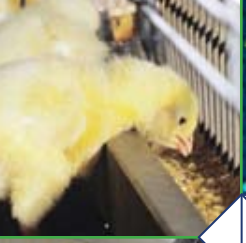
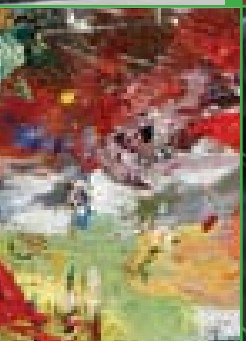


THE BETTER WORLD REPORT *PART ONE*

The Art of Collaboration:

The Relationships That Bring Academic Innovations to the Marketplace






AUTM

2008 Edition
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THE BETTER WORLD REPORT *PART ONE*

The Art of Collaboration:

The Relationships That Bring Academic Innovations to the Marketplace

2008 Edition
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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 third edition of the project focuses on collaborations among universities, governmental agencies, industry and others.

Materials and Support

The Better World Project includes:

- *The Better World Report Part One:* In-depth articles about 25 successful collaborations that have been key in bringing a technology to the market
- *The Better World Report Part Two:* Technology vignettes about academic discoveries realized in the marketplace from the U.S., Canada and abroad
- Better World Project Online: A searchable database to help you find stories of interest to you and your community

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

AUTM Better World Project
111 Deer Lake Road, Suite 100
Deerfield, IL 60015 USA
847/559-0846
betterworld@autm.net
www.betterworldproject.net

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 3,600 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.

Printed in the USA.

ISBN 0-9778444-5-5

AUTM extends its thanks to Nikki Borman for spearheading the 2008 Edition of the Better World Project; all members of the AUTM Board of Trustees for their ideas, feedback and participation, the Better World Project Committee, Kirsten Leute and all of the institutions and companies who told their stories.

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 *Better World Report* were researched and written by Sharyn Alden, Frank Bures, Brian Clark, Mark Crawford, Jill Ladwig, Nicole Resnik, Bill Shepard and Chris Thiede of The Blue Waters Group, a communications consultancy serving the knowledge industry. 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 Report*.

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The 2008 AUTM *Better World Report* you hold is the third in our series of reports making up the Better World Project. This report tells the stories of varied collaborations with partners and others who contribute to the success of academic 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 takes place in a complex ecosystem. Moving academic research into use requires continuous interaction and partnering at a number of levels in the public and private sectors. While patterns emerge, how these patterns may be used, merged or modified reflect a truth about technology transfer and relationships in general; each is different. Rather than explain, we feel the richness of these interactions speaks for itself.

The overall message of the stories comprising the 2008 *Better World Report* is that of the human face of the technology transfer practiced by our members on behalf of their academic institutions. Success in the short term may be measured in the initial relationships constructed through licensing as reported in AUTM's Licensing Activity Surveys. Success in the long term is measured by the success of ongoing relationships, the collaborations that ensue and ultimately the lives that are changed worldwide through products and services made available through those efforts.

The members of AUTM facilitate the movement of research into broad use through the relationships they help establish. The 2008 *Better World Report* highlights a few of these collaborative successes.

Patrick L. Jones, Ph.D.
AUTM President

The Innovation Ecosystem

By Vinod Khosla

The Better World project is fundamentally a story – an amalgamation of the people, institutions, entrepreneurs that are using the power of technology to improve the world around us – from the classroom to the boardroom, from a science project to a company. Like all stories, there will be setbacks, pitfalls, and obstacles, but the examples here prove that the happy ending is well within reach, waiting to be seized.

My focus here is on my own passion - green investing – an area that has seen an explosion of interest in the last few years as we start to come to grips with a climate change problem that is larger than any we've faced before. Meeting the needs of this challenge require an unprecedented coordination of capital, intellect, and pragmatism: and yet we remain confident that we will succeed. To show you how and why, let me share some stories of my own.

Under what set of circumstances would the world's best known academic plant biologist, molecular biologist and DNA sequencing expert, with the help of a malaria drug researcher, start working together on a new biofuels start-up? Chris Somerville, head of the Carnegie Institute of Plant Research at Stanford University, and professor of biological sciences at Stanford, is considered the world's foremost authority in plant biology. George Church, a genetics professor at Harvard Medical School, is widely considered the leading academic scientist in the country having been at the forefront of DNA sequencing, bioinformatics, systems biology and synthetic biology. Jay Keasling is a professor of chemical engineering at University of California, Berkeley, and is considered a leader in synthetic biology. he was named the "Scientist of the Year" by *Discover* magazine in 2006. They all have come together to start LS9, a promising renewable petroleum company based in San Carlos, Calif.

What about a company founded by a professor of chemical and biological engineering at Berkeley, with $40 million in funds from the Gates Foundation to develop artemisinin, used for the treatment of malaria - now transforming itself into a next generation biofuels company?

Professor Jay Keasling founded Amyris and came to us to suggest using their technology for pharmaceuticals – we suggested they look at biofuels and Amyris is now working on a proprietary diesel molecule.

How about a company originally formed casually in response to a bet? In a conversation with professor Frances Arnold of the California Institute of Technology, I suggested that "You can't do that with synthetic biology economically yet." She disagreed, and argued that a couple of graduate students working in the area could design bugs to make fuel – economically. Along with Matthew Peters and Peter Meinhold, also of Caltech, Gevo was formed. As subsequent events have proved – she was right, and the company is now well on its way to developing bio-butanol.

While academics form one very important leg of the stool, a second vital aspect is the industry's ability to attract entrepreneurial talent to run the companies. Today, alternative energy has seized the mantle as the "hot" area, attracting talent from people who want to make money – and make a difference. *Red Herring* magazine noted that business veterans are "joining cleantech startups in droves." It goes on to quote one venture capitalist as noting that "Some of the world's best entrepreneurs and executives are now focused on trying to be part of the cleantech revolution."

We've seen this dynamic in play in our investments - Mitch Mandich, former senior vice president of worldwide sales at Apple Computer, gave up the opportunity to run a $700 million public company in order to run Range Fuels, a biofuels company operating in the back of a pipe-fitting shop. And John Melo left a job as the president of U.S. Fuels Operations at British Petroleum in order to run Amyris Biotechnologies, a leading synthetic biology company.

The third leg of the stool, along with entrepreneurs and academia, is the need for intelligent capital and financial resources. As with the other two areas, people are stepping up to the challenge. Venture capital funding in cleantech has boomed to more than $3 billion in 2007 – up 70 percent from the year before. As recently as five years ago, funding in the area was just $250 million! Luminaries from John Doerr to Richard Branson have gotten involved, pledging

funds, and more importantly, their experience towards building businesses for the long run.

What is happening here? It is a classic example of the innovation ecosystem at work, solving large problems by harnessing the power of ideas fueled by entrepreneurial energy of our scientists, technologists, and entrepreneurs. Nothing signals opportunity than some of the best and brightest people working on solving a problem. And nothing results in more progress than people with very different backgrounds, from very different industries coming together and challenging traditional industry assumptions about what is possible and what is impossible! We find ourselves today at a great vantage point in the renewables industry. The impossible is becoming the improbable – and the improbable is becoming the reasonable. We have seen many debates on the Internet on why we don't have enough land, why the energy balance won't work, why we cannot scale fast enough, and on and on and on. If one follows a linear path, they are almost certainly correct — but these new ideas and approaches are attempting to bypass these limitations, find clever workarounds or alternative paths. Some will work and some will fail, but we suspect the world will be well on its way to meeting the climate change challenges. I'll conclude with my favorite quote, courtesy of Alan Kay, a visionary pioneer in the realm of computer science: "The best way to predict the future is to invent it."

Vinod Khosla was a co-founder of Daisy Systems and founding Chief Executive Officer of Sun Microsystems where he pioneered open systems and commercial reduced instruction set computer (RISC) processors.

Sun was funded by Kleiner Perkins and in 1986 Khosla switched sides and joined Kleiner Perkins Caufield & Byers (KPCB). In 2004, driven by the need for flexibility and a desire to be more experimental, to fund sometimes imprudent "science experiments", and to take on both "for profit" and "social impact" ventures, he formed Khosla Ventures. Khosla Ventures focuses on both traditional venture capital technology investments and clean technology ventures. Social ventures include affordable housing, microfinance and others.

Vinod holds a Bachelor of Technology in Electrical Engineering from the Indian Institute of Technology in New Delhi, a Master's in Biomedical Engineering from Carnegie Mellon University and a Masters of Business Administration from the Stanford Graduate School of Business.

University Researchers, Private Industry Work Together to Fight Tooth Decay

Chapter 1

Marketed by Cadbury Schweppes, RECALDENT™ (CPP-ACP) helps reverse tooth decay by replacing the minerals in the teeth. Developing and manufacturing RECALDENT™ (CPP-ACP) took a cooperative approach that brought together University of Melbourne researchers and private industry.

RECALDENT™ (CPP-ACP) works to strengthen teeth by delivering calcium and phosphate, the building blocks of teeth, to re-mineralize the enamel. Used as an ingredient in sugar-free chewing gum and other products, RECALDENT™ (CPP-ACP) is marketed internationally by Cadbury Schweppes.

The collaboration to develop the RECALDENT™ (CPP-ACP) technology was led by professor Eric Reynolds, head of the School of Dental Science at the University of Melbourne, Victoria, Australia, and included contributions from other areas of the university as well as from government and private industry.

Nature Provides the Solution

The project began in the 1980s, when even though levels of tooth decay in Australia had started to fall due to the introduction of fluoride, the disease was still a major public health problem. So Reynolds and his research team began researching ways to repair teeth by replacing calcium and phosphate ions in the enamel.

The first major obstacle was to find a way to deliver calcium and phosphate to the teeth. "Calcium and phosphate are insoluble," says Reynolds. "Our challenge was to deliver it in a practical way."

For a solution, Reynolds turned to nature. Dairy products were well-established as having dental health benefits, so Reynolds focused his attention on casein, the protein that carries calcium phosphate and is responsible for milk's white color. "We researched what part of casein is responsible for this ability to carry and stabilize calcium phosphate," he explains.

Working with his research team, Reynolds was able to easily and inexpensively isolate the active sequences in casein to form a new complex called CPP-ACP. This complex, which would eventually become RECALDENT™ (CPP-ACP), was found in laboratory and clinical trials to bind to the teeth and provide a reservoir of calcium and phosphate on the surface. Simply, it repaired teeth and reversed tooth decay.

To confirm these results, the team embarked on a two-year population-based study. In the study, 3,000 children were asked to chew sugar-free gum, which had been shown to reduce tooth decay on its own, for 12-24 months. In the double-blind study, some of the children received gum with CPP-ACP and others did not. The study showed that sugar-free gum with CPP-ACP produced 50 percent greater reversals of early signs of decay than did regular sugar-free gum. "It is the only technology apart from fluoride shown to slow development of decay," says Reynolds, "and it could actually repair teeth."

The study was used to build a case for regulatory approval to manufacture and market RECALDENT™ (CPP-ACP).

Working with Unimelb Pty. Ltd., which was the University of Melbourne's technology transfer office at that time, Reynolds applied for a patent for RECALDENT™ (CPP-ACP) and set about looking for a partner to manufacture it on a commercial scale.

Assembling the Team

The role of Melbourne Ventures, which now continues the work of Unimelb, is to build commercial value on the foundations of intellectual property developed at the university. "The major benefit we bring is bridging the divide between research and commercial enterprise," says Charles Day, Ph.D., general manager of Melbourne Ventures. "We tackle the intricacies of licensing, finance, intellectual property, and so forth."

Another role is bringing together a diverse set of skills, from outside the university and from within, to get technology into the marketplace.

A collaboration of a diverse set of skills was exactly what was required to manufacture RECALDENT™ (CPP-ACP), according to Reynolds. The project brought together Reynolds' group from the university's dental school, the chemical engineering department, and Bonlac Foods Ltd., an Australian dairy company.

Assembling an interdisciplinary team like the one assembled for the RECALDENT™ (CPP-ACP) project required funding. Reynolds and the team secured an Industry R&D grant through the Australian government to develop a commercial scale manufacturing process. Reynolds also attracted funding to clinically evaluate the CPP-ACP technology from the National Health and Medical Research Council.

But getting funding for tooth decay research was not easy, according to Reynolds. "The attitude was that fluoride eliminates tooth decay, and the funds go to cancer research and other areas," he recalls. They were able to secure the grants, however, and the project continued.

"For the government to see the quality of the science showed a lot of foresight," Reynolds says.

Above all, Reynolds points out that the interdisciplinary team effort was critical to the success of the project. "Manufacturing on a commercial scale was a completely new thing to us," he notes, adding that "Bonlac had no expertise in biotechnology."

Brought together by the government grant, the dental school and chemical engineering researchers created a form of the RECALDENT™ (CPP-ACP) material that could be produced relatively easily. Bonlac, meanwhile, built a pilot plant and provided guidance to the researchers regarding their needs for production. "It was frontier science," recalled Reynolds. "It was very exciting."

> "The major benefit we bring is bridging the divide between research and commercial enterprise."
>
> *Charles Day, Ph.D., Melbourne Ventures*

Impact on Health, Economics

Though RECALDENT™ (CPP-ACP) was developed several years ago, collaborative efforts are still ongoing to further develop the technology and find new applications for the product. Reynolds is working with dental academics in the United States, Japan and Europe on clinical trials.

These and other efforts have led to the further development of the technology and of several products featuring RECALDENT™ (CPP-ACP), including toothpastes, gum, mouthwash and professional products used by dentists. Global sales of products containing RECALDENT™ (CPP-ACP) have exceeded US$200 million. The most popular RECALDENT™-enhanced product is Trident White gum, which has generated annual sales of over $50 million in the United States. Other brands of gum with RECALDENT™ (CPP-ACP) have been successfully marketed in Mexico, Australia and Japan.

The development of RECALDENT™ (CPP-ACP) has enhanced the research reputation of University of Melbourne. Currently, the university is teaming up with Harvard University in Cambridge, Mass., and the Toronto Dental School on an international benchmarking exercise. Other research efforts to progress the technology are also ongoing. According to Day, it has been "an incredible magnet" to attract other researchers and opportunities to the university.

Reynolds believes the benefits of RECALDENT™ (CPP-ACP) are only beginning to be known. "Clinical data is showing that people who use RECALDENT™ (CPP-ACP) are having fewer cavities," he says.

This not only affects people's health, but also the economics associated with treating decay. RECALDENT™ (CPP-ACP) also has a positive cosmetic effect on the teeth, which can improve people's quality of life.

Reynolds notes, "With people living longer and having significant problems with their teeth, this can have a huge impact on society."

CLA: A Versatile Fatty Acid with Promising Applications

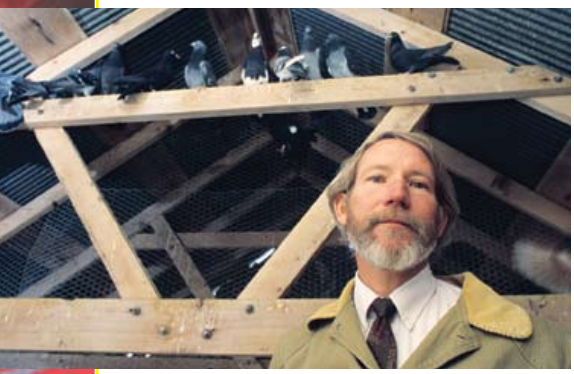
Chapter 2

For two scientists at the University of Wisconsin-Madison, a chance encounter on a running path led to the development of a dietary supplement with numerous health benefits.

Karen Albright, a senior research specialist in the laboratory of Dr. Mike Pariza, produces CLA from linoleic acid.

Photo courtesy of Wolfgang Hoffmann, UW-Madison

The pivotal collaborations that lead to groundbreaking inventions are typically born in the hallways of research institutes or during coffee breaks at scientific conferences. But on a running path? That's where two ambitious scientists with seemingly different interests bumped into one another one day while setting out for their respective daily exercise jaunts on the University of Wisconsin-Madison (UW-Madison) campus.



