product and on through the design of our business model," said Lee. "Now, we would like to successfully implement a two-tiered pricing policy to provide the tests to the developing world at near to manufacturing cost, and work with distributors as well as non-government organizations so the FirstBurst test is applied in settings where the more than 90 million people annually infected by chlamydia can be diagnosed and treated early."

John C. Herr, Ph.D. Photo courtesy of the University of Virginia Patent Foundation

Home Test Confirms Post-Vasectomy Sterilization

University of Virginia Patent Foundation

Similar to the convenience women have with home pregnancy tests, SpermCheck® Vasectomy allows men to check their post-vasectomy fertility status in the privacy of the home. The device tests sperm in the ejaculate without necessitating a trip to the physician's office or a laboratory with semen samples, as has traditionally been required to confirm sub-fertile sperm levels.

SpermCheck® Vasectomy is one of several products founded on technology developed by John C. Herr, Ph.D., professor, University of Virginia (U.Va.) Department of Cell Biology and director of the U.Va. Center for Research in Contraceptive and Reproductive Health. It is the first immunodiagnostic test to receive FDA clearance for monitoring sperm count after vasectomy.

With the at-home device, the paradigm for post-vasectomy sperm monitoring now shifts from the microscope to a simple, easy to use, highly sensitive, hand-held device that affords privacy and cost savings. "This is particularly important on a global basis where access to post-vasectomy testing is much more difficult," said Edward J. Leary, president and CFO of ContraVac Inc. a U.Va startup company. A number of global organizations, including the World Health Organization, have expressed interest in SpermCheck® Vasectomy for this reason.

"SpermCheck® Vasectomy is the result of many years of basic scientific research coupled with clinical chemistry know-how," said Herr. A 20-year collaboration with Stuart S. Howards, M.D., professor, U.Va. Department of Urology, began with a shared interest in studying the effect of anti-sperm antibodies. In the course of research, Howards pointed out that a simple test for sperm monitoring would be helpful. The challenge, said Herr, was to find a suitable biomarker. The interdisciplinary clinical collaboration included work with Charles J. Flicklinger, M.D., professor emeritus, U.Va. Department of Cell Biology.

The FDA approved SpermCheck® Vasectomy is based on more than a decade of research in Herr's lab on the sperm specific protein SP-10 and its encoding gene (ACRVI). Critical experiments validated that the SP-10 protein was useful in sperm detection and quantification. The work included efforts to develop immunoreagents (monoclonal antibodies) to bind with and detect SP-10 protein so it could be quantified. A correlation was found between the concentration of SP-10 and the concentration of sperm.

SP-10 is very soluble and highly expressed, making it an ideal target for diagnostic testing. SpermCheck® Vasectomy uses monoclonal antibodies that bind specifically to the SP-10 protein to detect as little as a few nanograms of SP-10 protein present in a sample.

Calibrated to detect extremely low levels of sperm, the portable device enables a man to determine the appropriate time at which to discontinue the use of other forms of contraception. SpermCheck® Vasectomy will return accurate results indicating fertile or infertile levels seven minutes after the semen sample is added to the device.

Translational research, as was executed in developing SpermCheck® Vasectomy, is essential to bringing new developments in basic-science biomedical research to patients, said Herr. "This was a team effort involving communities of basic and clinical scientists, a start-up biotech company, angel investors, a manufacturing partner, the cooperation of donor subjects in clinical and consumer trials, excellent patent counsel, and exceptional support from the FDA, who gave early advice on the design of clinical studies."

ContraVac and Virginia's Commonwealth Technology Fund funded the research on incorporating antibodies into a platform and recruited patients for clinical and consumer trials. In 2004 ContraVac entered into a strategic partnership granting Princeton BioMeditech Corporation the exclusive worldwide manufacturing rights of the SpermCheck® products. PBM held patents on the diagnostic

platform, which were combined with patents held by the University of Virginia Patent Foundation.

The 17 years from cloning of the ACRVI gene to FDA approval included various levels of support by the National Institutes of Health, CONRAD, United States Agency for International Development, Virginia Commonwealth Technology Research Fund and Schering AG, Berlin (now known as Bayer Schering Pharma). During that time span, Herr, Flickinger and Howards authored more than 60 papers on related topics.

"It's important to appreciate that there needs to be balance between basic funding and translation of discoveries," said Herr. "Careful basic science is the foundation of innovation, and I believe applied research is the responsibility of anyone who receives public money to do basic research." As an added benefit, Herr said it is very exciting to see "something you labored on at the bench to finally have a practical use in society."

On the flip side, Leary is grateful for the partnership agreement with U.Va. "In addition to a research agreement, U.Va. has a sperm donor program to develop and test our products."

Worldwide, approximately two million men undergo vasectomies each year. In the United States one in six men over age 35 has had a vasectomy, making vasectomy among the most popular contraceptive options among married couples, according to the National Institutes of Child Health and Human Development, a division of the National Institutes of Health.

Many studies indicate that a surprising number of men never return to their physician for post-vasectomy sperm testing to confirm the success of their vasectomy. In addition, most men never bother to confirm their sterility status in the years following a vasectomy in order to monitor the occurrence of recanalization (when a vasectomy naturally heals itself resulting in fertility). A study published in the *Journal of Urology,* July 2005, shows that of 43,642 vasectomies, 1 in 238 resulted in failure or recanalization.

"Louis Pasteur said it best—there is no fundamental distinction between pure and applied science, there is only science in the cause of man."

The inconvenience and indignity associated with returning to the physician's office or a laboratory to supply semen samples has created an environment where nearly as many as 35 percent of men do not return for their first post-vasectomy test and 72 percent of men may fail to return for their second test.

SpermCheck® Vasectomy can have a role in improving compliance and improving communication between patients and their physicians following a vasectomy. ContraVac recommends that testing at two different time intervals within the first three months following a vasectomy. Two consecutive negative results provide a high degree of certainty that a man is sterile. In addition, to detect possible recanalization, ContraVac recommends testing six months following a vasectomy with additional testing once per year for the first three years.

Herr said that research know-how developed in the course of creating SpermCheck® Vasectomy will be critical to the development of male birth contraceptive pills. "Availability of a sperm check test which can detect low sperm levels we hope will spur the clinical testing of male contraceptives for which a companion diagnostic test is also needed to monitor when men reach safe sperm levels." He believes there needs to be a seamless continuum between basic discovery, patenting and applied development. "Louis Pasteur said it best—there is no fundamental distinction between pure and applied science, there is only science in the cause of man."

Finding a Path to an Effective Shigellosis Vaccine

University of Maryland

In the worldwide attempt to combat disease, shigellosis may not garner considerable public attention, but its impact is devastating, particularly on the world's poorest children. Annually, the infectious disease causes some 165 million cases of severe dysentery worldwide, including more than a million deaths, according to the World Health Organization.

The group of bacteria involved, called *Shigella,* tends to inflict the most harm in developing regions with poor sanitation, as it is spread through contaminated food or water, as well as person to person. Those who don't die from the diarrhea and severe dysentery, including bloody stool, may be ill for weeks to months. Children in their first few years of life are most vulnerable both to becoming ill and the resulting long-term effects, according to Richard Walker, Ph.D., director of the Enteric Vaccine Initiative at PATH, a nonprofit international health organization. Even children who survive the infection may suffer damage to their intestinal lining and stunted growth, among other effects, says Walker.

Meanwhile, the antibiotics traditionally used to combat the microscopic organisms are becoming less effective, says Walker. "In the developing world, since they use antibiotics so frequently, a lot of pathogens have become resistant to them. *Shigella* is becoming much more resistant."

In 2007, PATH received a $50 million grant from the Bill & Melinda Gates Foundation to help develop two vaccines—one against *Shigella,* and one to combat another diarrheal illness called enterotoxigenic *Escherichia coli* (ETEC). With the funds, PATH is providing vital seed money for some of the most promising vaccine avenues.

According to Walker, ideally, one or two vaccine candidates for each disease will be identified that show sufficient promise to be pursued in Phase 3 trials, by far the most costly phase of vaccine testing. "Our job is to find good (vaccine) ideas and help move them along," he says. "And, if subsequent data warrants, get them to an organization that can actually manufacture (the vaccine) and distribute it."

Shigella Vaccine Hurdles

Shigella, first identified more than 100 years ago by a Japanese scientist named Shiga, is actually a family of bacteria. To date, more than 50 types and subtypes have been identified, falling into four species. For at least 40 years, researchers have been striving to create a live oral *Shigella* vaccine that can be safely tolerated, Walker says. Similar to other live vaccines, such as oral polio, the goal has been to incorporate a weakened—also known as attenuated—strain of the organism involved, thus inducing the body to develop a protective response.

The challenge, in terms of a *Shigella* vaccine, has been providing vaccine recipients with sufficient immunity without also exposing them to the bacteria's toxic side effects, such as diarrhea. The Center for Vaccine Development at the University of Maryland School of Medicine, led by Myron M. Levine, M.D., D.T.P.H., has made some intriguing discoveries toward resolving this challenge.

The center, founded in 1974, has been working for more than a decade to undercut the organism's toxicity while still fostering a sufficient vaccine response. The center also is relatively unique in that it contains not just research labs, but other facilities that enable it to conduct related clinical trials. So when PATH received the Gates funding, Levine's research team was one of the candidates they approached as they solicited requests for proposals.

Immunity vs. Toxicity

Safety has been an overriding concern, since young children will be any vaccine's primary target. How do you reliably disarm this organism, but don't totally disarm it so the body doesn't see it as a danger...and then the body doesn't create protective immune responses?" Levine asked. "You want to get immunity. You want to fool the body."

Levine, a long-time researcher, and his team had several critical breakthroughs as they worked to defuse *Shigella's* toxic elements. One breakthrough occurred in the mid-1990s when the center's researchers identified two enterotoxins in *Shigella flexneri* 2a that led to the onset of watery diarrhea. Once researchers knew those enterotoxins—enterotoxin 1 and enterotoxin 2—were present, the next step was to disarm them. Using genetic engineering, they were able to knock out the genes responsible for telling the organism to make those toxins.

Then the researchers were ready to test a vaccine prototype. In the Phase 1 study, Levine's researchers divided 28 healthy adult volunteers into two groups. Each group received one of two vaccine prototypes, each of which contained a weakened form of *Shigella flexneri* 2a. Levine describes *flexneri* 2a as the single most common *Shigella* culprit and maintains that in the developing world the strain is responsible for 25 to 50 percent of all cases.

During the Phase 1 study, the first group ingested a vaccine prototype that contained the weakened strain, but with the two enterotoxins also knocked out. At the highest dose tested, none of those volunteers experienced any diarrhea and only one developed a brief low-grade fever, according to the findings, published in 2004 in *The Journal of Infectious Diseases.* Of the 14 adults who received a vaccine that still contained the enterotoxins, six developed mild diarrhea.

"The differences were highly, highly significant and indicated that the enterotoxins were really important," says Levine. "And if you knock them out, you get a well-tolerated vaccine strain. But one that still gives immune responses that we consider protective."

Levine's group is not the only one that PATH is working with as they pursue several research avenues toward a *Shigella* solution. Walker states that PATH has a "high level of interest" in the vaccine prototype. "The key problem that Dr. Levine's group has overcome is they've greatly increased the safety of the product," he says.

Taking Concept to Market

In the fall of 2008, PATH signed a licensing agreement with the University of Maryland, Baltimore that included nearly $2.5 million to fund a Phase 2 trial of a vaccine prototype incorporating the *flexneri* 2a strain. Typically, the University of Maryland works with scientists to identify partners for promising research projects, said Elizabeth Hart-Wells, Ph.D., executive director of Commercial Ventures and Intellectual Property at the University of Maryland, Baltimore. "This one was definitely Dr. Levine's doing to find a partner to develop this technology," she says.

The Phase 2 trial, which will involve about 60 volunteers, is slated to launch in 2009. Levine is quick to stress that he is only part of a trio of *Shigella* researchers at the center, with Eileen Barry and Karen Kotloff performing much of the heavy lifting in running the related clinical trials and engineering the vaccine prototypes.

If the *flexneri* 2a prototype continues to look promising, the next step would be to test the vaccine on a trial basis in the developing world, starting with older adults and moving down in age, as the vaccine is assessed for relative safety and effectiveness. "The *flexneri* 2a that we are looking at right now is

the dominant strain of *Shigella* that's a problem in developing countries," Walker said. "So even by itself, it could be a significant vaccine."

Long term, Levine hopes to cast a more protective net. Eventually, he wants to build a *Shigella* vaccine that contains several strains and ideally five significant strains. Levine asserts that if the five-strain vaccine is used broadly in the developing world, it could theoretically guard against 80 to 90 percent of all *Shigella* disease, adding, "Our goal is the definitive broad-spectrum vaccine."

"Our job is to find good (vaccine) ideas and help move them along. And, if subsequent data warrants, get them to somebody that can actually manufacture (the vaccine) and distribute it."

— *Richard Walker, Ph.D., PATH*

You Say Potato, India Says More Income and Less Crop Destruction

Central Potato Research Institute
University of Wisconsin, Madison
Sathguru Management Consultants

Farmers in India and Bangladesh have become increasingly reliant on the potato over the past 50 years. Since the 1960s, Indian farmers have turned to this cash crop in lieu of more traditional crops such as buckwheat, hog millet and foxtail millet because of its high density of food per acre. Likewise, in Bangladesh, potato production has tripled since 1980. The highly nutritious potato provides essential vitamins, minerals and amino acids to the region's rice-dominated diets.

In 2007, 70 percent of India's 1.28 million hectares of potato crops were lost to late blight, a plant disease caused by a fungal pathogen. An estimated $236 million has been lost in India due to late blight infections. In Bangladesh, the disease has attacked 50 percent of potato crops, and an estimated $43 million has been lost. It is not uncommon, in either country, for a farmer's entire crop to be ruined.

Late blight is the best known as the disease behind the Irish Potato Famine of the mid-1800s. It causes potatoes and tomatoes to rot in fields or in storage. An entire crop can be destroyed within one to two weeks under certain conditions. The pathogen can survive from season to season in infected potato tubers, and infected plants produce millions of spores in wet weather conditions. Late blight is a tough disease to control, to say the least.