Poultry scientist Mark Cook extended his studies to examine the role of CLA in wild bird species. He is shown here at the University of Wisconsin-Madison's Arlington Agricultural Research Station with the pigeons he used in some of these trials.

Photo courtesy of Wolfgang Hoffmann, UW-Madison

Mark Cook, Ph.D., refers to himself as "the chicken guy" when recounting that fateful crossing of paths almost 20 years ago. A nutritionist in the department of animal science at UW-Madison, Cook was studying the influence of nutrition on the immune response in animals, particularly birds. At that time his work in chickens was demonstrating how certain immune molecules negatively affect their growth, and recent results indicated that a family of compounds — fatty acids — was involved in this response.

Meanwhile, the research of another UW-Madison scientist, Michael Pariza, Ph.D., a professor in the department of food microbiology and toxicology and director of the University's Food Research Institute, was burgeoning. Like Cook, Pariza cared greatly about fatty acids; in fact, he had established a reputation worldwide for his 1987 discovery of the anticarcinogenic effects of a fatty acid called conjugated linoleic acid (CLA). Pariza's work on CLA had led to a greater understanding of not only its anticarcinogenic properties, but also its effects on body composition and metabolism.

When Pariza stopped Cook to bid him a casual hello on the running path, he told him of his need for laying hen, and Cook realized the value of his molecule in his animal wasting model. Pariza could supply the CLA, and Cook would excute the chicken experiments. Their very first set of experiments resulted in a publication demonstrating the ability of CLA to prevent immune-induced growth suppression in animals. This marked the start of a fruitful collaboration that has since yielded hundreds of worldwide patents involving the use of CLA. From dietary supplements aimed at reducing body fat wasting to therapeutic treatments for autoimmune diseases, the versatile nature of CLA has proven to be valuable.

According to John Hardiman, licensing manager at the Wisconsin Alumni Research Foundation (WARF), the circumstances of how Pariza's and Cook's scientific interests first collided was "a good start to the serendipitous nature of this entire story. We're very

pleased about the commercial success of CLA," he says. "It represents a home run for WARF and we feel it has tremendous future potential."

About CLA

It helps to know something about CLA to better understand how this fatty acid can impact our health. CLA actually refers to a wide range of isomers (compounds with the same composition and molecular weight, but differing structures) in naturally occurring linoleic acid. A member of the omega-6 fatty acid family, linoleic acid is found in beef, dairy products and vegetable oils. One of the first health benefits CLA was found to impart was in weight and body composition management; the molecule both increases lean body mass and decreases fat mass.

CLA's mechanism of action involves the suppression of enzymes that normally help fat cells absorb triglycerides – the most common type of fat, or lipid, in our body. Instead of being taken up by fat cells, triglycerides are diverted to the muscles and used as fuel. CLA also induces the breakdown of fat by stimulating the release of other enzymes linked to that process.

Pariza and Cook are considered two of the world's pioneers of CLA research. Their research has spawned studies that have since demonstrated additional health benefits of CLA including immune system support, cancer reduction, antioxidant protection, and positive inflammatory response.

The Licensing and Manufacturing of CLA

As Pariza and Cook's collaborative animal studies demonstrated convincing results in the realm of body composition and feed efficiency, the potential for commercialization of CLA was clear. Together they approached WARF about patenting CLA for its ability to prevent against body wasting in animals, and once the idea caught on, WARF took an active approach in obtaining licenses. Cook does admit feeling surprised when WARF decided to first license CLA as a dietary supplement, a field of food and nutrition that was in its early stage of development, but now says that "it turned out to be a good move."

One of the first major nutritional companies to get excited about the potential of CLA was EAS. Now owned by Ross Products, a division of Abbott Laboratories, EAS is a leading manufacturer of athletic and sports training dietary supplements. The company recognized the value of CLA as a preventative agent in the phenomenon of immune-induced growth suppression. Bodybuilders and athletes are often susceptible to wasting and loss of muscle mass when they become sick — a phenomenon that Cook first demonstrated in his research on chickens. One of the companies that supplied CLA to EAS, Natural ASA, based in the Netherlands, (and now called Aker Biomarine), contacted WARF in 1995 about licensing opportunities.

"If not for Natural we might have lost our momentum," says Hardiman. "Many big companies looked at CLA but failed to pull the trigger. And some

major American firms obtained rights and then terminated them."

What followed was a succession of large international manufacturing companies requesting the right to license CLA either directly from WARF or from Natural. Currently, in addition to several smaller licenses, Cognis, headquartered in Germany, and Lipid Nutrition, headquartered in the Netherlands, possess licenses to use CLA in dietary supplements and food ingredients. BASF, also in Germany, and Lipid Nutrition secured the rights to manufacture CLA for use in animal nutrition. The original partnership between Natural and the University of Wisconsin/WARF is the reason why CLA is now available worldwide, and supplements containing CLA can be found at nutrition stores and pharmacies and are widely used.

CLA technology developed at the University of Wisconsin was funded primarily by the University's Food Research Institute and gifts to Pariza's and Cook's research program. In its earlier stages, their research was funded by local companies and not-for-profits such as Wisconsin Milk Marketing Board and the American Meat Institute. Natural provided significant financing for early stage research as well.

CLA on the Horizon

The animal studies designed by Cook and Pariza to study the effects of CLA in body composition have since led to another exciting avenue for CLA — the treatment of autoimmune diseases. One autoimmune disease, lupus, which is characterized by inflammation of different organs in the body such as skin and kidneys, is currently being tested for its response to CLA. The fatty acid is believed to be effective in preventing body weight wasting in lupus patients. This is because it plays a role in regulating leukotrienes, inflammatory substances that are released by mast cells during allergic reactions. In individuals with lupus, the inflammatory pathway typically overacts, forming damaging immune complexes that then attack vital organs.

As more research is conducted on the various ways CLA affects our health, more benefits are identified and the significance and versatility of this nutrient may continue to expand. Pariza is pleased with how his early work on the anticarcinogenic effect of CLA in hamburger has led to applications now worthy of annual international research symposiums and that may be just the beginning.

"The role of CLA in controlling body fat remains the main application at this point, although I do think its other positive effects such as those found in the immune system will be important," he says. "While most of the attention first focused on CLA's effect on preserving muscle in bodybuilders, I think it will turn out to have a much greater effect in the general population."

From Diagnostic to Vaccine: The Fight Against Tropical Disease Continues

Chapter 3

The University of Virginia and TechLab are working together to create a vaccine against amebic dysentery, an illness that causes millions of deaths around the globe.

University of Virginia

Each year, more than 3 million children around the world die of diarrhea and other gastrointestinal ailments, primarily in developing countries.

Scientists at the University of Virginia (U.Va.) and TechLab, a medical diagnostic manufacturer based in Blacksburg, Va., are working together to make a dent in the disease and, if all goes well, come up with a vaccine against amebiasis, or amebic dysentery.

The story begins in 1989, when Dr. William Petri, a trombone-playing researcher at U.Va. received a National Institutes of Health (NIH) grant to study a protein on the surface of *Entamoeba histolytica,* a parasite that causes dysentery. Petri is the chief of the Division of Infectious Diseases and International Health at U.Va. in Charlottesville.

Pictured are participants in TechLab's diarrheal illness study conducted in Dhaka, Bangladesh.

Photo courtesy of TechLab

With the help of colleague and long-time friend, Dr. Barbara Mann, they were able to successfully clone the surface protein so it could be used to develop antibodies that would result in an accurate diagnostic test. This test, which has been cleared by the U.S. Food and Drug Administration (FDA), identifies the *E. histolytica* organism in children and adults suffering from diarrhea and dysentery. It was licensed by the U.Va. Patent Foundation to TechLab in 1992.

The company is now collaborating with Petri to develop a low-cost dipstick-like device similar to a home pregnancy test that changes color when used to analyze infected fecal matter. The dipstick, which is being tested in Bangladesh, uses TechLab's diagnostic technology. But it will deliver it in a simpler form, Petri says.

Providing such a low-cost kit would allow the most impoverished nations to have greater access to the technology, thereby allowing for proper diagnosis and treatment of dysentery.

Petri says he believes FDA clearance of the dipstick test may occur by the end of 2008. The current form of the test is a bit more complicated, but can also be used in the field, he says.

Debi Hudgens, a licensing associate at the U.Va. Patent Foundation, calls the collaboration between her school and TechLab "extremely productive."

Joel Herbein, who heads TechLab's parasitology section, says working with Petri is important because he has collaborators all over the world and can set up clinical evaluations in places where gastrointestinal diseases are endemic.

"We want our products to be used in very simple settings to diagnose disease without a lot of supplemental expensive equipment," says Herbein, who earned his Ph.D. in cell biology from Duke University in Durham, N.C. "There is always a push for these tests to become simpler and cheaper, faster to run and more sensitive."

TechLab came into being in 1989, when it was spun out of the Virginia Tech Anaerobe Laboratory in Blacksburg, Va. It was founded by microbiologists Tracy Wilkins and David Lyerly, whose work had focused on *Clostridium difficile,* a bacteria that can also cause gastrointestinal illnesses. The company now has 72 employees and more than 15 products on the market, including the *E. histolytica* test.

Lyerly said TechLab is always trying to push basic research to improve its products.

"We go to the top institutions in the country," he says. "That's why we started the collaboration with U.Va., because it is a top-notch university doing work that dovetails perfectly with what we do here."

A Chance Meeting Leads to Collaboration

Petri and Wilkins crossed paths in 1992 when Petri made a presentation at an American Society of Microbiology chapter meeting held at Virginia Tech.

"Very fortunately for me, Tracy happened to be there," says Petri. "The presentation was about our attempts to make a better diagnostic test for amebiasis. We'd had some limited success doing that, but Tracy and his company were and still are today, the world's experts in how to make diagnostic tests for intestinal infectious diseases."

The pair spoke during the meeting and decided to work together.

"There were no research grants or anything," he recalls. "We agreed to take some of the antibodies that we had made against this parasite and turn it into a diagnostic test that would work and could pass muster at the FDA."

Petri calls the importance of the collaboration between the two "enormous for the field of tropical medicine and amebiasis. There still is no other diagnostic test specifically for *E. histolytica*. Since then, it has gone through three generations of FDA approval, with each one better than the last generation."

Petri says the importance of the collaboration goes well beyond simply having a good diagnostic test.

"We have been able since 1999 to work with a cohort of 500 children in Dhaka, Bangladesh, who have been monitored every other day for diarrheal illness," he says. "With their tests, we have been able to quickly ascertain when the children have diarrhea if it is due to amebiasis, which often leads to malnutrition. And malnutrition in turn is the most common cause of death in children in the developing world."

Before there was a good diagnostic test for amebiasis, Petri says no one knew how common it was or if those who had it were resistant to being reinfected.

"A number of very fundamental questions were unresolved," he says. "If you don't have a good way of reliably diagnosing an infection, there is no way to study it in humans. All this was made possible by the TechLab test."

Petri and his colleagues in Bangladesh learned that amebiasis

is quite common in the children they are following.

"About 40 percent of Bangladeshi children we are following are infected with this parasite every year," he says. "We also discovered that the infection is linked to malnutrition. So if you are malnourished, you are four times more likely to become infected."

Hope for a Vaccine

Petri and his team learned that when the body creates antibodies against this parasite, reinfection is less likely. In other words, they discovered that these intestinal antibodies can lead to immunity to the infection.

"We can use this information to try to rationally develop a vaccine against the infection," he says. "All because of the TechLab test. Without that, none of this work would have gone forward. This has been the perfect collaboration where both parties benefit equally. This has been win-win from the very beginning."

Petri said his current work with TechLab is being supported by the National Institutes of Health through cooperative research agreements that are part of the Vaccine Initiative and with Small Business Technology Transfer program funding.

But the work Petri is most devoted to is the amebiasis vaccine.

Petri said he believes the vaccine will be tested on humans by 2011.

"If I can help achieve a vaccine against amebiasis, I will be overjoyed," he says. "That will be a huge accomplishment by many people working together."

"The biggest winners, I think, are going to be children in the developing world," he says.

"What is coming out of all this is a better way of understanding what contributes to malnutrition in the developing world.

"That is the biggest killer of children in the first five years of life. What we have discovered so far from this work is the contribution of cryptosporidiosis, amebiasis and giardiasis to malnutrition. Having a better way of diagnosing means you have a better way of treating it to try to help prevent malnutrition.

"And it's malnutrition that makes children so susceptible to the other diseases like pneumonia that kill so many of them around the globe."

> "We want our products to be used in very simple settings to diagnose disease without a lot of supplemental expensive equipment..."
>
> *Joel Herbein, Ph.D., TechLab*

Ohio University Researcher Discovers Key to Producing Cheap Hydrogen Fuel

Chapter 4

Ohio University researcher Geri Botte has developed technology that efficiently converts ammonia into hydrogen to produce inexpensive fuel. She and her university have partnered with American Hydrogen Corp. to initially power small generators for homes, offices and eventually cars and space shuttles.

During a 2005 visit by then Congressman Ted Strickland (elected Ohio governor in 2006), Ohio University engineer Gerardine Botte demonstrates ammonia's potential as a fuel by using it to power this toy car.

Photo courtesy of Rick Fatica, Ohio University

What do nuclear submarines and petrochemical plants have in common?

Both use ammonia.

Ben Schafer learned about this colorless, pungent gas during a stint as a submariner — or "bubble head" — in the U.S. Navy. Gerardine Botte, an associate professor of chemical and biomolecular engineering at Ohio University in Athens, became familiar with it from her studies and while working in her native Venezuela.

The two ended up putting their heads together after attending a Denver meeting of the Electrochemical Society in December 2005. Botte was there representing her university's Russ College of Engineering and Technology, while Schafer was attending on behalf of his company, the Hydra Fuel Cell Corp.

The result — less than two years later — was a collaborative private sector-university partnership to develop inexpensive hydrogen from ammonia, while also producing clean wastewater in the process. This partnership led to the establishment of a new company, American Hydrogen Corp. in the Ohio University Innovation Center, which aims to produce inexpensive hydrogen from ammonia and clean wastewater in the process.

Schafer, a computer engineer, was scouting for a cheap source of hydrogen to power small electric generators made by the Hydra Fuel Cell Corp., a subsidiary of American Security Resources Corp. (ASRC).

"I'd been looking for six months," says Schafer. "I was continually being pinged (a submariner term) by people asking me 'where you gonna get the hydrogen?'" he says.

"Like all fuel cell companies, we'd kind of ducked the question and said the problem will get solved eventually," he recalls. "But I was getting tired of the questions."

Schafer knew that nuclear submarines had used ammonia in their reactors' coolant. "We used lots of it and I was exposed to its chemistry back then," says Schafer, a proud bubble head for seven years.

An Auspicious Lunch

Fast forward 30 years to the conference in Denver. Schafer encountered Botte and the two sat down for lunch. It was an auspicious meeting.

"I said I worked for a fuel cell company and was trying to find ways to provide hydrogen," he recalls. "She asked if I'd considered ammonia, and I told her I had, but hadn't found a way to reduce it to nitrogen and hydrogen. She said 'let's talk' and that's how it started. It wasn't long before we were communicating near the speed of a couple of Cray supercomputers."

In a nutshell, Botte had developed a patent-pending ammonia catalytic electrolyzer (ACE) technology to efficiently convert ammonia into hydrogen.

Botte, director of Ohio University's Electrochemical Engineering Research Laboratory came up with the idea of passing ammonia through the electrolyzer after attending a Honda Initiation Grant Conference in Columbus, Ohio, in 2002.

"One of the presenters at the conference said fuel cells are great because you start with clean water, clean energy, and in return you can produce clean water and clean power," she recalls.

"I went back into my lab after that conference and spent the whole night doing calculations and realized that the thermodynamics of the reaction were wonderful. I said I have to work on this right away," she says.

Botte did the initial experiments herself and then got her students involved.

"In the beginning it was like using a magnifying glass to look at little bubbles of what we have right now, which is a process that produces tons and tons of hydrogen," she says (figuratively speaking).

"I started with an idea and a small piece of paper, which had the potential for a commercial application. And now it has become a company."

Room Temperature

One of the things Schafer liked about Botte's discovery is that it takes place at room temperature and under low pressure, requiring less energy and expense than high-pressure, high-temperature processes.

The cost is also reasonable, too, he says.

"It's not the horse that costs you, it's the feed," Schafer explains. "And in this case, ammonia is inexpensive. A tremendous amount of it goes into the environment as waste and we see that as a tremendous potential for recovery in energy use."

Schafer figures Botte's process involving the ammonia catalytic electrolyzer will be able to process a kilo of hydrogen for $2, far less than the $8 to $10 it costs in today's market. And a kilo of hydrogen, he notes, is the equivalent of one gallon of gas.

Schafer explains, "It's our intention to take the ACE to market in conjunction with our Hydra Fuel Cell products as the first commercial ammonia-to-energy process in the one-to-five kilowatt range.

"We also have the grander dream of really getting the hydrogen economy moving by using ammonia as the feedstock to run stationary fuel cells to supply electricity to sites and also to dispense hydrogen for hydrogen-powered vehicles.

"What you store locally is ammonia and then convert it to hydrogen for your vehicle," he says. "Or you store ammonia in a gas tank and convert it onboard to feed an electric fuel cell."

> "I started with an idea and a small piece of paper, which had the potential for a commercial application. And now it has become a company."
>
> *Gerardine Botte, Ohio University*

Environmental Benefits and Profitable Solutions

The sources of ammonia are wide-ranging, according to Botte.

"There is a lot of ammonia in the waste slurry from animals, for example, and it is a byproduct of plenty of other processes," she says.

But on the drive back from the Columbus conference in 2002 to her Ohio University campus in Athens, she says she had an epiphany.

"I said 'wow,' ammonia from wastewater would be a wonderful source to produce hydrogen because it is abundant and independent of fossil fuels," she says.

"And if I put the wastewater through an electrolyzer. I remove the ammonia waste from the water and produce clean power and clean water," she says. "It is a beautiful picture."

Besides the obvious environmental benefits of removing ammonia from wastewater, there are great benefits for companies that have to dispose of ammonia they use or produce as a byproduct in their manufacturing processes. In some cases, this disposal can be costly, and can require additional time and resources. But now there's an alternative.

Instead of spending money on ammonia disposal, these companies could potentially use the ammonia catalytic electrolyzer to remove ammonia and resell it to companies that can use it to produce hydrogen, or they might even convert it to hydrogen themselves and resell it. Bottom line, it amounts to transforming a costly waste item into a profitable commodity.

"The great thing about this is that it can go so many places. It could drive a car or even be in a shuttle in a mission to Mars in the future," she says.

Botte says the ACE technology dovetailed with other work she had been doing in her lab during the past several years, such as hydrogen storage.

Schafer, who likes to move fast, visited Ohio University not long after the Denver conference. He toured Botte's facilities and went back to his board seeking $50,000 to fund a project to scale up her "lab project" from 250 milliwatts to five watts.

The results, he says, were "impressive."

Fruitful Negotiations = Collaborative Relationship

Ohio University's Technology Transfer Office and ASRC soon entered negotiations to license Botte's technology. As a result, the university had a substantial license package, including up-front payment, minimum annual licensee payments, running royalties for fuel cells and hydrogen production, and a sizable equity stake in ASRC for the Ohio University Foundation. And, just as important, Botte's lab had a two-year, $600,000 sponsored research contract to support her ACE-related research and development project.

At the same time, ASRC created American Hydrogen Corp., which has exclusive worldwide rights to commercialize the technology for hydrogen production and fuel cell

applications, and set up the new company in Athens at the Ohio University Innovation Center, further strengthening the collaborative ties between ASRC and the university.

Robert Malott, associate director for technology commercialization at the university, says gaining equity in ASRC was a key to the deal. In addition to American Hydrogen and Hydra Fuel Cell, ASRC also owns a third company called American Wind Power. ASRC may also make more acquisitions in the energy field, he said.

Malott says the collaboration between the university and ASRC and American Hydrogen Corp. has gone well.

"We liked Ben's demeanor and found him and the others we dealt with to be straightforward and down-to-earth, the kind of people we like to do business with," Malott recalls. "There was no "smoke and mirrors" or any game-playing."

Schafer agrees.

"It's been great dealing with the Ohio University folks," he says. "And their Innovation Center, especially if you are in the early stages of starting up a company, is super. The flexibility is nice and you can't beat the cost in terms of services that are available. It takes a lot of the pain out of being a startup, that's for sure."

Botte, a consultant for American Hydrogen, is pleased, too.

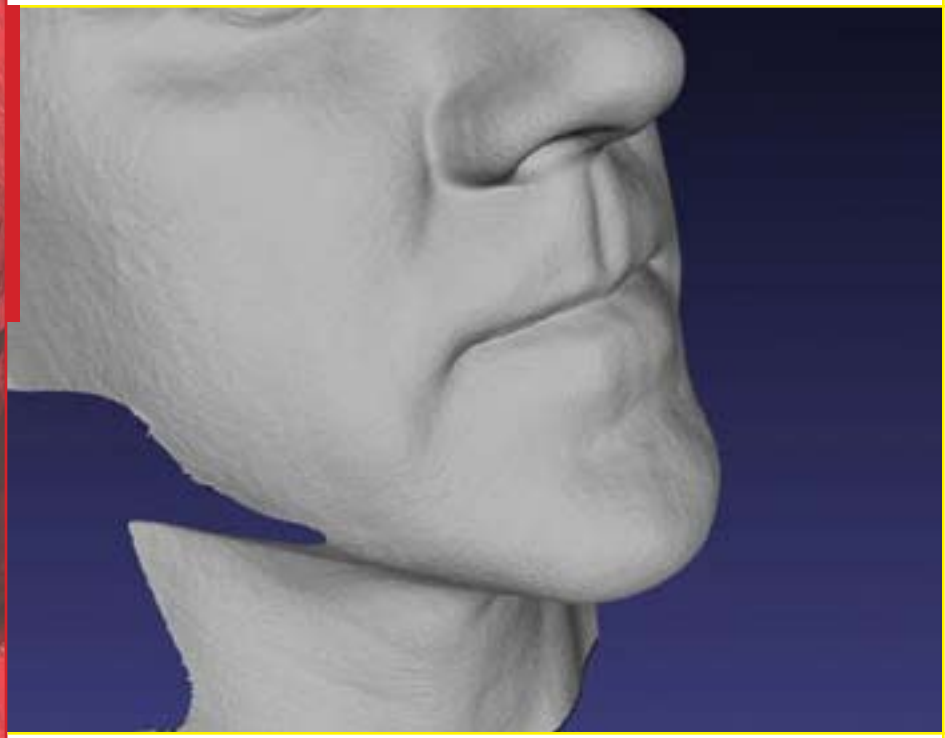
Not only is her future research being solidly funded, but her graduate students are finding work at the fledgling company.

"There is a lot of interaction between their personnel, myself and my students," she says. "And I'm advising them on different market and R&D opportunities for the project.

"I think I will always be a professor," she says. "But I have some ideas for the future of additional things I'd like to start."

Aguru Images Shines New Light on Digital Imaging

Chapter 5



A tale of three technologies on opposite coasts are now the heart of a groundbreaking company.

A five million polygon mesh image, captured by the Aguru Dome.

In the world of academic technology transfer, one contact often leads to another, ultimately resulting in new discoveries that enter the marketplace.

That is the story of Aguru Images, which merged brilliant academic discoveries from universities on opposite sides of the United States — New York University (NYU) and the University of Southern California (USC).

The result is creating a buzz in the computer graphics community because the technology can be used in a variety of applications. They range from making strikingly accurate digital images in motion pictures, videos and computer games to improving renderings by interior, fashion, architectural and industrial designers.

In fact, just about anyone who wants realistic lighting on everything from faces to brushed aluminum to fabrics may be able to benefit from Aguru's technology.

The Virginia-based company now sells equipment and services and will eventually add software and a library of illumination data to its products. Appropriately, one of the meanings of Aguru in the Sanskrit language is light.

Steve Gray, the chief technical officer and executive producer of Vykarian, a Shanghai-based game developer, says Aguru has made a great leap forward.

"It's pretty remarkable what they've done working with NYU and USC," says Gray, who formerly was the executive producer for Electronic Arts' "Lord of the Rings" video games.

This is not a photo, but a photorealistic rendering.

The Right Mix of Technologies

In the computer graphics world, getting textures right is extremely difficult, Gray points out.

"But along came Aguru, working with NYU, which has a scanner that uses a kaleidoscopic array," says Gray. "You can stick anything on it and it basically figures out how the light, including light that is being scattered below the surface, is reflected. That's something."

Next, in conjunction with USC, he notes, Aguru added a dome that is a three-dimensional scanner.

"It essentially takes pictures simultaneously from many different angles," Gray explains. "Then, using image-based modeling techniques, allows you to reconstruct a 3-D model of the thing that was inside the dome. One of the first applications was scanning people's faces and it achieved

really, really high resolution. It uses five million polygons, which is essentially more resolution than can be rendered back with film."

The third component, also from USC, is called the Linear Light Source (the Aguru Scanner). It is a larger type of scanner that captures flat object reflection, the different colors of shine and the surface bumpiness, among other features.

The technologies work together well, Gray says, because the USC dome recreates the subtleties of 3-D shapes and textures for really difficult objects and materials, like the human face, while the NYU and USC scanners capture the properties of countless other materials.

"It's exciting stuff, and it's 99.9 percent photorealistic," Gray says. "It makes it cheaper, faster and unlocks these capabilities for everyone, like small game developers and boutique studio effects studios."

Collaborating With Researchers on Two Coasts

Aguru's story began in 2005, when Saul Orbach was hired by ANGLE Technology Ventures, a publicly traded British firm, as its entrepreneur in residence. Back then, Orbach knew little about computer graphics, kaleidoscopic technologies, properly illuminating textured surfaces or getting the light right when scenes with real actors are meshed with virtual backgrounds.

Nor did he know that the quest for truly photorealistic digital images had long been the holy grail of the three-dimensional computer graphics industry.

In the past two years, however, he has become something of an expert of sorts in the field of virtual lighting — thanks in large part to researchers at NYU's Courant Institute of Mathematical Sciences and USC's Institute for Creative Technologies.

Orbach is modest about what he put together.

> "The goal of our institute is to foster collaboration between academic researchers and the entertainment industry to develop the next generation of simulation and virtual environments."
>
> *Paul Debevec, USC's Institute for Creative Technologies Graphics Lab*

"I'm no scientist," says Orbach, a serial entrepreneur. "When I started out, my job was to find technologies that we could commercialize and turn into a company. So I looked at a lot of things."

Because of his NYU connections — Orbach earned undergraduate and M.B.A. degrees from the university — he met with Robert Fechter, associate director of the NYU Office of Industrial Liaison, who led him to the Courant Institute.

Fechter introduced him to Ken Perlin, a computer science professor, and Jeff Han, a research scientist at Courant. They showed Orbach a variety of computer graphics projects they were working on.

"One was the kaleidoscopic technology that was capturing reflectance data for textured materials," Orbach says. "This was exciting stuff.

"In fact, it was a 'Eureka!' moment," he said. "The existing methodologies for doing the same thing were very complicated. But Ken had come up with a simple, brilliant device with no moving parts that was quick and easy to operate.

"I like simple, innovative solutions to problems that no one has thought of," he said. "This was really cool.

"Ken's device allowed you to capture all angles of illumination. Then you could look them up from his database. His device could capture all those angles in 15 seconds. Learning about that was what started it all."

Appropriately, Perlin was a fan of kaleidoscopes as a child.

"Wasn't everyone?" Perlin asks. "As part of my research, I learned that the kaleidoscope was invented by Sir David Brewster in the early 1800s. It was so wildly successful that it became the symbol of science and progress. It was the iPod or computer of its time."

Prior to this invention, in order to see a surface from multiple points of view you either needed an array of cameras or to mechanically move a single camera to different locations.

"I thought, 'Why not use a tapered kaleidoscope to do the same thing?'" Perlin recalls. "Then I talked to my colleague Jeff Han and we set about to build it."

As part of his due diligence, Orbach says he learned everything he could about the industry and the difficulty of getting realistic lighting on computer-generated images.

"Along the way, I talked to 50 people and companies who were possible users of this technology. I got a good feel for the market, what the applications were, how much and for what price," notes Orbach.

Orbach also met with Paul Debevec, a research associate professor at USC's Institute for Creative Technologies Graphics Lab and a friend of Perlin's who had come up with a complementary technology.

Debevec's Light Stage 2 process was used by Sony Pictures Image Works to create photorealistic digital actors as part of its Academy Award-winning visual effects in "Spider Man 2," the Academy Award-nominated visual effects in "Superman Returns," and most recently "Spider Man 3."

Debevec, who most recently led the development of a Light Stage dome that measures 26 feet in diameter, says his research began in 1999 and is funded by movie studios and digital imaging corporations. The institute's basic research funding came from the U.S. Army.

"The goal of our institute is to foster collaboration between academic researchers and the entertainment industry to develop the next generation of simulation and virtual environments," Debevec explains.

"With Aguru commercializing some of our technologies and pushing them

further forward, that will help meet these goals," he says. "It will allow more people to benefit from these physically based rendering and realistic model acquisition techniques. Aguru is going to take proven technologies, make them more robust, more economical and will adapt and evolve them to better meet the specific needs of the industry. And that will inspire our group to work on the next generation of these technologies."

Making Its Marketplace Debut

Aguru Images was launched in March 2007 with an initial $1 million in financing from ANGLE. NYU licensed its technology to Aguru in exchange for equity and revenue. USC negotiated a similar deal.

By August 2007, Aguru was ready to show its products at the 2007 SIGGRAPH trade show in San Diego. (SIGGRAPH stands for Special Interest Group for Graphics and Interactive Techniques.)

John Sweet, a senior licensing associate at USC's Stevens Institute for Technology Commercialization, calls working with Aguru Images a "pleasure."

"Saul Orbach is an experienced entrepreneur and has assembled a good group of guys," he says. "It's nice to collaborate with people like that who know what they are doing."

Orbach estimates the company will have revenues of between $5 to $7 million in 2008. And after that, who knows?

"As for future applications, we quickly came up with a short list of 15 or 16 that includes online commerce, cosmetics, catalog shopping, medical applications and even military stuff," says Orbach.

"There is no shortage of how this technology could be used," he muses. "The sky's the limit."

Chapter 6

Mixed Reality Creates Powerful Learning Tool

Interactive computer technology from the National University of Singapore creates the next generation of children's books.

Children are captivated by wIzQubes.™

When science fiction author William Gibson introduced the world to the concept of cyberspace in his novel "Neuromancer" in 1984, readers were intrigued by the notion of human beings living immersed in a computer-generated reality. Today, more than 20 years later, the notion of cyberspace and virtual reality are readily understood and even embraced by society.

The Interactive Multimedia Lab at the National University of Singapore is taking this understanding to a new level and stands poised to change the way we live, work, learn and play. By combining technology and creative art, researchers at the lab are developing new software interfaces using "augmented" or mixed reality technology developed at the university's Mixed Reality Lab. The technology is aimed at making machines more natural, more intuitive and easier to use. Mixed reality merges the physical with the virtual worlds to allow users to interact with imaginary or fictional three-dimensional objects as if they were in the real, physical world.

MXR Corp.: A Collaboration of Two Laboratories

Kenny Lew was the NUS intellectual property manager who evaluated and patented the interactive computer technology developed by professor Steven Zhou, director of the Interactive Multimedia Lab, and professor Adrian Cheok, director of the Mixed Reality Lab. After working with the Singapore military to develop training programs using interactive human computer systems, the two researchers worked together to spin out the Mixed Reality Corp. to commercialize related technologies.

Steven Zhou, Ph.D.
founder of MXR Corp.

In the beginning, this new collaborative venture needed critically important funding to get off the ground. NUS Venture Support, which promotes innovation and entrepreneurship within the National University of Singapore community, provided a $40,000 grant that matched $10,000 from Zhou. This grant sustained MXR Corp. through its first year of existence. Thanks to its partnership and support, NUS Venture Support gives fledgling startups like MXR Corp. a strong foundation on which to thrive.