Farmers in India and Bangladesh attempt to control the disease with pesticides, herbicides and fungicides. These primarily subsistence farmers can barely afford the high price of these chemicals, and, often times, the plants are resistant to them. Bangladeshi farmers apply more than 20 treatments a year. This not only cuts into their profits, but also poses heath and environmental risks to the region.

Solanum bulbocastanum is a wild relative of the potato. It comes equipped with a gene that makes it resistant to late blight infection. Researchers first attempted to fight late blight by cross breeding the resistant variety with common cash crop potatoes, but they were unsuccessful.

However, researchers at the University of Wisconsin-Madison were able to isolate the resistant gene, Rb, and use genetic engineering to insert it into popular U.S. potato varieties.

Sathguru Management Consultants in India coordinated with the university to use this gene technology pro bono and develop resistant cultivators in India and Bangladesh. A global consortium under the United States Agency for International Development's Agricultural Biotechnology Support Project II (ABSPII) was formed for this project, including the University of Wisconsin-Madison, Sathguru, Cornell University, Central Potato Research Institute in India and Bangladesh Agriculture Research Institute.

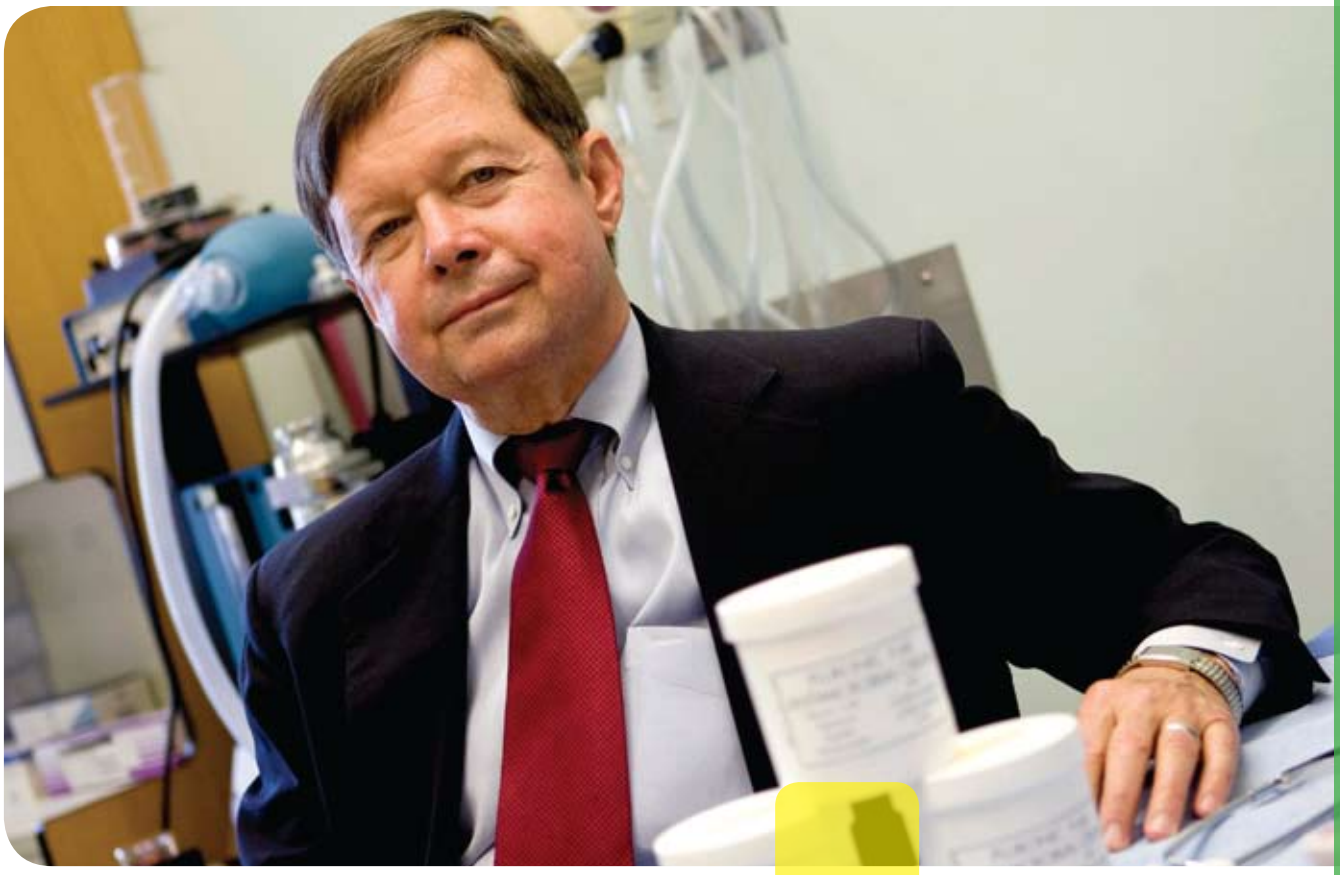
With funding from ABSPII, governments in India and Bangladesh, Cornell, Sathguru and the University of Wisconsin-Madison, researchers have introduced the Rb gene to popular local potato varieties. In India, Kufri Jyothi and Kufri Bahar varieties have been modified and tested, and in Bangladesh, Diamant and Cardinal varieties are being assessed. These field trials judge the Rb-infused varieties' effectiveness against local strains of late blight.

Successful trials have led researchers to believe that soon new products will be available to farmers and become an integral part of pest management systems for late blight.

The new products will be licensed to both public and private enterprises. Commercial farmers will have access to seeds through private companies' seed catalogues, while poorer farmers will receive seeds through local distribution channels. These channels will distribute literature and show audio-visual programs in key Indian languages to educate farmers about the new product, address safety issues and show the benefits of adopting the new technology.

The new product could save farmers between $160 and $200 million in chemicals alone. George Norton of Virginia Tech University, in partnership with national economists in India and Bangladesh, conducted a detailed socio-economic impact assessment that shows farmers using late blight resistant potatoes will double their income. The study also found that labor would decrease by 11 percent and potato yields would increase 25 percent. Chemical applications would also decrease and benefit local health and environment conditions.

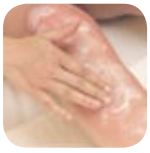
This international effort in technology transfer and development will benefit both the farmers of these countries and consumers, who get a safe, high quality product that is free of chemicals.



George T. Rodeheaver, Ph.D. Photo by Jane Haley

PluroGel Advances Wound Care, Eliminates Infections and Saves Lives

University of Virginia Patent Foundation



PluroGel™, an antimicrobial gel used by the University of Virginia (U.Va.) Health System, is under review by the FDA for commercial approval, a testament to the physicians and patients who have benefited from the product and demanded that the gel be made available beyond the university hospital.

The antimicrobial gel has proven significantly more effective than existing therapies in treating severe burns and chronic wounds, such as diabetic ulcers, pressure ulcers and venous leg ulcers. The topical treatment is unique in that it thickens at high temperatures (such as body temperature) and liquefies at cooler temperatures. As a result, PluroGel effectively delivers healing medication when applied to the body but is easily removed by cool water, making it much less painful to remove than existing therapies.

The U.Va. Patent Foundation named George T. Rodeheaver, Ph.D., professor of biomedical research, U.Va. Department of Plastic Surgery, as the 2008 Edlich-Henderson Inventor of the Year for his work on the revolutionary wound-healing technology and its overriding benefit to society.

Rodeheaver began research on a burn and open wound treatment with his colleagues in the 1970s. The resulting product, PluroGel, has been successfully used to fight infection and heal burn and chronic wounds in more than 2,000 patients with superior results.

“The fact is that in our burn center, we have been able to eliminate infection, which was the leading cause of death 15 years ago. And we have had great success in healing chronic wounds, many of which (with traditional remedies) had not healed for numerous years,” Rodeheaver says.

Because of the level of success achieved within the U.Va. Health System, word quickly spread to neighboring states such as West Virginia, North Carolina and Tennessee. The health system saw an increase in patients who traveled 300-400 miles to get this treatment. In addition, Rodeheaver said he began to receive calls from former U.Va. wound and burn care surgeons he had trained who were frustrated by the lack of access to PluroGel at other hospitals.

“The benefits and success with our patients was so overwhelming that the university got behind the process of encouraging us to make it available to a wider audience than just U.Va.,” says Rodeheaver.

Technology transfer was uncharted territory for Rodeheaver. However, he was able to tap into resources U.Va. had in place to assist faculty members in moving their products from concept to commercialization. With support from the U.Va. Patent Foundation, Rodeheaver and colleague Adam J. Katz, M.D., Department of Plastic Surgery, patented and licensed the technology. Next, the duo turned to Spinner Technologies, a for-profit branch of the Patent Foundation that exists to encourage faculty start-up programs. With the help of Spinner, and with the aid of an M.B.A. student from U.Va Darden School of Business, they completed a business plan and named their company PluroGen Therapeutics.

The PluroGen plan was entered in U.Va Batten Institute’s Business Plan Competition, earning the company $10,000. In addition, they were given a spot in the Darden Progressive Incubator, a program that offers start-ups a team of business school advisors, office space and an intern. With the help of the Darden students, the company began an ambitious marketing campaign to secure funding to cover early start-up expenses.

Finally, Katz and Rodeheaver tapped into the T100 U.Va. Alumni Mentoring program, which provided business experts to help them further refine their

business plan and hire their first CEO and president, Neal Koller. As a result, Rodeheaver says, "PluroGen became much more polished and professional."

The company has been focused on the commercialization of PluroGel for more than five years. "We're still in negotiation with the FDA, but we are very encouraged."

"The process has been a successful litmus test for the entire technology transfer program," he says. "Developing PluroGel with the support of the entire U.Va. system has been the best source to drive the product to success, rather than a corporate entity."

"It's important to remember that the whole motivation was driven by the patient benefit and success we achieved for patient improvement. It was not driven by any commercial incentive. We wanted to make the material available to patients outside of U.Va."

"The technology has had a dramatic impact so far," said Rodeheaver. "We are only in the beginning of benefits of PluroGel and what it can bring to the health care community on a global basis," he says. "In third world countries the availability of an anti-microbial gel for treating burns and chronic wounds will have tremendous impact. Look what it did to the U.Va. Burn Center, which was already at the advanced edge of burn care," he adds. "We thought we were the best, and we still had infections."

Rodeheaver hopes to continue his research on PluroGel with other applications beyond infection. He believes that he is at the beginning of a pipeline of products to enhance healing for the masses. "We can use this unique gel to carry active ingredients such as anti-inflammatory agents or whatever you think the tissue needs to heal—to improve blood flow and cellular repair of damaged tissue, and optimize the healing process."

"Entrepreneurship in particular is something I see as a brand-new adventure," he says. "It's been unique and exciting."

Continued efforts will brings its benefits to patients everywhere, said Marie C. Kerbeshian, Ph.D., executive director of the Patent Foundation.

"It's important to remember that the whole motivation was driven by the patient benefit and success we achieved for patient improvement. It was not driven by any commercial incentive..."

— George T. Rodeheaver, Ph.D., University of Virginia

The Sentricon® Termite Colony Elimination System: Termite Control Without Using Toxic Insecticides

University of Florida

Taking advantage of termites' own biology and behavior, this innovative method of termite control uses small amounts of an insect-specific agent to kill the whole colony, reducing pesticide use by an estimated 6,000 metric tons since it was commercially introduced in 1995.

They live underground, they eat wood, and every year they cause billions of dollars in damage to wooden buildings and other structures worldwide. Subterranean termites. "You can't see them. You can't find them. They are somewhere in the soil," says Nan-Yao Su, Ph.D., professor of Entomology at University of Florida, Fort Lauderdale Research and Education Center. Su invented an environmentally sound treatment for subterranean termites that can eliminate whole termite colonies without the use of conventional insecticides. It is effective against both the common subterranean termite and the Formosan "super termite."

Recognizing the value of Su's research, Dow AgroSciences LLC, Indianapolis, Ind., licensed this pest-control technology and developed the Sentricon® termite colony elimination system, available through authorized pest control operators.

"I thought maybe there is a way to kill the colony. If we can kill the colony, we have a real, final solution."

— Nan-Yao Su, Ph.D., University of Florida

The Sentricon system has found wide acceptance, and Dow AgroSciences has continued to support Su's work. "The Sentricon system represents one of University of Florida's most successful technology transfers," says John Byatt, Assistant Director for Life Sciences in the Office of Technology Licensing at University of Florida, Gainesville. "This is due not only to the commercial success of the technology, but also due to the good working relationship that has developed between the University and Dow AgroSciences."

This approach to termite control uses subterranean termites' own biology and behavior to wipe out a whole colony that is attacking a house or other structure. It is based on a simple concept of monitoring an area for termite activity, and then providing bait that the termites themselves carry back to their colony. This allows control of termites without the use of conventional insecticides.

In commercial use since the mid-1990s, the Sentricon system has protected more than two million structures, including the White House, the Statue of Liberty, Independence Hall, the Alamo, and houses in the French Quarter of New Orleans, as well as buildings throughout the world. In 2000, the Sentricon system won the U.S. government's Presidential Green Chemistry Challenge Award. Also, the bait used in the system was the first to be registered under the U.S. Environmental Protection Agency's Reduced Risk Pesticide Initiative.

"When I was in graduate school studying termites," says Su, "we found out that if you have a house infested with subterranean termites, what you're seeing in your house is really the tip of the iceberg. Underneath [the ground] is the nesting structure, which may stretch up to 300 feet away from your house."

"So you spray a couple of hundred gallons of pesticide and pray, 'Please, termites, stay away from my house.' They will come back. If you spray the soil, you're treating a symptom, you're not treating the disease.

"When I found this out, I said, 'This is ridiculous.' I thought maybe there is a way to kill the colony. If we can kill the colony, we have a real, final solution. My basic idea was to try to use the termite to do the job for us. These termites are social insects. The nest is a network of small nests, connected with tunnels. There are several million termites in there. And sometimes they exchange food with each other."