The company's flagship commercial product is wIzQubes™, a virtual, three-dimensional storytelling tool. Zhou and Cheok worked together to develop this brilliant educational toy, which took top honors at the prestigious International Idea2Product Competition in 2004, held in Austin, Texas.

Zhou says he got the idea for wIzQubes on a whim. "I was thinking of a natural and intuitive interface for storytelling," he says. "I happened to

see the foldable story cube of 'Noah's Ark,' and thought that it would be a great experience for kids if the story could be played in three-dimensions using mixed reality by physically manipulating the cubes."

It took three years of hard work and $1,200,000 to develop the technology on which wIzQubes™ is based, but it eventually paid off.

A New Way of Learning

Frequently referred to as the "next generation of children's books," the colorful plastic cubes allow children to actively participate in storytelling and directly engage with fictional characters. In early tests of the toy, children said they enjoyed the magic cubes more than a picture book.

The wIzQubes work with two small cubes, each with images on them. Each cube is made up of smaller plastic cubes connected at various edges. Cheok and Zhou worked together to combine the cube structures with virtual reality software and a digital camera to superimpose computer graphics on the real world, creating an animated version of the story.

A Web camera in one of the cubes captures the image on the cube and software calls up an animated story, which is stored on a CD. The user watches the story unfold on a computer screen that displays the scenes. The technology allows the users not just to view the story in an all-around three-dimensional format, but also to interact with the characters and play an active part in the story by simply manipulating the cubes.

The new medium opens up a new avenue for education. Educational researchers have long studied how children learn, and found they do it best by taking in visual and auditory information that reinforce each other. This unique combination of media increases their understanding of new concepts. Adding a third sense — the sense of physicality — mixed reality provides a new dimension to learning.

"Education has always been an important topic in our everyday lives," says Zhou, who today serves as CEO and director of the company. "The tools of the trade have changed over the times, but interaction has always been necessary to provide children with a better understanding of the topic."

> "Not only are the cubes a fun way for kids to learn, it's a boon to parents and teachers, too, because it is proven to increase the attention span of kids."
>
> *Steven Zhou, Ph.D., MXR Corp.*

Zhou says it's difficult for children to get their minds around topics for which hands-on material is not available. He cites scientific topics such as how dinosaurs once lived, and sociological and historical topics like the ancient Roman city of Pompeii. The wIzQubes product can bridge that gap by providing a physical experience.

"With mixed reality, we bring together the physical and virtual world and allow the user to fully interact

with the virtual contents in physical surroundings," he says. "This in turn allows the user to absorb what is being taught faster, because of the clarity and detailed modeling in three-dimensional graphics and the interaction element thrown into the mix."

Children, Zhou says, "learn by doing, using their hands, and feeling the entire link with the imaginary world."

Not only are the cubes a fun way for kids to learn, it's a boon to parents and teachers, too, because it is proven to increase the attention span of kids, according to Zhou. "The wIzQubes achieved a record of 3.5 hours of continuous usage by an eight-year-old girl during the product launch at IT Show 2007," he says. The product also may develop children's language skills, and encourage innovative and critical thinking, as well as sharpen their psycho-motor skills, he adds.

The cubes differ in size; some are as small as a deck of cards. Creating a computer reality game in this portable size was one of the key technological challenges, according to Zhou.

"Mixed reality requires using a camera to do the real-time tracking of physical objects," he says. "The portable size means that fewer pixels are being captured by the camera and hence, there is less tracking accuracy. In addition, portable-sized objects are easily held by hands, which introduces a lot of occlusions that make the tracking harder."

The product, which was licensed by MXR Corporation in 2004, has been available at stores in Singapore since early 2007 and will soon be available at retailers in the United States. The cubes, which feature classic tales such as *Cinderella, Little Red Riding Hood,* and *Jack and the Beanstalk*, sell for approximately $85 U.S.

Math for Business Decisions: An Equation for Success

Chapter 7

University of Arizona mathematics and business faculties collaborate to develop a revolutionary approach to teaching sophisticated mathematics to business students.

Most tales of technology transfer collaboration don't begin with a thorny, difficult situation. But that's how *this* story begins.

For years, the University of Arizona (UA) mathematics department faculty had been teaching finite mathematics and brief calculus to undergraduate pre-business students. This two-course sequence was required for students who hoped to enter the Eller College of Management as business students at the start of their junior years.

Just one problem.

"These courses were not popular with the students," says Richard Thompson, now a retired professor of mathematics at UA. "We were failing to teach them in a way that related to their world."

What's more, the mathematics professors didn't enjoy teaching students who weren't interested in the material and did not want to learn it.

Professor Chris Lamoureux, head of UA's department of finance, adds that although the traditional courses were theoretical in nature, they were scaled back for pre-business students.

"It was as though these pre-business students were considered 'little math students'," he explains. "Yet these students *were* capable of handling rigorous math."

Recognizing the need to change, Thompson convened a group of deans and faculty to explore the problem. The group unanimously agreed that mathematics and business professors would have to work together to find a better approach.

So in 1997, Thompson took the next step — or several hundred steps, as it were.

"I remember walking across campus to discuss this with Chris Lamoureux for the first time — it took a while to get there!" recalls Thompson with a chuckle.

You might say the physical distance between Lamoureux's and Thompson's offices on campus was a metaphor for the gulf between their respective disciplines, at least as far as teaching pre-business mathematics was concerned. The mathematics department's approach was more abstract, while business faculty focused more on applied learning.

Fortunately, Lamoureux and Thompson hit it off, and started creating a brand new way of teaching math to pre-business students.

The Experiment Begins

After a series of meetings and lengthy discussions, Thompson and Lamoureux fashioned a brand new set of courses, Business Math I and II, incorporating three key "pillars" designed to engage the students.

"Real World" Examples

Within each of the semester-long courses, the students had to solve two major business "problems," using the mathematical concepts at the core of the classes. The problems included:

- Loan work outs: Using bank records to decide whether to foreclose or attempt to work out repayment on a delinquent loan.
- Stock option pricing: Determining

the value of stock options.

- Technology marketing: Developing a marketing strategy for computer hard drives.
- Auction bidding: Bidding on an offshore oil lease.

Each of these problems involved realistic amounts of data, giving the students a sense of the scope, depth, and complexities of an ever-changing business environment.

Technology

In the business world, computer applications — namely Microsoft® Excel®, PowerPoint® and Word® — are common tools of the trade. Both courses integrated these software programs commonly used by business professionals, particularly Excel, into the real-world tasks of preparing reports and making presentations.

Working in Groups

In contrast to "traditional" math courses, in which students work individually on assignments, students in Business Math I and II are required to work in groups.

While Lamoureux was largely responsible for designing the overall structure of the projects, Thompson provided the mathematical content and developed the texts supporting the courses. Instead of offering texts in print, they were available in an electronic format, in keeping with how students learn in the digital age.

Professor Richard Thompson, former Arizona Congressman James Kolbe, and UA students Jason Haun and Kelly Peck, pictured during the June 2003 visit to Washington, D.C.

Photo courtesy of Sharon and Richard Thompson

You might think that even though the new courses were based heavily on experiential learning, the sophistication and difficulty of the math involved may have been compromised, or at least less rigorous than traditional math classes.

Think again.

"The mathematics underlying two of the courses actually is based on Nobel prize-winning economic theories," explains Lamoureux.

The auction bidding project involves the Nash equilibrium game theory, for which John F. Nash (who was depicted in the Academy Award-winning film, "A Beautiful Mind"), John C. Harsanyi and Reinhard Selten won the 1994 Nobel Prize in Economics. The stock option pricing project entails the Black Scholes formula, which is part of the work that earned Robert C. Merton and Myron S. Scholes the 1997 Nobel Prize in Economics.

"It would take about five years to learn the math involved in these projects," says Thompson. "But we use computer simulations, based on

historical data, to help the students understand the concepts and methodology."

During 1998-1999, Lamoreaux and Thompson taught the new courses, and quickly realized they were onto something big.

The students, it turned out, were energized by the new format, and wholeheartedly embraced this new approach to learning business mathematics. They realized that math was vitally important to helping them solve real-life business problems.

After that first year, the Business Math I and II replaced their unpopular predecessors — finite mathematics and brief calculus. In a survey of students, the new two-course combo was ranked "number one" among incoming juniors in UA's business program. This was quite a contrast from just a few years earlier, when students eschewed UA's pre-business math courses.

It wasn't long before Thompson and Lamoureux realized Business Math I and II could become part of pre-business curricula at other colleges and universities.

Licensing Opportunities

Don Albers, editorial director of the Mathematical Association of America (MAA), had heard rumblings in the mathematics community about the UA's "experimental" business math project.

"These courses vividly demonstrated how interdisciplinary experiences for students can be shaped through the active collaboration of academic departments — in this case, mathematics and business," says Albers.

He was so dazzled that he began to explore ways the MAA could promote and even license Business Math I and II. After making successful presentations to the MAA's publications committee, Albers entered negotiations with Thompson and Patrick Jones, director of UA's Office of Technology Transfer, to license Business Math I and II.

In 2003, the MAA gained rights to publish and distribute the courses in the United States under the name "Mathematics for Business Decisions," while international distribution would be handled by Cambridge University Press. As part of the deal, the Arizona Board of Regents retained all copyrights for the University of Arizona, so the university could coordinate expanding work on new opportunities for Mathematics for Business Decisions.

For its part, the MAA made editorial enhancements to Mathematics for Business Decisions, and started selling it in a CD-ROM format complete with Microsoft® Excel® workbooks, internet links and video clips.

Paradigm Shift

Meanwhile, in 2003 the UA received a $500,000 grant from the National Science Foundation (NSF) to continue the development and promotion of Mathematics for Business Decisions.

A telling example of the national recognition Mathematics for Business Decisions was receiving occurred in

> "Everyone on the Math for Business Decisions team felt it was important for others to be able to contribute their creative ideas, allowing for customization within a coherent framework."
>
> *Patrick Jones, Ph.D., University of Arizona*

June 2003, when Thompson, Albers, two UA undergraduate business students and NSF representatives paid a visit to Washington, D.C. The delegation made presentations to members of Congress, showcasing the tangible, beneficial impact of NSF-funded projects like Mathematics for Business Decisions. Jason Haun, one of the UA students taking part in the visit, says the course has benefited him since graduation.

"I'm in real estate development, and a lot of what we learned — from auction bidding to using modeling tools for pricing — continues to help me in my work," he notes.

Yet Albers notes that getting business and mathematics faculty around the country to embrace Mathematics for Business Decisions has not been an easy task.

"It's a major paradigm shift for these people," says Albers, whose background includes serving for 23 years as a mathematics professor and dean at Menlo College in Atherton, Calif. "You're asking them to uproot their way of thinking about applied mathematics, and to change. Professors aren't always willing to change."

Nonetheless, a number of academic institutions have incorporated Mathematics for Business Decisions into their curricula. Today, Kent State University in Ohio, Texas A & M in Corpus Christi, Pima Community College in Tucson, Ariz., Texas Christian University in Fort Worth, and Seattle Central Community College have joined UA in teaching Mathematics for Business Decisions. It's also being used at the American University of Kabul in Afghanistan.

Professor Deb Hughes Hallett is intimately familiar with Mathematics for Business Decisions, having taught Thompson's and Lamoureux's Business Mathematics I and II at the UA. She also teaches mathematics at Harvard University's John F. Kennedy School of Government, and is an internationally renowned expert on teaching mathematics at the college level.

"We're exploring ways to use this same collaborative approach to teach applied mathematics in other disciplines, such as biology, agriculture or journalism," says Hughes Hallett.

Protecting Intellectual Property, Promoting Adaptability

With the success of Mathematics for Business Decisions came new challenges.

At schools that used Mathematics for Business Decisions in their curricula, a few students would purchase the CD-ROMs, and then make copies for their friends.

"This diminished the self-sustaining revenue generated from sales of the CD-ROMs, and was forcing the MAA

to raise prices, which increased the likelihood of copying," says Jones, who also served as president of the Association of University Technology Managers (AUTM), 2007.

To address this growing problem, Jones and the UA Office of Technology Transfer provided their expertise in rights management to devise an effective solution for the MAA: site licenses incorporating a course fee concept with download-accessible content.

By providing such licenses for the software, the academic institutions themselves were responsible for dispensing the content provided by the MAA and collecting fees for use. The purchase price of Mathematics for Business Decisions could be substantially lowered compared to previous versions, also solving a vexing problem of increasing textbook costs, while still generating enough revenue to allow the MAA to continue offering, and improving, the content.

Jones points out that while the intellectual property at the heart of Mathematics for Business Decisions is protected, it can be customized to meet the academic institutions' unique requirements.

"It has been designed in the spirit of a collaborative community," he explains. "Everyone on the Math for Business Decisions team felt it was important for others to be able to contribute their creative ideas, allowing for customization within a coherent framework."

The Future

With the success of Mathematics for Business Decisions at U.S. institutions, the UA and the MAA have translated it into Spanish, and are investigating new markets for the software in Latin America, as well as in Spanish-speaking areas of the United States. Additionally, educators in Tunisia and Senegal have expressed interest in Mathematics for Business Decisions, so French-language versions may be in the offing. It also is being considered for use in elementary and secondary schools.

"Through our ongoing partnership, we're eager to continue promoting and improving Mathematics for Business Decisions," says Jones.

Partnership Results in Advanced Energy Solutions

Chapter 8

Los Alamos National Laboratory and Chevron have formed a partnership to address innovative ways to deliver reliable and environmentally sound energy.

Pictured is riser assembly in the moon pool of the ENSCO 7500 semi-submersible drilling rig. TAP will be implemented off-shore using a similar drilling rig. The riser assembly in the moon pool allows drilling fluid to be pumped down and back, without losing any to the ocean environment.

Photo courtesy of Los Alamos National Laboratory

It's been the dream of researchers for years — to revolutionize the development of energy resources. Consider that in the last 125 years, according to Cambridge Energy Research Associates, the world has used one trillion barrels of oil and the demand keeps growing. In the next 30 years, another trillion barrels of oil are expected to be needed.

Availability of fuel is taken for granted by some, but not those who work in the energy industry. Los Alamos Industrial Fellow assigned to Chevron, Kevin Jakubenas says, "It takes an increasingly sophisticated technology to keep the lights on and our cars running."

The Alliance for Advanced Energy Solutions, a partnership between Chevron and Los Alamos National Laboratory, is working on innovative solutions.

"They are drawing on every area of expertise, from fundamental physics, chemistry and materials science to satellite engineering and earth and environmental sciences," says Jakubenas.

It takes an enormous amount of effort and money to fill up a car with gas. If you're filling up in the United States, approximately one in 10 gallons comes from the Gulf of Mexico, and it doesn't come easy.

"Reaching oil in the Gulf of Mexico requires a platform the size of a city block located more than 100 miles offshore," Jakubenas explains. "Up to two miles below that platform on the sea floor is a completely automated village in which the only business is moving oil to the surface. The oil itself starts as many as five miles below the village, locked away in an environment with such high pressure that rock can flow like taffy."

Cutting-Edge Science

Technology plays a significant part when the oil reaches the surface and is then sent through miles of pipeline to a refinery or a molecular factory where atoms are pulled apart and reassembled into products such as gasoline. In discussing the cost Jakubenas says, "These processes involve billions of dollars of cutting edge technology and thousands of highly trained engineers, technicians and scientists."

What happens when oil that is easy to access now becomes difficult to attain? Finding, recovering and processing the next trillion barrels in an efficient and environmentally responsible way is a formidable challenge. Scientists unrelated to the oil industry are beginning to solve some of the oldest problems in the industry, including how to reduce the United States' reliance on foreign oil.

The collaborative partnership has given Chevron the opportunity to work with Los Alamos scientists of widely different backgrounds. For example, a polymer chemist is using laser technology to prevent collapse of wells in the Gulf of Mexico while a space scientist is enabling breakthroughs in sensors miles underground, and a materials

scientist's expertise is measuring complex flows in oil pipelines.

In 1987, the relationship began with Manuel Gonzalez, a senior drilling engineer in the oil and gas industry who is now co-manager of the Alliance. Gonzalez first encountered Los Alamos technology during his time in the U.S. Army.

"The Los Alamos technology I worked with in the military was impressively advanced, but more importantly it always worked when needed," recalls Gonzalez.

When he left the Army for the oil business, Gonzalez remembered his previous encounters with the innovative equipment from the scientists "on the hill" and how he had come to trust their ability to make advanced technology reliable. Subsequently, Gonzalez worked with Los Alamos technology both in an innovative oil well logging tool and in a company he started to track fraud in retail gasoline distribution.

Building Partnerships

In 2003, while working at Chevron, Gonzalez initiated conversations with Los Alamos' Technology Transfer Division on yet another technology, wireless communication. The technology, called Inficomm, implies "infinite communication."

It was the initial Alliance project and grew out of technology originally developed for military communications. Gonzales and Don Coates, a technical staff member in Los Alamos' Physics Division and an Intellectual Property Coordinator for Los Alamos' Technology Transfer Division, proposed to adapt Inficomm to allow down-hole wireless communication in oil and gas wells. Inficomm is expected to allow data rates up to a million times faster than conventional techniques without the need for any power source located in the well. This would enable the collection of real-time, broadband production data and revolutionize the way in which oil fields are managed, potentially allowing much more oil to be recovered from existing fields.

Los Alamos and Chevron realized the project was just one in which Los Alamos' technology could help Chevron face its growing challenges in extracting oil from increasingly difficult environments. They also recognized an opportunity to build a lasting relationship to meet long-term goals that would continually benefit the United States and possibly the world.

The Alliance for Advanced Energy Solutions was established in 2004 in order to coordinate efforts across multiple project areas. This formalized

Pictured is the BakerHughes Drilling Fluids high pressure/ high temperature EMF-350 testing laboratory. This laboratory is used to test various formulations of the TAP spacer fluid under simulated conditions that are found in the actual drill holes (both on-shore and off-shore applications).

Photo courtesy of Los Alamos National Laboratory

partnership is guided by an Alliance Agreement that states that the parties will collaborate to advance energy security and help Chevron and the entire oil industry deliver reliable, affordable, and environmentally sound energy. This is also a strategic goal of the Department of Energy.

Los Alamos has designated John Russell as its Alliance Coordinator to coordinate technical projects, agreements, and strategic planning. "The Alliance allows Los Alamos to apply world-class science to Chevron's greatest challenges that in turn helps Los Alamos advance these sciences further benefiting the Laboratory's mission in energy security," Russell says. Twice each year, the Los Alamos-Chevron Alliance Decision Review Board meets to discuss new and ongoing projects. The Board consists of Chevron and Los Alamos senior managers who set the strategic direction for the Alliance.

The structure of the Alliance provided the framework and eventually the contractual mechanism — an umbrella Cooperative Research and Development Agreement, or CRADA — to build effective relationships, select and manage projects, and to ensure early success.

The umbrella CRADA sets the overall contractual terms of interaction including protection of proprietary information and expectations for licensing of intellectual property. A separate Alliance Agreement has also helped build a bridge of trust and clear communication that is making the Alliance increasingly successful.

A second early project developed through the Alliance is trapped annular pressure mitigation, or TAP, used in deepwater drilling. Trapped annular pressure is a problem in deepwater drilling when hot oil from miles under the seafloor first flows in wells located in cold deep ocean water. The temperature differential can cause extremely high pressure that can collapse wells like a cheap soda straw. The elegant solution developed under the Alliance uses a new compound as an ingredient in the drilling mud. This compound is a monomer (small, simple molecules that chemically bond to other monomers to form polymers) liquid that combines to form a solid polymer upon exposure to heat. The monomer solution was first brainstormed in early 2005, and then was tested in the laboratory and scaled up and demonstrated in a test well within a year. When these monomers are present in the drilling fluid, they cause a reduction in volume that eliminates the pressure buildup.

Robert Hermes, lead scientist on the TAP project, says, "I've had this solution sitting on my desk for 25 years, but I didn't know it. I had never heard of the problem until Chevron came to Los Alamos."

Through a partnership with Baker-Hughes, a leader in oilfield services, Chevron and Los Alamos have been able to field test TAP. Chevron believes that the use of the Los Alamos TAP technology has the potential to prevent catastrophic failure in every one of their deep-sea wells — an insurance policy for billions of dollars in

investment, much of it in the U.S. Gulf of Mexico where a single well may cost well over $100 million to drill. TAP is one of the technologies that may be commercially available to the oil and gas industry within the next two years. The Alliance has agreed that once tested and successful in working wells it will partner with outside companies to manufacture and market TAP for the rest of the industry.

Developing New Technologies

Los Alamos and Chevron also have a strong commitment to the environment and are studying methods for oil shale recovery that can be done with as little environmental impact as possible. The Alliance is also drawing on expertise at other national laboratories and universities. Through the Alliance, Los Alamos provides opportunities for Chevron to work with some of the most knowledgeable scientists in the world along with other research collaboration.

The Alliance is constantly trying to develop new technologies to solve the industries' toughest problems. One example is the development of oil shale in the western United States. The work includes reservoir simulation and modeling, as well as experimental validation of new recovery techniques. The project demonstrates Los Alamos' and Chevron's interests in basic research for unconventional fuels, in addition to applied problems facing the industry like trapped annular pressure.

The Los Alamos-Chevron Alliance is successful because it is built on the common goals of applying first-class science to problems of compelling need. The Alliance has established a strong structure to guide and organize the efforts while also allowing sufficient flexibility for the unexpected confluence of ideas that leads to true innovation.

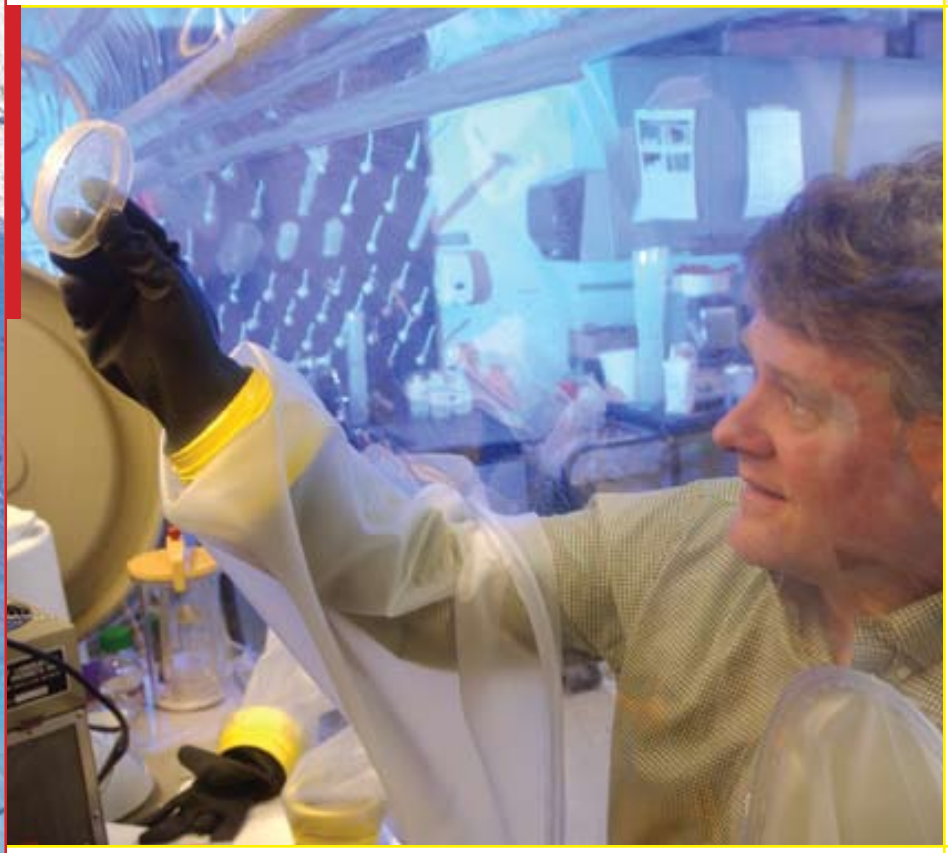
The broad breadth of projects is an indication of the value of the Alliance to both parties. "We have 15 projects in place — Inficomm and TAP are current projects that address every aspect of the oil industry. Our projects are in advanced well performance, oil shale, deep water exploration and high efficiency separation processes," says Russell.

Chevron and Los Alamos continue to work together to identify new areas of potential collaboration in refining, equipment reliability and advanced geologic imaging. The Alliance expects to see these technologies advance into field trials and deployment within the next two years. Through commercialization, these projects not only help Chevron better provide energy but they are also consistent with the Department of Energy's mission of energy security.

There's no doubt about it. Future opportunities exist to develop technologies to enhance oil exploration, which improve efficiency, save money and reduce environmental impact. Together, Chevron and Los Alamos are championing the future.

Cellulosic Ethanol Technology Holds Key to Inexpensive Fuel

Chapter 9



It took years for the world to wake up to the need for alternatives to gas and other petroleum-based fuels. Dartmouth College's Lee Lynd has been working on cellulosic ethanol technology for nearly three decades and believes grasses, wood scraps and other forms of biomass can be converted to ethanol at a reasonable price.

Timing, alas, is nearly everything.

For years, Alla Kan, the director of the Technology Transfer Office at Dartmouth College in Hanover, N.H., shopped around the cellulosic ethanol technology developed by professor Lee Lynd at Dartmouth's Thayer School of Engineering.

No luck. Just lots of frustration.

No one, it seemed, was interested in investing in research that would turn grasses, crop residue, paper pulp, wood scraps from mills and other forms of biomass into ethanol in one step called consolidated bioprocessing.

Not when gasoline was selling for $2 a gallon or less.

But gas prices topping $3 a gallon, oil selling for more than $90 a barrel, acceptance of global warming as a real threat, military conflicts in the Middle East, other geopolitical concerns — to say nothing of achievements in cellulosic ethanol technology — all combined to shift opinion.

"I have mailing lists and mailing lists over various periods of time," says Kan, whose scientific background in chemical research includes tertiary oil recovery to wring more petroleum out of underground reservoirs.

"I knew the time would come, but it would depend on many factors, a lot of which were political, not scientific," she says. "Altogether, I probably presented the technology to 200 different companies and dozens of technology brokers over many years."

Lee Lynd is a professor of engineering and adjunct professor of biology at Dartmouth College, and he also serves as chief operating officer, co-founder and director of Mascoma Corp.

Meanwhile, Lynd had found success in getting government grants for his research as Dartmouth assembled a considerable patent portfolio.

But the big break, in terms of commercializing the technology, came in 2005 when Lynd and businessman Bob Johnson were able to convince renowned venture capitalist Vinod Khosla to back a nascent company called Mascoma. The firm now has more than 70 employees, roughly half doing research in Lebanon, N.H., and the remainder in the company headquarters in Cambridge, Mass.

"Why was it so difficult for all those years?" muses Kan.

"The time was not ripe and the companies we approached did not have the foresight," she says. "But the geopolitical realities are such today that it is recognized that we need to look for alternative sources of energy so we don't have to depend on oil-rich countries that are not particularly friendly to the United States.

"It's also because we are starving for new energy," she says. "That reality finally began to sink in and became a hot topic in the news. Yes, it was frustrating, but I was always confident that one day people would recognize

the need for this technology. Time has proved us right."

Kan credits Khosla with giving Mascoma, which is now building cellulosic ethanol plants in several states, a kick-start. With Khosla's $4 million initial investment — and reputation for backing winners — others took notice. Now more than $39 million has been raised from private backers. In addition, state and federal grants currently total $75 million.

"He is a brilliant man with a good foresight for technology that can be commercialized," she says of Khosla, who co-founded Sun Microsystems. He then joined a venture capital firm that financed many successful Silicon Valley firms when they were small.

"We felt he would be able to help put together the right team to make this happen," she says. In the process, Dartmouth licensed Lynd's technology to Mascoma and took an equity share in the company. In addition, Mascoma is funding some of Lynd's continuing research at Dartmouth.

Khosla, whose interests in ethanol have been well publicized, says in a statement that he believes "Mascoma is poised to transform the current model for ethanol production.

"Mascoma's research and innovation in the field have solidified our leadership position in commercializing cellulosic ethanol technology and we expect a great and positive impact on the industry and consumers alike."

In an interview with CNNmoney.com, he says, "I think we have a replacement for oil today. It's cheaper, cleaner, it doesn't require a change of infrastructure, and it appeals to most of the lobbies. What is this platform? It's ethanol.

"In the past, ethanol was made from corn, which isn't that great environmentally and isn't very efficient — for every one unit of energy you get 1.5 units of fuel," he says. "Now, with bioengineering, we can make ethanol from agricultural waste, which is four to eight times as efficient."

Lynd Persevered

Lynd, who began his research on cellulosic ethanol in the late 1970s, says the lack of interest in his work gave him pause, causing him to think it might not be worthwhile.

"Frankly, in the time between then and 2005 or so, there was not much enthusiasm in this field," he says. "And I did ask myself if perhaps there was something wrong that I just didn't see.

"But I was committed, though for much of that time, it seemed I was one of the few persistent ones who maintained faith in it.

"That meant that when venture capitalists got interested in the summer of 2005 — others began to take note somewhat earlier — I found myself in the position of being one of relatively few people who had long-standing activity in the field."

As for the conversation he and Johnson had with Khosla on Oct. 7, 2005, Lynd remembers it as if it were yesterday.

"We had about a two-hour conversation about cellulosic ethanol,"

he recalls. "At the end, Vinod said, and I quote, 'Let's do this.'"

Lynd, a co-founder of Mascoma, which is named after a lake near Dartmouth, sits on the company's seven-member board. He is also Mascoma's chief scientific officer, dividing his time between his Dartmouth lab and Mascoma. The other co-founders are professor Charles Wyman, who is now at the University of California, Riverside, and Bob Johnson.

"I continue to lead research in my academic capacity at Dartmouth, which complements Mascoma's activities," Lynd says. "We see ourselves as scouts at Dartmouth. We are ahead of the main file, which at this point is Mascoma."

Currently, that research is focused on developing a new generation of enzymes, microbes and processes for economical conversion of cellulosic feedstocks into ethanol. With this conversion will come a complete rethinking of the ways in which we fuel our economy, Lynd says.

"I got into this not to start a company, but as a service," he says. "I believe that a transition to a world supported by sustainable resources is probably the defining challenge of our time."

Plants in New York, Tennessee and Michigan

"One hundred years from now, people will look back on us and ask how well did humanity do on this issue. Frankly, I don't think we're doing too well with it now.

My gift to the world, as modest as it may be, is going to be advancing cellulosic biofuel technology."

With backing from venture capitalists, Mascoma has built a multi-feedstock demonstration-scale biorefinery located in Rome, N.Y., that is being developed in partnership with several New York state agencies.

Construction was expected to start at the end of 2007 on a $40 million plant in Tennessee that will use switch grass to make 5 million gallons a year. This joint effort is backed by the University of Tennessee and will include $27 million for research and development activities.

> "One hundred years from now, people will look back on us and ask how well did humanity do on this issue. Frankly, I don't think we're doing too well with it now."
>
> *Lee Lynd, Dartmouth College*

Also in 2007, Mascoma and the state of Michigan announced plans to build one of the nation's first commercial scale biorefineries using wood as a feedstock. This project is being developed with the Michigan Economic Development Corporation, Michigan State University and Michigan Technological University.

Lynd said the collaboration between Dartmouth and Mascoma has gone well.

"If I take a step back from the details, Dartmouth's fundamental mission is to educate people and serve humanity," he says. "Mascoma's

mission is to be a successful business in a direction that serves the world. A lot of our momentum is because of that service aspect.

"To some extent, this story is still very much in progress," he adds. "Dartmouth has its mission rewards, with students being educated and the school getting credit for groundbreaking research. If all plays out well, Mascoma will be successful and help solve what is today one of our biggest problems."

Five years down the road, Lynd says he can foresee Mascoma producing well over a billion gallons of ethanol a year for transportation fuel. While one billion is a big number, Lynd notes that the United States now uses 140 billion gallons of gasoline annually.