In a subterranean termite colony, the workers leave the nest and forage for food – wood or other sources of cellulose. They may travel as far as 300 feet underground in their search. When they find wood, they chew it up and bring it back to the nest to feed the other termites in the colony: soldiers and reproductive termites. When a worker termite discovers a food source, it leaves a scent trail as it returns to the colony, so other workers can also find their way to the food.

"So, when I was a student, I thought if we can find some chemical that would not kill them right away when they come and eat, they wouldn't die right away, so they would go back and give the chemical to everybody else. Give them several weeks or several months, maybe that would be enough to spread the poison to the entire colony and wipe it out."

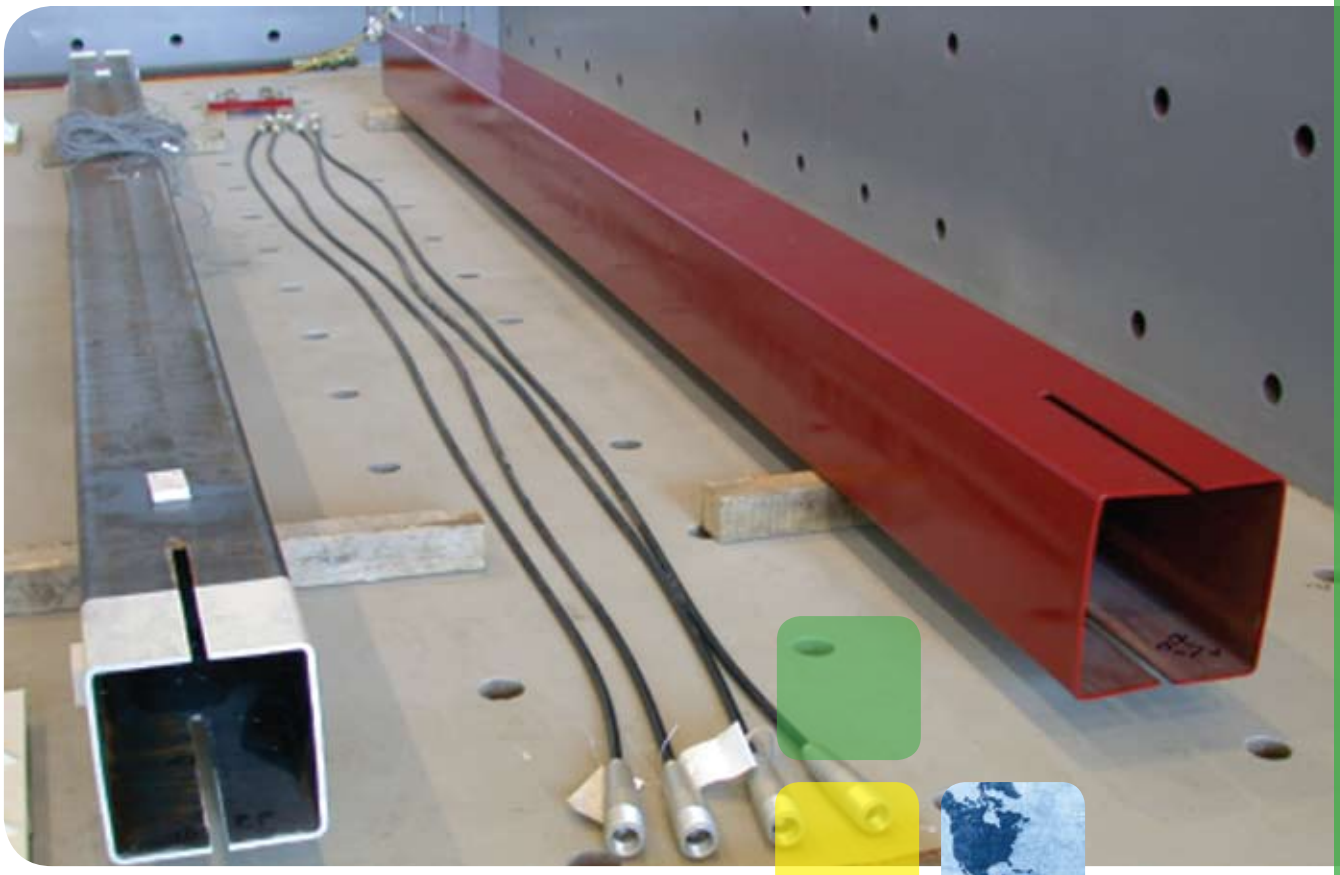
When Su came to the University of Florida in the late 1980s, he contacted companies asking if they had any compounds that would do what he wanted. Dow Chemical responded that it had a chemical, hexaflumuron, that might work. Hexaflumuron is not a typical insecticide. It is a chitin synthesis inhibitor. Chitin is the main component of the exoskeleton (skin) of insects. Hexaflumuron prevents proper formation of chitin. It affects insects, but it is not toxic to most other animals.

"Insects have to molt every now and then, to shed their skin so they can grow. This hexaflumuron keeps them from making a new skin. They will try to molt – the old skin is shedding, but the new skin is not coming out. It takes a while, but it kills them."

Initially, Su put wooden stakes in the ground and monitored them periodically. When he found termites had started eating the stakes, he replaced the stakes with bait made from wood material laced with the hexaflumuron. "When I tried this, it actually worked. I found that I was able to wipe out quite a few colonies of Formosan and native termites." Su refined the process, using slotted plastic cylinders placed in the ground to hold the wood and the bait material.

After the intial research, Dow AgroSciences licensed the technology and developed it into the Sentricon termite colony elimination system. Since then, Dow AgroSciences has supported Su's research. Additional work has included an electronic monitoring technique for the in-ground stations, an above-ground bait station for use where termites are found inside a structure, and use of a more potent, faster-acting chitin inhibitor.

Twelve U.S. patents for Su's inventions have been licensed to Dow AgroSciences, says Byatt. The university also applies for foreign patents in areas where subterranean termites are active and Dow AgroSciences markets termite control products.



Brace Buffers Buildings to Protect People and Profits

École Polytechnique de Montréal, University of Toronto

It's less than two to three inches, but it's an amount big enough to allow buildings and their occupants to avoid a close call. That's the amount of sway allowed by a new self-recentering brace that is designed to let buildings give a little during stress—such as an earthquake—and then right itself to within a few millimeters of its starting position.

Keeping Profits and People Safe

The technology, which is the brainchild of civil engineering professors Robert Tremblay, École Polytechnique de Montréal, and Constantin Christopoulos, University of Toronto, is designed to play a critical role in maintaining a building's structural integrity, not only keeping its occupants safer, but allowing the businesses it houses to remain up and running after a natural disaster. Something that is especially critical for first-responders such as firehouses, hospitals and police departments.

"The technology provides affordable ways of achieving superior performance for structures, including buildings, subjected to extreme loading conditions," explains Didier Leconte, manager, business development, sciences and engineering at Univalor in Montréal, Quebec, Canada. "For example, those induced by earthquakes, wind storms or explosions, thus saving lives and protecting infrastructures."

Bracings are regularly used to support buildings and help them absorb energy. They are structural elements set diagonally between the floor levels to make structures resist lateral loads and shocks. Current bracings are made from steel; however, this material, when loaded beyond its limit, yields and deforms permanently. The new device, which can be used for new construction or worked into an existing building, is also made from steel but is designed to work a bit like an elastic band to absorb and dissipate some of the energy, says Leconte.

"The tendons in the bracing exert a steady restoring force, a bit like a spring, when a building deforms and puts pressure on it," he explains. "At the end of the earthquake, the spring realigns the building and brings it back to its initial position."

Close Calls on the Way to Market

Interestingly enough, the technology itself had several close calls on its way to market. In fact, its very origin was a simple matter of coincidence.

The researchers, who knew each other during graduate school but had since went separate ways, decided to reconnect over coffee one afternoon. From their café conversation sprung the idea for the new spring.

Aware of the potential of this invention, the researchers filed invention disclosures with their respective universities as soon as the concept was defined. The universities then alerted their commercialization entity—Univalor, which serves several Canadian institutions.

After meeting with the researchers, Univalor staff decided to take over the project and moved swiftly to secure the patents and move the commercialization aspects of the technology forward. Simultaneously, the professors continued testing their invention.

"The researchers actually built a full-scale prototype that was about 29 feet wide and 12 feet high and used bracing that was about the normal scale," explains Leconte. "Then they submitted the model to tremors equivalent to those of a major earthquake."

Meanwhile, the technology was so promising that Univalor continued to work on an international patent, knowing that its market would most likely be the Pacific Rim.

But financing further research was proving tricky. "There came a moment when we had to invest some big money to keep the patent protection going," says Leconte. "It looked like the project was going to die. But the researchers believed so strongly in the technology that they asked to share the costs of prosecution and eventually contributed about $50,000 [Canadian] of their own money."

Set to Shake up the Market

Eventually however, their gamble paid off and Univalor was able to strike a deal with a South Korean company, Dongil Rubber Belt Co. Ltd. (DRB), which agreed to collaboratively develop the technology. The company, which has worldwide distribution channels, also agreed to help finance further testing of the device. The company hopes to start sales this year and to have the first device installed early in 2009 or 2010 at the latest.

But even this industrial partnership happened almost by chance. One of Christopoulos' doctoral students, Hyung-Joon Kim, Ph.D., who worked on the experimental validation of the system while he was a student, mentioned DRB as a potential partner and made first contact. Subsequently, Univalor cultivated a close relationship with DRB, one that was significantly reinforced by a trip to Montréal by three DRB executives and engineers. They visited the laboratories at École Polytechnique and liked what they saw. From there, they explored possible commercialization partnership strategies with Univalor.

"It took us a little while to find the right company to license the technology," says Leconte. "Because the device had not been tested in real-life conditions and it looked like it might take some years to go to market. That made some companies a little skeptical. But based in part on the credibility and reputation of the researchers and the direct link to the company that Dr. Kim provided us with, we were able to eventually find a really good fit."

It remains to be seen, however, if the new bracing will shake up the market, because it is more expensive than the traditional methods. But Leconte thinks that even with a price premium, the market is ripe for a device such as this. Not only are building regulations getting stiffer, but manufacturers and other businesses in high-risk areas realize that investing upfront in the structure could mean avoiding costly downtime later.

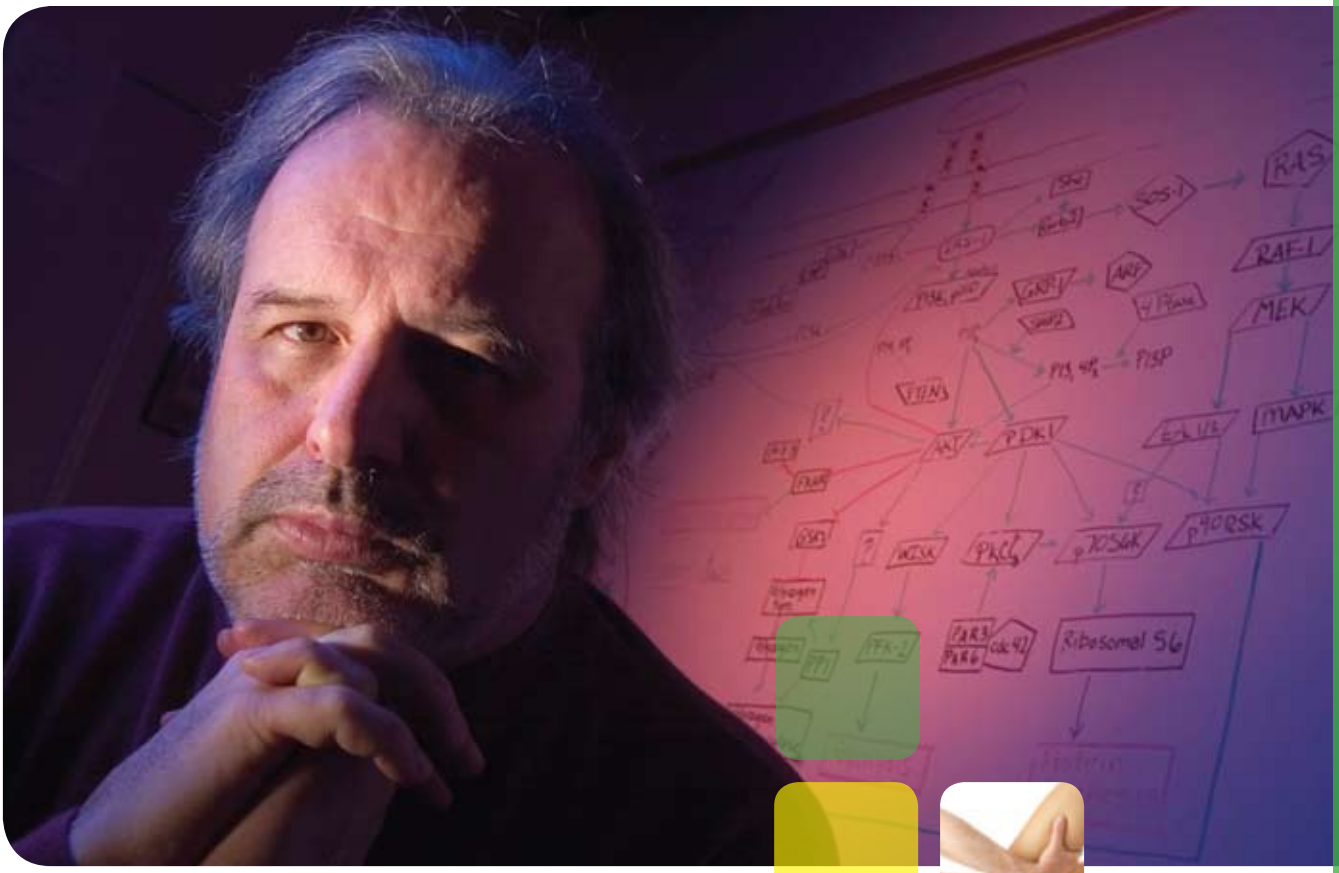
"Countries exposed to earthquakes and other natural disasters are constantly seeking out ways to shelter their buildings from catastrophe," says Leconte. "Through this deal, countries will have access to high-performance protection technology."

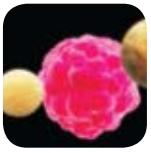
But in addition to helping shepherd a life- and property-saving product to market, for Leconte, there is further satisfaction in knowing that he and the researchers didn't give up.