But growing the industry to 10 billion gallons of ethanol per year or more may come soon after, he says.

"To increase it to 1 billion, it has to be profitable, the technology has to work and you have to do a lot of things for the first time," he says. "By the time you are at a billion gallons, however, you are replicating success and growth can be very rapid. It's one of those things that starts very slowly and if things are properly aligned, can accelerate.

"Two thirds of the value of gasoline is the cost of oil," he says. "Fuel production is dominated by raw material costs. (Think $80 plus for a barrel of oil.) So a very good question is what is the cost of cellulosic biomass. The answer is around $50 a metric ton, which is the equivalent of $17 a barrel.

"When you are starting with something that inexpensive and you have biotechnology on your side, which is arguably the transformative science of our time, it seems realistic to think that we can make fuel pretty cheaply."

UltraCell: A Portable Power Plant

Chapter 10

Researchers at Lawrence Livermore National Laboratory realize the dream of a truly portable power source with hydrogen fuel cells.

UltraCell XX25 ™ Fuel Cell

After Hurricane Katrina ripped up the United States' Gulf Coast in August 2005, countless hospitals, clinics and nursing homes were left without electricity for days and even weeks. In the city of New Orleans alone, some two dozen hospitals had to be evacuated because of the loss of power, water and sewage service, according to a 2006 report by the Urban Institute. While portable power generators pumped electricity to critical care areas, many people died sweltering in temperatures that exceeded 100 degrees Fahrenheit.

Natural disasters such as Katrina revealed just how much we depend on energy during an emergency. They also demonstrated the need for making energy last longer, and for portable devices that can go where they're most needed.

A company called UltraCell in Livermore, Calif., is working to address these needs. UltraCell is making the world's first micro-scale fuel cells, which run on clean energy — methanol — and due to their compact size, are highly portable. While these innovative fuel cells currently can power computers, they're being developed for larger applications, such as power generators, that could make a big difference in future Katrina-like disasters.

A Small Energy Solution for Big Energy Problems

A fuel cell is an electrochemical energy conversion device that produces electricity quietly and efficiently, without pollution. Unlike power sources that use fossil fuels, the byproducts from a hydrogen fuel cell are benign — heat and water.

The UltraCell technology is a high-power, high-energy-density fuel cell system for portable electronics applications, ranging from military to laptop computing, to police and industrial use.

Demonstrating a preproduction device at an Intel Developers Forum in 2006, UltraCell Chief Executive James Kaschmitter said, "Our fuel cell systems literally cut the cord to electrical dependence."

While fuel cells have been around for a while, UltraCell has managed to address one of the major stumbling blocks associated with their widespread use: energy density. An interdisciplinary team at Lawrence Livermore National Laboratory in Livermore, Calif., figured out how to get the most bang for the buck in fuel cell technology — reducing the size of the cell while at the same time increasing the amount of energy it can store.

The project that led to the development of these micro fuel cells began in the Chemistry and Materials Science and Energy Directorates of the Lawrence Livermore National Laboratory, with funding from the U.S. Department of Energy. While many years of work had gone into the use of hydrogen in fusion, in the 1990s researchers at the lab began looking into developing hydrogen as a source

of fuel. Right away it was clear they needed to create smaller-scale devices.

"Fuel cells had always been very large in scope and size," said Alan Jankowski, one of the inventors of the technology and now a professor of mechanical engineering at Texas Tech University in Lubbock. "You could power a bus with a fuel cell, but the fuel cell would be about as big as the bus."

With a background in materials science, Jankowski had been working on creating thin film coatings for application in fuel cells, trying to develop the cells on a smaller scale. When he began collaborating with Jeff Morse, an electrical engineer at Lawrence Livermore with a specialty in microelectromechanical systems (MEMS) and nanofabrication, the results were revolutionary.

"When people started looking at smaller fuel cells, they were looking at taking a large (90 watt) device and making it smaller," Morse said. "We decided to take MEMS and microscale approaches and blend them together to create a new paradigm."

In other words, instead of using existing technology to take something big and scale it down, Jankowski and Morse decided to start — and stay — small.

"People were trying to minimize the real estate of a fuel cell with traditional machining," Morse explained, "but if you want to work on the scale of cubic centimeters, you need MEMS."

Teamwork Leads to Commercialization

The team of inventors made their first invention disclosure to the Lawrence Livermore Office of Technology Partnerships and Commercialization in 1997. The group, led by Jankowski and Morse, included chemists and chemical engineers, mechanical engineers, materials scientists and energy experts, as well as doctoral and post-doctoral students from the nearby University of California, Berkeley. This group worked collaboratively for five years to miniaturize the components of a hydrogen fuel cell.

> "Today's soldiers increasingly rely on portable electronics, such as GPS systems and radios, so portable power can be a critical life-protecting component for them."
>
> *James Kaschmitter, UltraCell*

Although the benchtop devices were demonstrated, they still didn't have a commercial product.

Then came Kaschmitter, a former Livermore staff engineer and serial entrepreneur with a background in energy storage, who saw a real need for the new, small-scale fuel cell technology. As soon as the concept had been sufficiently proven, he wanted to bring it to market.

"I wanted to take an interesting technology and make a product that people would really use," Kaschmitter said. "Jeff and his group had proved the viability of the technology. We saw the potential to turn it into a product."

Kaschmitter says collaboration was critical to the success of the project. "Scientists at the lab are working in basic research, they're not thinking about the market, so they needed practical information, which I could bring."

He worked with the researchers for several months and when it became clear it would work, formed the company UltraCell, which licensed the technology in 2002. The company recently opened a plant in Vandalia, Ohio, and is expected to generate more than 300 jobs in the region.

Aside from offering a clean source of energy, hydrogen fuel cells offer a safer, better way to store energy, especially as compared with lithium batteries, according to Kaschmitter.

"Cell phone and laptop lithium-ion batteries have reportedly exploded or caught fire, and if you try to put more energy into them, it could create a safety hazard," he said.

The number one advantage of fuel cells over batteries, according to Kaschmitter, is that they are lighter weight, and offer more energy. Batteries in today's cell phones and laptops last only three or four hours. He says soldiers in the field today routinely carry up to 30 pounds of batteries on missions that can last a week or more.

He's heard anecdotal evidence from military leaders — stories about batteries going dead in the middle of an air strike, for example. "Today's soldiers increasingly rely on portable electronics, such as GPS systems and radios, so portable power can be a critical life-protecting component for them," Kaschmitter said.

The military is the company's first customer, and it's a good place to start, according to Kaschmitter. "The military provides field testing with very high standards, plus it gives us a higher price point during production startup," he says. "Now, we're going from military to industrial markets, to provide portable power that will run for a long time."

While UltraCell technology is currently geared toward small devices, such as laptops and portable telecommunications equipment, Kaschmitter says it may one day have larger-scale uses. These include providing power at remote construction sites, or backup power for homes, apartment buildings and hospitals. UltraCell could also be used in the rental power market, which provides electricity for concerts and other large public events.

And, as mentioned earlier, UltraCell technology could be a vital resource in disaster relief efforts. It's a small-sized solution for large-scale problems.

Letting Cooler Roofs Prevail

Chapter 11

Berkeley Lab and Oak Ridge National Laboratory test a panel of cool roofing materials outdoors.

Photo courtesy of Bill Miller of Oak Ridge National Laboratory

Researchers at two federally funded laboratories partnered with a group of committed companies to develop and enhance "cool roof" technology, which can significantly reduce energy consumption and negative impacts on the environment.

Imagine it's a hot summer day, and you can choose between walking barefoot on a black asphalt sidewalk or one that's concrete. Unless you're a glutton for punishment, you'd probably choose the relatively cooler, light-colored concrete sidewalk, which reflects the sun's heat.

This idea of reflecting the sun's heat is at the heart of "cool roof" technology, which is growing in popularity in the United States. Developed through a collaborative partnership of federal researchers and companies, this innovative technology can be a powerful weapon in the battle to cut greenhouse gas emissions, while reducing urban pollution and energy consumption.

The basic idea underlying cool roofs is nothing new under the sun.

Lighter colors tend to reflect sunlight and heat, which is why people in tropical climates typically wear white or light-colored clothing. The same holds true for roofing materials. Buildings with dark-colored roofs are hotter than those with light-colored roofs. Employing the same principle, cool roofs are made of materials that reflect the sun's energy, so they're much cooler.

How much cooler? Cool roofs generally reduce the roof surface temperatures by 50 to 60 degrees Fahrenheit, and in some cases by as much as 90 degrees.

Consequently, this decreases the heat transferred to the building, which can reduce energy costs associated with cooling the building. Not only that, but cool roofs have other potential benefits, such as lower maintenance costs, longer-lasting roofs, and generally improved comfort for the building's occupants.

Cool roofs translate into environmental benefits by lowering greenhouse gases and emissions that go hand-in-hand with energy consumption. Also, since cool roofs last longer, they don't have to be replaced as frequently which, in turn, reduces roofing waste that ends up in landfills.

But there's another big environmental win that cool roofs offer – especially to city dwellers — the reduction of heat islands and concomitant smog.

What's a heat island? Think of it as an expansive canopy of warm, polluted air that covers an urban area where the temperature is higher than in the surrounding areas. So, these urban areas are islands of heat, surrounded by suburban and rural areas where trees and vegetation lend themselves to cool temperatures. Dark, heat-absorbing rooftops are big contributors to the growing problem of urban heat islands.

The Birth of a Collaborative Partnership

While cool roofs have become more common in the marketplace in recent years, they have been years in the making. For decades, two separate federally funded research institutions have been researching the possibilities of making roofs reflect the sun's heat and radiation: Lawrence Berkeley

National Laboratory (Berkeley Lab) in Berkeley, Calif., and Oak Ridge National Laboratory (ORNL), managed by UT-Batelle for the Department of Energy, in Oak Ridge, Tenn.

"We've conducted building envelope research since the 1970s, and our first cool roof experiment took place in 1986," explains Andre Desjarlais, group leader of Building Envelope Research at ORNL. Building envelope research involves investigating the energy efficiency of a building's "skin" – its roof, walls, foundation and windows, as opposed to internal "working parts" such as the furnace, appliances, etc.

Meanwhile, the Environmental Energy Technologies Division (EETD) at Berkeley Lab had been studying solar reflectance of roofs since the early-1980s.

"Within the last 25 years, we have achieved global recognition for our work on heat mitigation and cool roof research," notes Hashem Akbari, head of the Heat Island Group at Berkeley Lab.

However, the two institutions had been approaching cool roof research from two distinctly different vantage points.

"We received U.S. Department of Energy funding for our research on building energy efficiency, whereas Hashem's Heat Island Group received U.S. Environmental Protection Agency funding to explore the environmental benefits of cool roof research," says Desjarlais.

But in time, a series of emerging trends and events brought the two institutions together in a collaborative partnership to bring cool roof technology to the marketplace.

As the new millennium dawned in 2000, the concerns over the environment and global warming became widespread in the U.S. Case in point: 71 percent of Americans reported being either actively involved in the environmental movement or sympathetic toward it.

Around that same time, concerns over the environment and energy consumption became particularly acute in California. From November 2000 through May 2001, Californians experienced a series of brownouts – planned partial shutdowns of energy for limited durations, designed to ease the demand on the power grid to avoid a complete energy blackout.

It became clear that controlling peak demand, rather than investing millions of dollars into new power plants, would be necessary to deal with California's looming energy shortage problem. Utility companies and energy policy experts soon discovered that cool roof technology offered an effective means to control peak demand. One of its biggest advantages is that it doesn't rely on changing or influencing people's energy consumption habits, such as turning off lights, doing laundry at off-peak times or using energy-efficient appliances. Once the cool roof is installed, significant energy savings start adding up.

By 2001, the California Energy Commission began promoting cool roof technology, running ads to

increase awareness of its benefits, and offering more than $20 million worth of rebates to building owners who installed cool roofs.

But the California Energy Commission took its mission a step further. In 2002, it brought together researchers at the Berkeley Lab and ORNL for a collaborative Public Interest Energy Research (PIER) project aimed at improving cool roof technology and expanding its availability and use in the California marketplace.

"The project also involved industrial partners representing 95 percent of the roofing material-type market in the United States," added Akbari. "They were essential to our success."

Among the originally participating companies were 3M, American Rooftile Coatings, BASF, Custom-Bilt Metals, Elk Premium Building Products, Inc., Ferro Corp., GAF Materials Corp., Hanson Roof Tile, International Specialty Products Minerals, MCA Tile, MonierLifetile and the Shepherd Color Co.

"We already had been working with a lot of these manufacturers before 2002, but our cooperative research project with ORNL made the relationship with our industry partners more 'formal,'" says Akbari. "Since then two dozen other manufacturers have expressed interest in joining us."

The Cool Color Challenge

One of the biggest challenges facing the partnership between Berkeley Lab, ORNL and the manufacturers was to develop cool roof technology available in a rainbow of colors appealing to a wide range of residential customers.

At the time, existing cool roofs were available in just light colors. For commercial buildings, having a white or light-colored roof is a non-issue. This is because commercial buildings' roofs typically are flat and out of the public eye, so it really doesn't matter what color the roof is.

But most homeowners are very particular about the color of their roofs. Many U.S. homeowners may not buy lighter-colored cool roofs, even it could help them save money by cutting their air conditioning bills.

With this in mind, Berkeley Lab scientists worked with industry partners, including Ferro Corp. and Shepherd Color Co., testing different types of materials and pigments, with the goal of creating a large palette of cool colors. Using solar spectrometers, the researchers identified the pigments contained within colors that reflect what is known as "near-infrared" radiation, which comprises more than half of the energy in sunlight. Armed with this new information, they developed software enabling manufacturers to use these pigments to create roofing materials with "high solar reflectance" – the ability to reflect solar radiation both in the visible and near-infrared parts of solar spectrum.

The next step involved the development and testing of roofing materials containing these "cool colors." Residential roofing experiments involved roofing made of coated asphalt shingles, clay or

concrete tiles, or metal. And this is where the industrial partners came into play.

Companies donated materials and shared information, working with Berkeley Lab researchers on developing experimental cool-colored materials with just the right combination of pigmentation to achieve optimal reflectivity. Utilizing these prototype materials, Berkeley Lab and ORNL conducted field tests to determine their effectiveness.

"These experiments typically involve using sensors to measure the amount of heat flowing into the house from the attic," explains Desjarlais.

Frank Klink, Ph.D., a laboratory manager in 3M's Industrial Mineral Products Division, notes that the cool roof initiative resulted in great enhancements to the sand-like granules 3M manufactures for coated asphalt shingles.

"The value of increased reflectance is further enhanced by the granules' naturally high thermal emittance," he explains. "This means that whatever solar energy is not reflected is readily dissipated, further helping to keep the roof cool. Incorporating these factors into roofing helps reduce building cooling costs, especially on the hottest days of the year when electrical demand peaks."

The Success Story Continues

An interesting aspect of the cool roof PIER project is that the resulting technology has not been patented or licensed. It's available free of charge to any roofing product company wishing to take advantage of it.

Akbari says the project has successfully achieved its goal of promoting the use of cool roofs in the marketplace, not only in California, but beyond.

"The popularity of cool roofs is catching on in other parts of the country," he says.

In different cities throughout the U.S., the projected annual cost savings from using cool roofs is considerable. For example, Phoenix can save as much as $26 million in annual cool energy costs, while Los Angeles can save $15 million.

As for the environmental benefits, a single 3,000-square-foot home with a cool roof can reduce its yearly carbon dioxide emissions by one ton. And based on field tests, cool roofs can save residents and building owners 20 percent in annual cooling energy use.

Given these great benefits, it's no surprise that the Berkeley Lab research team is exploring other uses for cool colors – for car surfaces, clothing, tools and camping gear.

Tony Chiovare is president and CEO of Custom-Bilt Metals, a partner in the project and one of the first manufacturers to use cool roof technology in metal shingles. For him, the cool roof "revolution" makes good sense from both an environmental and a business standpoint.

"I'm a capitalist, there's no question about that," he says. "But if we can promote technologies like this one that help us reduce energy consumption and benefit the environment, we all win!"