"The takeaway message in this story," says Leconte, "is to think twice before withdrawing from a potential patent....one day, you just might have a deal."

"It looked like the project was going to die. But the researchers believed so strongly in the technology that they asked to share the costs of prosecution and eventually contributed about $50,000 [Canadian] of their own money."

— Didier Leconte, Univalor





Stopping the Progression of Disorder for Acromegaly Sufferers Shows Additional Implications for Breast and Prostate Cancer Patients

Ohio University

It's easy to hail any cure that relieves the suffering of many, and just as easy to overlook the treatments so crucial to so very few. They call these "orphan drugs" as though these life-saving potions for less than 60,000 or so sufferers have no place in societies with much bigger plagues. But to each individual person so afflicted, "orphan drugs" are life-changing, soul-saving, hope-charged miracles of epic proportions. One such drug is called Somavert and the life-threatening disease it attacks is known as acromegaly.

Acromegaly is a hormonal disorder that results from too much growth hormone (GH) produced by benign tumors on the pituitary gland. If these tumors bloom before the onset of puberty, the victim becomes a giant with myriad health problems. If onset is after puberty, the victim suffers from enlarged limbs and organs, including the heart, and a variety of related health consequences such as diabetes, debilitating arthritis and cardiovascular disease. Other consequences add insult to injury: bony changes can lead to disfigurement, for example, a huge protruding jaw or super-sized hands and feet, while the skin thickens and exudes excessive perspiration.

"Acromegaly is associated with a proven increased mortality rate," says Dr. A.J. van der Lely, a clinician in Rotterdam, Netherlands, who, along with Dr. Peter Trainer in Manchester, England, did most of the original work with the GH antagonist—called Pegvisomant and sold as Somavert by Pfizer—in acromegalic patients.

The discovery of Somavert was a huge advancement in the successful treatment of the disease.

"Currently available treatment modalities for acromegaly consist of surgery, radiotherapy and medication," explains van der Lely. "Unfortunately, surgery cures only 60 percent of patients overall and less than half of patients with macroadenomas, which constitute the majority of patients with acromegaly. The effect of radiotherapy is delayed and variable with poor efficacy and a high incidence of panhypopituitarism. Available medical treatment modalities still leaves at least one third of patients eligible for a more effective medical therapy."

"In conclusion, Pegvisomant is the most effective medical treatment for acromegaly to date," he says.

John Kopchick, Ph.D., Goll-Ohio Professor of Molecular Biology and his research team were the first to discover and characterize the molecular aspects of GH antagonists. "Somavert is the first drug of its kind; the very first large molecule antagonist," he explains.

Kopchick and his team spent 25 years studying growth hormone in mouse models. "We were trying to come up with a more potent agonist, instead we came up with an antagonist—180 degrees from what we were shooting for," he says.

Ohio University and Kopchick were awarded several U.S. and European patents for the discovery. The drug was approved for use in acromegaly patients in 2003.

Kopchick was instrumental in founding a company, called Sensus, with Rick Hawkins who served as chairman and has since founded an unrelated new company called LabNow. Sensus has since been sold to Pfizer which now distributes and markets Somavert.

"Patients immediately feel better after using Somavert. The letters have poured in from patients and their family members lauding both physical and psychological changes from using Somavert. It's very satisfying to make a difference in their lives," says Hawkins.

Hawkins points out that the drug will not reverse bony changes that have already formed, but that it does stop the progression of such changes. "It stops the production of (insulin-like growth factor 1) IGF-1 and normalizes patients," he says.

As it turns out, Somavert may not be an orphan drug for long. "There is big indication for the drug in the treatment of breast and prostate cancer," says Hawkins.

van der Lely said that the first association between GH and diabetes was made in 1937 in a showing that anterior pituitary extracts precipitated diabetes in dogs and furthered when Campbell (and others) showed that daily injections of highly purified GH made dogs permanently diabetic. Thirty years ago it was shown that diabetic patients present with GH hypersecretion at about the same time the "GH-hypothesis" was launched, suggesting that GH plays an important role in the development of diabetic micro-vascular disease such as retinopathy (damage to the eye's retina).

Increased circulating GH concentrations are believed to stimulate local IGF-1 concentrations in non-liver tissues, for example, in the kidney, blood vessels and the eye. Researchers believe that suppressing the circulating GH levels will minimize the harmful effects on diabetic metabolic aberration and could prevent long-term diabetic complications.

"In this context GHR antagonists are interesting candidates," says van der Lely. "Experimental data suggest that GHR blockade, by the use of GHR antagonists, may present a new concept in the treatment of diabetic renal complications. Future studies are warranted to fully characterize the clinical potential of GHR antagonists as drugs for treatment of diabetic complications in general."

The role of GH in a variety of cancers also points to potential successful treatment by Somavert.

"A series of epidemiological analyses have linked circulating IGF-I concentrations, or IGF-I/IGFBP-3 ratios, with the risk of developing several different types of cancer, including prostate, breast and colon cancer," explains van der Lely. "With respect to modulating tumor growth once neoplastic transformation has occurred, numerous pre-clinical studies have defined IGF-I as potent growth factor for dozens of different tumor types."

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— Rick Hawkins, LabNow

Reports of colonic cancer in patients with acromegaly have been increasing in frequency. van der Lely says several experiments have been performed with Pegvisomant using a variety of colon cancer models. In one study, Pegvisomant therapy reduced the volume and weight of xenografted COLO 205 tumors by 39 percent and 44 percent respectively as compared to untreated animals. In a model designed to look at colon cancer hepatic metastases, Pegvisomant was found to be an effective therapy and the combination of Pegvisomant and the commonly used Topoisomerase 1 inhibitor, Irinotecan, was found superior to either therapy alone. The growth of several breast cancer cell lines, including both estrogen receptor positive and negative representatives (T-47D, MCF-7 and MDA-MB-231) has been reported to be reduced by 42-62 percent of that observed in control animals.

"In a nutshell, there is a big indication that Somavert can successfully treat breast, colon and prostate cancers because it works in animals," says Kopchick.

Hawkins says it took eight long and trying years to get Somavert past the various logistical and regulatory obstacles and out to acromegaly patients who so desperately needed it. Beyond improving lives in this relatively small group, this "orphan drug" has cleared the way to potentially save millions of others afflicted with diabetes and cancers. "Somavert has already been thoroughly tested for safety and cleared for human use," says Hawkins." That could speed relief to cancer and diabetes patients who need help now."

Arsenic Removal: Fixing Drinking Water for Millions

Lehigh University

It certainly seemed like a good idea in the 1970s to improve the health of millions of people in India and Bangladesh by replacing their reliance on polluted river waters with access to small-tube wells. By drawing clean water from underground aquifers UNICEF, World Bank and Indian and Bangladeshi officials hoped to reduce the diarrhea, dysentery, cholera and hepatitis that were constants of life in the Gangetic Delta. And it worked – Bangladesh saw its infant mortality rate, one of the highest in the world, cut in half.

But by the 1990s, it was clear there was an unwelcome trade-off: A fifth of the eight million wells in place by then were contaminated by arsenic. Today, says the World Health Organization, tens of millions of people in Bangladesh and the eastern Indian state of West Bengal are being poisoned by drinking water laden with toxic levels of arsenic.