Chapter 12

TyraTech: Bringing "Green Pesticides" to the World Marketplace

TyraTech's flagship product, the ready-to-use Crawling Insect Spray.

Photo courtesy of TyraTech, Inc.

What began with a power failure resulted in a university-private sector partnership to develop a new environmentally friendly technology for killing and repelling mosquitoes and other bugs.

One day in the early 1990s, it was business as usual for Essam Enan, Ph.D.

Enan was performing cancer-related research on essential plant oils in his laboratory at the University of California, Davis, where he was working as a research professor. Suddenly, the lights went out. After waiting a bit, he realized the power was not going to come back on right away, so Enan opened the door to his lab to try to keep cool in the summer heat.

Other scientists in the building did the same thing, and soon flies and other insects started coming in from outside. But as he walked by the labs next to his, Enan noticed a strange thing: they had many more flying pests than his lab did.

This got him to thinking. Could it be possible that these essential plant oils had something to do with the absence of insects in his lab space?

Essential oils — the volatile aroma compounds of the oils that can be extracted from any plant — have been around for ages. They have been used in the perfume industry, and have been on the Environmental Protection Agency's list of exempt chemicals, considered safe for people and animals.

But it was also known that these oils had the power repel, and even to kill, insects. However, scientists did not know why essential plant oils had these insect-killing and repelling qualities. So in his spare time, when he wasn't doing his cancer research, Enan began to investigate this question, out of pure scientific curiosity.

A few years later, in 1996, he unlocked the mystery: essential plant oils disrupt certain external olfactory and protein receptors that only invertebrates have. This causes rapid and abnormal calcium production which either kills or repels the bugs.

TyraTech screens essential oils for the most potent synergistic combinations possible.

Photo courtesy of TyraTech, Inc.

Filling a Potential Marketplace Need

For several years, Enan went on investigating the properties of these oils. He developed oil combinations that could repel mosquitoes, kill ants, and he even found a way to screen for oil combinations that would target specific insects. Yet it wasn't until 2003 that his mind turned from curiosity about the process, to how it might be applied to the needs of people in the marketplace. Enan took stock of his discoveries, and decided this was something that could benefit society while filling a key market niche: green pesticides.

"I looked at everything I had," says Enan, who was then a research professor in biochemistry at Vanderbilt University, where he is still based, "and I decided, this is not just about the science, or about the publication. There is something behind it, and I need to see if I can make something out of it. That's when I decided that this should be a product, not just a publication."

Enan gathered up his things, and went down to Vanderbilt's Office of Technology Transfer and Enterprise Development, where he made his pitch to Brian Laden, who remembers it well.

"It's very unusual that someone would walk in the door here with a technology related to agriculture," says Brian Laden, the university's senior technology commercialization associate, "At Vanderbilt, we don't do much with that. But then, in walks Essam, and he starts telling me this story of how he's come up with some essential oil combinations that are very effective at repelling or killing insects."

Laden was impressed, but skeptical. Together, he and a colleague walked over to Enan's lab, where Enan gave them a little demonstration, by dripping a few drops on a tissue covered with ants, and watching the ants scatter.

Laden was even more impressed, and could see the obvious market possibilities for a benign pesticide that didn't even need to be approved by the Environmental Protection Agency. So they took some of his samples and sent them to an independent lab for testing. "Lo and behold," says Laden, "they were very, very effective, compared to typical products."

Partnering with XL TechGroup

Vanderbilt had already been in touch with XL TechGroup, a Melbourne, Fla.–based company that is publicly traded on London's Alternative Investment Market (the U.K.'s equivalent of the NASDAQ), and that has pioneered what it calls a new "value creation" model, different than the traditional venture capital model. Instead of putting money into a host of promising new technologies and pushing them out into the market, XL TechGroup works with the business community to identify needs that exist in the current marketplace. XL TechGroup then scours university systems and other technology sources looking for technology platforms that can meet those needs. When they find such technologies, they build companies based on them. It's a model that has proven remarkably successful.

When XL TechGroup was alerted to Enan's oils by Vanderbilt's Technology Transfer office, according to senior vice president Harold Gubnitsky, they liked what they saw: a technology platform, an innovation, with massive development potential to do everything from revolutionizing agriculture to stamping out intestinal parasites, to making our barbeques that much more pleasant.

As it happens, just when Enan was getting his oils tested and verified, the demand for "green pesticides" began to grow in Europe. Under strict new environmental laws, traditional

pesticides were being banned by the hundreds. Clearly, there was market demand in Europe and elsewhere for environmentally friendly pesticides, and XL TechGroup could help bring Enan's laboratory discovery to consumers around the world.

Laden and his colleagues, Tom Noland and Christopher Rand, sat down with Gubnitsky and others at XL TechGroup to negotiate the formation of a company called TyraTech in June 2004. In exchange for an equity stake in the company for Vanderbilt, the technology was given to Tyratech, which would take responsibility for developing the technology into marketable products. Then the XL Techgroup, which founded TyraTech, began cultivating partnerships with large companies like Scotts Miracle-Gro, Kraft Foods, Syngenta, Arysta LifeScience and others to fund the development of the various essential oil products. These companies are currently in the process of developing (or have developed) products that can kill bedbugs, lice, mosquito larvae, cockroaches and other pests. They are also working on agricultural pesticides, and a variety of other applications. One of the more surprising developments is the possibility that Enan's oils could help to eradicate intestinal parasites. Since essential plant oils have no effect on humans, the company has developed a range of combinations that target the so-called *Helminths* that plague many areas in developing countries where water quality and sanitation are a persistent problem.

After three years of building partnerships and growing the technology from its initial platform, TyraTech went public in June 2007, on London's AIM. The company had a first-day market capitalization of $219 million, before its products have even gone on sale. XL TechGroup expects this to increase significantly over the next several years.

> "The ultimate goal for any scientist is to translate your science into something people can benefit from."
>
> *Essam Enan, Ph.D., Vanderbilt University*

Needless to say, all of this is immensely gratifying for Enan, who has made a power failure into a powerful idea that will have a real impact on the world. That is all he ever wanted.

"The ultimate goal for any scientist," Enan says, "is to translate your science into something people can benefit from. Besides the publicity, besides all of that, what will really give you satisfaction is to see the community benefit from it."

Cleaning up the Environment Faster and More Cost-Effectively

Chapter 13

Lehigh Nanotech LLC develops nanoscale iron products for toxic and hazardous environmental remediation, based on innovative and patented technology first developed by Lehigh University professor Wei-xian Zhang.

Lehigh Nanotech offers cost-effective solutions for a range of environmental cleanup projects, such as this one.

Photo courtesy of Lehigh Nanotech LLC

Tiny, ultrafine particles of pure iron are making a big difference in aiding environmental cleanup and helping make the world a better place.

This critical progress in environmental restoration is due to technology that was pioneered and invented at Lehigh University, Bethlehem, Pa. Huge rewards sometimes come in tiny shapes and sizes, and Lehigh Nanotech LLC, which produces the nanoscale particles, is making that happen. It only takes six ounces of the tiny nanomaterials, versus a ton of larger compounds, to make sweeping changes in cleaning up contaminated environments.

This revolutionary breakthrough in nanotechnology is helping clean up hazardous waste sites and toxic industrial sites faster and more economically than ever before.

Throughout the United States numerous industrial sites have toxic contaminants in the soil and groundwater. And while environmental remediation is a logical solution to improving the environment, cleanup is often extremely costly and exceedingly time consuming. It can take many years to transform the environment from a previously unusable site to one that is free of contaminants.

Technology invented at Lehigh University is successfully cleaning up a wide range of soil and groundwater sites with toxic materials, heavy metals, fertilizers and pesticides in about a tenth of the time of typical environmental remediation.

This is how the technology, using nanoparticles comprised of pure iron, works to clean up contaminated sites. The particles are so small they remain suspended in water. When they are injected into contaminated groundwater, the iron reacts with contaminants. Paul Osimo, who has more than 25 years of experience in the environmental field as both a consultant and a client, and serves as vice president of the new company, explains, "The complex molecules of chlorinated hydrocarbons, such as industrial degreasers and chemical solvents are broken apart into simple, non-toxic compounds and the iron combines with oxygen and turns to rust. The quantity of iron injected is relatively small compared to the amount of iron which occurs naturally in soils."

Since environmental remediation has a history of arduous, expensive cleanup, many cities are not receptive to bringing in new industry. Yatin Karpe, senior manager of technology transfer at Lehigh University says, "Some cities are simply unwilling to welcome new industry into the area due to a history of pollution and the long, expensive road to cleanup when industry leaves. But now Lehigh Nanotech's products, using technology developed at the university, is changing that direction."

Environmental remediation is a worldwide issue that will continue to be needed as the world's population continues to grow and industry expands. World population is expected to increase to approximately 7.2

billion people by 2015, and about 95 percent of that increase is expected to be in developing areas of the world. Additionally, about 70 percent of the world's industrial wastes in developing countries are discharged into water supplies without treatment, often resulting in pollution.

A Better Way to Clean Up the Environment

Twelve years ago, Wei-xian Zhang, Ph.D., associate professor of civil and environmental engineering at Lehigh, began his research on the use of iron particles for removing hazardous waste contaminants like explosives and highly toxic material from the soil and groundwater. About four years later, he began working with nanoparticles. Ultimately, Zhang successfully developed nanotechnology that uses less energy more efficiently and at a fraction of the cost of expensive pump and treatment procedures to clean up polluted sites.

The Lehigh Nanotech nanoiron, which is composed almost totally of ultrafine iron particles, is injected into the contaminated groundwater area by gravity or through pressure. It remains in the groundwater for long periods of time attacking contaminants like chlorinated hydrocarbons and pesticides.

Zhang's research regarding contaminated groundwater has been seen as unique in more ways than one and has received support and recognition from the U.S. Environmental Protection Agency (EPA), the National Science Foundation and other agencies. Karpe explains that Zhang's work in the field of nanoparticles is an extraordinary accomplishment. His work has been featured in a wide range of media including academic publications such as *Technology Review, Environmental Science and Technology, Chemical and Engineering News,* and major newspapers, TV and radio outlets.

"Recently, published reports from the University of Pennsylvania show there are about 120 scientific publications in the field of nanotechnology for every three patents issued, and for about every one product developed," says Osimo.

Collaboration Leads to a Startup

Lehigh Nanotech hit the ground running, selling products just four months after it was founded in 2006. But the path to success did not occur overnight. A crescendo of collaboration between the university, the private sector and the state preceded its marketplace debut.

Lehigh University's School of Engineering and Environmental Science had long attracted industry

An injection setup for nanoiron slurry.

due to its history of innovation. It didn't take long for industry to react to Zhang's work with nanoparticles for environmental remediation.

"When we read about professor Zhang's work in publications, abstracts and conference papers, we made our first contact with the university," says Osimo. Karpe notes, "Professor Zhang's research was promoted by two Lehigh University innovation seed grants and a Keystone Innovation Zone (KIZ) grant. The resulting company, Lehigh Nanotech LLC, came about through efforts of the Office of Technology Transfer, was an extensive collaborative venture between the university, the startup company, and the Pennsylvania Department of Community and Economic Development that funds KIZ programs."

Lehigh Nanotech also received funds from the Ben Franklin Technology Partners (BFTP), and the Lehigh Valley Economic Development Corporation provided grants to assist production and control procedures.

Osimo says, "A year after professor Zhang and Lehigh University filed a patent application to protect his technology, we had established a company, licensed the technology from the university and were producing and selling a product."

Osimo credits the expertise of the Technology Transfer Office at Lehigh University in quickly and successfully negotiating the necessary licensing agreements with the startup company, Lehigh Nanotech LLC.

"Lehigh's technology transfer office was technically efficient and helped make the process work smoothly," says Osimo. "Once the company was established, it was a challenging and exciting time. We had several product orders before we even opened our doors. Even as we were getting the electrical system in the production facility completed, orders were coming in!"

A True Success Story

The collaboration has proven to be an enormous success. "The technology that originated with professor Zhang's research has been successful not only for the university but also for the state of Pennsylvania," says Thomas Meischeid, director of Research & Sponsored Programs, and interim director for the Office of Technology Transfer at Lehigh University.

No toxic chemicals are used in the production of Lehigh Nanotech's nanoscale iron products, which have been used for environmental remediation projects by the federal, state and local governments, as well as for projects in the private sector.

The following is an example of how Lehigh Nanotech nanoscale iron products are helping make the world a better place. For several years, the owner of a former industrial manufacturing site in Ohio was paying to operate a pump and treat the system. But when the company's engineering consultant learned of Lehigh Nanotech's nanoiron, Lehigh was brought in and was able to achieve complete elimination of the serious contaminant in the groundwater in the treated area in

only a few weeks time. Additionally, a full-scale remediation is planned for early 2008.

At another site in New Jersey nanoiron is being used to treat chromium contaminated wastes known as COPR (chrome ore processing residue), which is left over from industrial production in the 1940s, 1950s and 1960s. Nanoiron is being used to stop the leaching of hexavalent chromium from contaminated soils into the groundwater.

Osimo says, "This is breakthrough technology and it affects every consumer. Currently, the technology is being used to treat groundwater where industrial leaks and discharges have contaminated drinking water supplies. At hazardous waste sites, it can take 10 to 20 years to clean up. These small nanoparticles are solving big problems. They allow us to clean up a toxic site in less than a year. This is a huge breakthrough."

Behind the scenes, Zhang's technology led to widespread collaboration among the university, companies and Pennsylvania state agencies in order to make Lehigh Nanotech's products available. The university and affiliated regional organizations such as the Lehigh Valley Small Business Development Corp. and the Ben Franklin Technology Partners were instrumental in getting Lehigh Nanotech in front of the Secretary of the Pennsylvania Department of Environmental Protection and other state and regional agencies who could utilize the technology at sites throughout the state.

And Lehigh Nanotech's partnership with the university continues to grow stronger and stronger. Since Zhang was well-known regarding his scientific and technical symposiums, Lehigh Nanotech has arranged meetings for a potential client, who was considering various technological approaches to treat contaminated groundwater at industrial sites, to visit the laboratory and meet the professor.

Osimo says, "This dialogue helped Lehigh Nanotech be more responsive to the client, and allowed the client to have a greater confidence that the product would do the job."

Osimo says, "Moreover, as we continue to look for ways to produce more materials on the nanoscale, we will create products that allow development of more efficient and less expensive solar panels, heat transfer materials, and many other products that reduce energy consumption and improve the environment."

Undoubtedly for areas in the world where environmental cleanup is not being done because of the high cost and time it takes to treat contaminated sites, Lehigh University's technology will become even more beneficial.

Meischeid adds, "Lehigh Nanotech's products manufactured in Bethlehem, Pennsylvania, will continue to impact the world environment."

FluMist® Reshapes the Fight Against Flu

Chapter 14

A University of Michigan public health researcher devoted his lifetime to developing the vaccine that led to FluMist®, the first and only nasal spray flu vaccine in the U.S. marketplace.

A healthcare provider administers FluMist® (Influenza Virus Vaccine Live, Intranasal) to a seven-year-old girl. For information on indications and usage, dosage and administration, as well as safety information, please see www.flumist.com.

Photo courtesy of MedImmune

Many children, as well as adults, cringe at getting an annual flu shot. But now, with the development of FluMist®, there is a needle-free, highly beneficial alternative to getting a shot in the arm.

FluMist®, which has been available in the United States since 2003, is a trailblazer in the annals of flu prevention. The research behind its innovation spanned seven presidencies, but for millions of people nationwide, the nasal spray vaccine, which has its origins in research at the University of Michigan, was well worth the wait.

While many viruses can make people moderately ill, true influenza can cause serious illness. The Centers for Disease Control and Prevention point out that each year more than 200,000 people are hospitalized with flu complications and about 36,000 people die from the flu.

Since the flu virus mutates and changes quickly, prevention is an ever-challenging issue. FluMist® has demonstrated protection against both matched and drifted strains of the flu. "That alone makes this product vastly different," explains James Young, Ph.D., president of research and development at MedImmune, the company that manufacturers the vaccine.