"We're used to thinking of contaminated water as a man-made problem but arsenic is a natural contaminant of groundwater found throughout the Earth's crust, including in the United States," says Arup K. SenGupta, PhD, a Lehigh University professor whose career has focused on removing trace contaminants from water. "In some places arsenic levels are quite high, and it's become a very serious public health problem."

Compared to the World Health Organization's acceptable standard of 10 parts per billion (ppb) of arsenic to water, 46 percent of Bangladeshi wells are above that level and 27 percent are above 50 ppb. It is, a WHO scientist said in 2000, "the largest mass poisoning of a population in history."

"A similar crisis has since emerged in Cambodia, Laos and Vietnam," notes Tom Meischeid, Interim Director of Lehigh University's Office of Technology Transfer. "It's a case in which research in a university setting can be translated into potential relief for entire populations."

SenGupta, P.C. Rossin Professor of Civil and Environmental Engineering and of Chemical Engineering at Lehigh, has found a novel way to impregnate tiny polymeric beads, known as anion exchange resins, with ferric hydroxide nanoparticles to create a safe, effective mechanism for separating arsenic from the water in wells and public water supplies. The technique is the basis of LayneRTTM, an advanced filtering medium manufactured by Northborough, MA-based SolmeteX®, Inc.

Chronic, Long-term Effects

Unlike its "Arsenic and Old Lace" image, arsenic poisoning doesn't automatically lead to one's keeling over and expiring on the spot. Individuals' responses to it can vary – some people do have acute reactions that include nausea, heart failure and death within a few hours and some can tolerate large doses without ill effect. For most, arsenic poisoning is a matter of chronic, long-term, possibly fatal diseases – including skin, lung, bladder and kidney cancers. Studies have linked arsenic to cardiovascular disease and Type II diabetes. Hyperkeratosis – blotchy thickenings and changes in pigmentation of the skin – are common. It's an ingestion issue. Arsenic-laden water is safe to use for bathing and laundry.

"Arsenic is found in drinking water in more than 70 countries, from Argentina to Taiwan, but its presence varies from region to region and even from well to well," SenGupta says. "It's a severe regional problem in eastern India, Bangladesh and southeast Asia."

In the United States, arsenic levels are not as toxic as in other regions but a 2006 Environmental Protection Agency tightening of acceptable levels from 50 ppb to 10 ppb has meant that many areas are now considered to have excessive levels. That's estimated to be the case for more than a third of wells in Arizona and California.

The Iron Factor

SenGupta's involvement in arsenic removal began in the 1990s, when he started collaborating with staff at the Bengal Engineering College in India on developing a sustainable well-based system to filter out the poison. Placed in some 150 villages, the manually operated pumps used granular activated alumina to generate arsenic-reduced water.

The devices yield arsenic levels of less than 20 ppb. For their work, SenGupta and his associates were awarded the 2005 Mondialogo Sustainable Engineering Award by Daimler-Chrysler and UNESCO, the 2007 Grainger Silver Prize Award by the National Academy of Engineering and the 2008 Dhirubhai Ambani Award from the Institution of Chemical Engineers in the United Kingdom.

In his laboratory at Lehigh, SenGupta focused on other filtering substances. He saw iron oxide nanoparticles as an excellent medium for arsenic separation – but one that clumps and clogs the filter column when water is run through it. He thought it should be possible to disperse ferric oxide through a substrate base to achieve a stable structure.

The Massachusetts-based SolmeteX, Inc., had been focused on remediation of arsenic in industrial wastes when the EPA announced plans in 2001 to lower the acceptable levels for drinking water in the United States as of 2006, notes SolmeteX CEO Owen Boyd. The company began looking – with little success – for a technology that would do that when, in 2003, Boyd and his team came across accounts of SenGupta's work.

"We talked to him on the phone," he says. "We drove down to Lehigh that afternoon. And we signed an agreement not long afterwards."

SenGupta worked with doctoral candidate Luis Cumbral at Lehigh for several years before they found a way to place a hybrid ion exchanger ("HAIX") in columns of tiny polymeric ion-exchange beads that could be irreversibly impregnated with hydrated iron oxide nanoparticles.

The LayneRT™ Factor

In 2007, SenGupta and Cumbral received a U.S. patent for their invention, a HAIX dubbed ArsenXnp and produced by SolmeteX. After SolmeteX was acquired by Layne Christensen Company some 18 months later, the technology was further modified and commercialized as LayneRTTM,, a substance offering enhanced performance economically and safely.

"The beauty of Arup's approach," Boyd says, "is that by embedding iron oxide into a polymeric structure, he's created a very durable product that lasts a long time and generates very little waste. They're both positively charged and should repel each other. He figured out how to get a positively charged iron oxide solution onto a positively charge polymer."

Certified by the EPA in early 2009, LayneRT offers a capability for reducing arsenic levels to the U.S. and WHO standards of 10 ppb. By mid-2009, it had been installed in 30 to 40 systems throughout the United States, the largest a 1,500 gallons/minute application in Arizona serving about 4,000 homes.

"We're working with companies in India to try to get products made in that country for use there," Boyd says. "It's not feasible to simply install and maintain these systems from here. It's essential that the materials and services be available locally."

The newest hot spot in the arsenic crisis is Cambodia, Laos and Vietnam, notes Yatin Karpe, Ph.D., Associate Director in Lehigh's Office of Technology Transfer. Working with the Technology Office, in early 2009 SenGupta received a grant from the National Collegiate Inventors and Innovators Alliance to install sustainable arsenic removal systems in Cambodia.

“He’s collaborating with the Institute of Technology of Cambodia to develop arsenic-selective adsorbents, emphasizing indigenous materials available locally,” Karpe says.

SenGupta notes that he and his team spent more than a year developing two grams of HAIX material in the early 2000s, then refined and upscaled the process. Today, there are more than one million pounds in use or available. He believes that the HAIX technology has the potential for applications to separate other heavy metals. He also notes that other companies have started manufacturing similar materials.

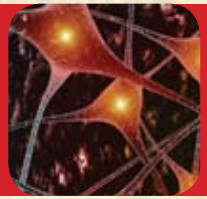
“That’s not necessarily good for business,” he says, “but it’s good to see that science is following up on this.”

Technology Transfer is about more than transferring innovations to local communities. In some cases it is about improving lives of people who live nowhere near the university where the innovation first originated.

The 2009 *Better World Report* celebrates real world examples of technologies that directly impact the health and well being of people everywhere. Here are a few examples of the innovations profiled in this book:

- A program equips health care workers in developing nations with the skills they need to improve quality of care for the communities they serve
- A group of scientists find a creative yet simple way to make life safer for refugee women.
- Groundbreaking HIV medication that is available in developing nations as quality, low cost generics.
- A small nonprofit company with a focus on serving the developing world first
- A truly green biofuel that spares the environment while preserving the global food supply
- An “orphan drug” that truly serves the underserved
- A university that developed global access principles—guidelines for how the university provides global access to its technologies

Read more about the diversity of academic innovation and the world of technology transfer at www.betterworldproject.net.



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