Flu shots have been around since World War II, but it wasn't until 2003, when FluMist® first became available, that the world had an alternative. That's when the Food and Drug Administration (FDA) approved the new nasal spray vaccine for healthy people between the ages of five and 49 who are not pregnant.

Recently, the FDA approved FluMist® for children between the ages of two and five years. MedImmune also has developed a new refrigerated version of the vaccine, which was first available in the 2007/2008 flu season. Freezer storage is no longer needed as it was during the first four flu seasons the nasal spray was on the market. Young says, "It was more difficult to transport it to schools or other sites, but now, because it's available as a refrigerated product, we anticipate that it will have higher usage."

For those who wonder why the vaccine was developed as a nasal spray, Hunein "John" Maassab, FluMist's® inventor and professor of epidemiology at the University of Michigan, has the answer. The vaccine, which contains three live (weakened) flu viruses, stimulates the body's immune system to develop protective antibodies. Maassab says, "The viruses, which are attenuated, cold-adapted, and temperature sensitive, can grow in the nose but not in the lower respiratory system and in the lungs where the body's temperature is warmer."

Maassab further explains that the cold-adapted live vaccine has shown to be highly successful in warding off the flu. "As the virus mutates, it becomes temperature-sensitive," he says. "The weakened virus used in FluMist®, which does not cause the flu, will not grow well at higher temperatures in the lungs."

Since flu is transmitted from one person to another as an airborne pathogen, the nose is a logical place to stop the virus where it enters the body. Maassab adds, "By squirting the vaccine in the nose it induces a more complete, broader immune response."

University-Business Collaboration

In 1955, Maassab, a public health graduate student, was in the audience at the University of Michigan, Ann Arbor, when Dr. Thomas Francis, Jr., Dr. Jonas Salk's teacher and mentor, announced that the polio vaccine developed by Salk was safe and effective. Maassab, who was born in Damascus, Syria, in 1926, was young enough to have heard about the accounts of the pandemic flu of 1918, designated the Spanish Flu. The devastating outbreak was responsible for the deaths of more than 20 million people throughout the world.

Maassab's interest in developing a vaccine for the nasal passages became his life's work. By 1960, he had isolated the "A" Ann Arbor influenza virus, which he used to create the cold-adapted live influenza virus. Over the next 20 years, he worked with scientists at the Laboratory of Infectious Diseases in the National Institute of Allergy and Infectious Diseases in Bethesda, Md. refining the cold-adapted virus.

In the late-1970s and early 1980s the National Institutes of Health funded clinical trials to test the efficacy of the new vaccine. In 1995, the University of Michigan licensed the vaccine technology to Aviron, a biopharmaceutical company.

Partnering with Aviron and later MedImmune, after its purchase of Aviron, researchers at the University of Michigan provided information from earlier research studies and materials from the University of Michigan School of Public Health laboratories to assist with the commercialization efforts. By 1997, the vaccine was proven effective in a major study in children at 10 centers throughout the United States.

In 2003, the FDA approved FluMist® as a nasal spray commercially available through MedImmune Vaccines, Inc., a wholly owned subsidiary of MedImmune, Inc. Dr. Maassab's dream, to develop an effective flu vaccine without the need for needle injection, was becoming a reality due to his pioneering efforts and the collaboration among Aviron, MedImmune and the University of Michigan.

First Line of Defense

Since preschoolers and school-age children are often considered the vectors in transmitting the flu, one important strategy in reducing its spread is to vaccinate this age group.

Robert Belshe, M.D., professor of medicine and pediatrics at Saint Louis University School of Medicine in St. Louis, was the lead investigator on the pivotal pediatric FluMist® trial. This trial was key to the recent expanded approval of FluMist® for use in children as young as two years. The double-blind study included approximately 8,500 children between six months and five years of age in 16 countries at 249 sites. The study was conducted between 2004 and 2005 and published in 2007.

"It was the biggest influenza vaccine trial ever done with children," Belshe comments.

For the 2006-2007 influenza season, MedImmune made about 3 million doses of FluMist®. Now, with the approval for FluMist® use with children as young as two, Young says, "We intend to make approximately 4.5 million doses this year."

MedImmune has invested about $2 billion in FluMist® since commercializing the technology. Young points out, "Based on current data, there may be an increased cost savings to communities who vaccinate more people. Fewer parents may need to stay home from work, and fewer children may have to stay home from school."

By some estimates, over 1.5 million work days are lost in a single year due to the flu. Research published in December 2006 in the *New England Journal of Medicine* showed that school-based influenza vaccination programs using FluMist® may represent an effective and feasible strategy to help lessen the impact of seasonal influenza on households and communities.

In this study, researchers found that households with children who attended schools with influenza vaccination programs reported missing approximately two fewer school days per 100 school days during the flu season (4.34 vs. 6.63 days) than households with students in schools without programs. While not statistically significant, there was a trend toward adults missing fewer workdays due to being ill or staying home to care for a sick child.

As more pediatricians choose FluMist® during the flu season, there is the potential for an even greater effect on fighting the flu.

Belshe sees new applications for the technology ahead. Instead of going to the flu clinic or medical clinic to receive FluMist®, he envisions vaccination centers where people congregate.

Although FluMist® is not right for everyone and proper screening is necessary, Belshe says, "There may come a day when you'll see the vaccine available at kiosks at shopping malls. FluMist® has changed the world of public health. It's easy to give — no special skills are needed to administer the nasal spray, and children and parents love it."

And there is nothing like it in the U.S. marketplace. That fact alone is remarkable, but when coupled with the astonishing talent, vision and scientific strides that took 40 years of research to bring FluMist® to market, it could be called a medical marvel. The collaborative work between university research and industry has opened the door to a brand new way of helping protect people from debilitating flu.

For important safety information and additional facts about FluMist®, visit www.flumist.com

Improving One of the World's Oldest Inventions

Chapter 15

Ultreo® is the only power toothbrush to combine patented ultrasound waveguide technology with precisely tuned sonic bristle action.

An exploration of new applications for medical ultrasound led to the latest innovation in oral health care – the Ultreo® ultrasonic toothbrush.

When is a toothbrush *not* a toothbrush?

When it's an ultrasonic device that propels thousands of tiny bubbles, pulsing at high speeds and providing a long-lasting feeling of clean.

In a feat of collaboration that involved medical physicists, periodontists, pediatric dentists and public health specialists at the University of Washington (UW), and a businessman known for a Midas touch with oral health care products, the device, now known as the Ultreo toothbrush, was born.

Like many great ideas, the brainchild hatched while its inventor was thinking of something else.

As a medical physicist, Pierre Mourad had spent much of his career considering the unlimited potential of ultrasound technology in medicine. These tools harness the energy of sound waves that have a frequency of greater than 15-20 kHz — above the range of human hearing.

While most of us know ultrasound as a way to view the inner workings of the human body, Mourad was looking beyond that. Fascinated by the mechanical aspects of bubbles, he had been considering how ultrasound might work with bubbles to help clean the mouth.

About the same time, Jack Gallagher, an angel investor, was invited to the UW Medical School on the Seattle campus. He had been asked to evaluate an investment in a novel ultrasound technique that would provide neurosurgeons with a minimally invasive means of measuring deadly swelling in the brain.

Mourad, also a research associate professor in the UW department of neurological surgery, had developed this brain monitoring technique. Although Gallagher passed on the technology, he clicked with Mourad, and the two soon began exploring how they might use ultrasound waves to make a better toothbrush.

Teamwork Leads to Great Results

With initial funding from Gallagher and other angel investors, and a boost from the Washington Technology Center, the new toothbrush was created. Mourad and his colleagues at the Applied Physics Lab conducted extensive development research and, with assistance from periodontists, pediatric dentists and public health specialists, tested his concept. The team, augmented with staff scientists, eventually garnered three research grants from the state and two from the National Institutes of Health, totaling almost $2 million. Clinical studies ensued, proving the Ultreo toothbrush removed up to 95 percent of hard-to-reach plaque in the very first minute of brushing.

"We wanted to employ ultrasound to create a toothbrush that was truly efficacious," says Gallagher, former president of Optiva, the company that brought the Sonicare toothbrush to the world. "We had no idea if it would work — but if it did, it would be uniquely differentiated."

A Closer Look at the Toothbrush

In case you think the toothbrush you use now is adequate, Mourad, referring to published studies, says traditional brushes leave behind about 50 percent

of the plaque that's found on teeth. Plaque is the sticky film you can sometimes feel on your teeth between brushings, which can lead to the buildup of tartar. It's literally a "biofilm" made of bacteria that can, over time, cause cavities and gum disease.

Numerous studies have shown a link between oral health and general health. The 2006 Surgeon General's Report on Oral Health says gum disease may be a risk factor for health complications such as heart disease, diabetes and premature births. Gum disease has been correlated with a decrease in immune system efficiency and problems as serious as arteriosclerosis, a hardening of the arteries that causes cardiovascular disease.

Historians believe the first toothbrush was created in China more than 3,000 years ago, when someone plucked a few coarse bristles off a wild pig and tied them to a piece of bone to clean their teeth. Aside from the materials, the basic elements of the brush have remained the same over the years, and just recently the toothbrush was chosen as the one invention Americans could not live without according to the Lemelson-MIT Invention Index, beating out the automobile, the telephone and the computer.

Ultreo: The Next Wave in Dental Hygiene

The latest development in personal oral health care came about in 1959, when the power toothbrush was introduced and launched into the world marketplace the following year. More recently, companies have developed high-speed brushes that have been touted by consumer advocates, recommended by dentists, and endorsed by the American Dental Association.

And then came Ultreo.

"While other power toothbrushes have high-speed bristle motion, they don't have ultrasound," says Gallagher. "Only Ultreo has ultrasound waveguide technology."

The key advantage of the Ultreo over any other power toothbrush is its use of a patented "ultrasound waveguide" to transform plain bubbles into bubbles pulsating with ultrasound energy.

According to Lisa Norton, licensing officer with UW TechTransfer, the ultrasound waveguide enables the ultrasound to activate the bubbles, causing them to pulsate and provide a long lasting feeling of clean.

First disclosed to UW TechTransfer in 2003 and licensed by Ultreo in 2004, the company now has seven U.S. and international patents and eight patents pending, proving the novelty of the instrument and its benefits over existing technologies. The company has attracted more than $23 million in private investments, many from dentists and alumni of the UW dental school. The toothbrush, which costs around $169, is sold at Sharper Image, and online retailers such as Amazon.com and Drugstore.com.

High-Tech Partnership Yields Technological Innovations for Our Aging Population

Chapter 16

Researchers at the Oregon Health and Science University and Intel have teamed up on high-tech research that should enhance independent living and provide early clues to diseases such as Alzheimer's, Parkinson's and others.

Elly Steacy uses the Medtracker — a pillbox that tracks medication adherence.

Photo courtesy of Tamara Hayes, Ph.D.

Portland resident Pat Graves has literally opened her home to the digital age.

That's because her house is outfitted with tiny sensors that track her movements and behavior, as part of a special research project jointly conducted by the Oregon Health and Science University (OHSU) and Intel.

Graves, who is 77, is optimistic that the data gathered from the study will contribute to greater understanding of diseases and health issues affecting the elderly.

"If not me, it should help the baby boomers down the road," quips Graves, who says she has the spirit of a 45-year-old. "And I have grandchildren and a great grandchild who I believe will benefit, too. But in any case, helping science is a good thing to do."

Graves has been involved since early 2007 in this longitudinal research effort coordinated by the OHSU's interdisciplinary Oregon Center for Aging & Technology (ORCATECH), which is directed by OHSU neurologist Dr. Jeffrey Kaye. ORCATECH has been supported since 2004 by federal agencies, including the National Institutes of Health and the National Institute on Aging.

In October 2006, Intel's Digital Health Group signed a three-year, $3 million collaboration agreement with OHSU called the Behavioral Assessment and Intervention Commons (BAIC). The alliance with OHSU is designed to initiate and accelerate research into behavioral markers of disease, such as changes in walking and performance on computer games. The research should eventually translate into health-related products, services and personalized medicine.

The collaboration between Intel and the university is unique because Intel recognizes the value of a university research partner. "We are inquiry-driven, not product-driven, and we need to publish our research. Intel not only understands that but they value it," says Kristin Rencher, a licensing associate in the Office of Technology and Research Collaborations at OHSU. "They are keen to see us publish and recognize the power of scientific publications in enabling the adoption process of health technologies."

Arundeep Pradhan, director of the Office of Technology and Research Collaborations at OHSU praises the BAIC and says it "represents an emerging model for creating university-industry collaborations in the appropriate context."

"Because of the size of the market we expect that the collaboration will result in products, but that is not the focus. We didn't walk into negotiations with the expectation of royalties," he says. "For us the bottom line is creating a partnership that furthers the research."

Signing up her Friends

Graves notes proudly that she was the third or fourth person to enroll in the BAIC project.

"I thought it was such an admirable thing that I got several of my friends to sign up too," adds Graves, who is a semi-retired communications coach.

As part of the project, OHSU and Intel researchers placed dozens of sensors around Graves' home to track her daily movements around the clock. The resulting data will provide hints of changes in the heart and lung diseases from which she suffers or, detect early indications of Alzheimer's disease, should they arise.

"These sensors are throughout the house," she says. "On the doors, along the walls and attached to my refrigerator. I even have a special pillbox that pays attention to when I take my vitamins."

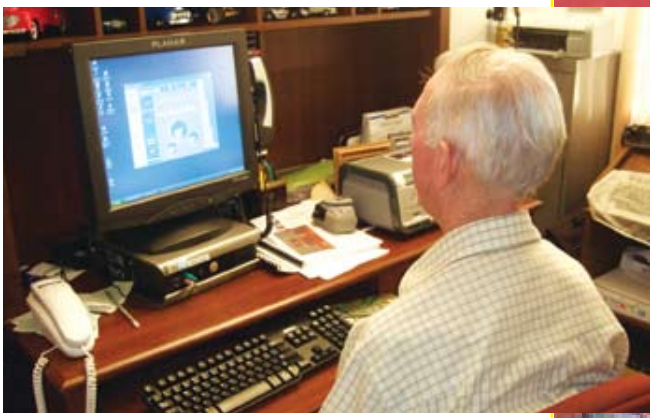
In addition, she wears a belt one week a month that monitors her physical movements. She also has a cell phone with a global positioning system to track her whereabouts when she leaves her home.

On Monday mornings, Graves gets an automated call to remind her to take a memory test on a computer provided by Intel. In addition to the quiz, she is asked questions about her health status, including if she has fallen, changed her medicines or even if she has moved her furniture — the latter being important because it could affect how the sensors function.

"They say they are trying not to overwhelm me with too much technology, but I find this sort of stuff fascinating" she says. "How they think up and implement all these things is beyond me."

Tamara Hayes, assistant professor of biomedical engineering at the OHSU School of Science and Engineering and the BAIC project's lead investigator, says BAIC is a complement to the university's National Institutes of Health-based studies of age-related health outcomes.

"It will allow us to make significant progress in developing continuous assessment and in-home technologies that have clinical relevance," she says. "The initial living lab of homes that were funded in 2005 allowed us to test out technologies and make sure we were ready to go forward with Intel and BAIC."



Brent Steacy plays letter lotto.

Photo courtesy of Tamara Hayes, Ph.D.

She said Intel chose OHSU because it is "able to deliver critical information for the development of truly useful independent living technology. They could come up with products and solutions that they think will work. But with no way to test them on patients there is no guarantee they will hit the mark."

In addition to the core set of sensors, she said some participants wear radio frequency identification (RFID) tags, so the monitors will know who is moving about the house when guests are in the home.

> "There are 600 million people on this earth who are over the age of 65 today. That will double to 1.2 billion by 2025, then double again in the next 20 years."
>
> *Eric Dishman, Intel*

Other components include coaching and intervention to encourage individuals to take their medications. "Right now, we are creating algorithms based on our data that will tell us the right time to prompt patients to take their medications," she says.

And there are also games to keep their minds alert and to be used as ongoing assessment tools by recording changes in how well the seniors score when playing the games.

Hayes said it has been remarkably easy to get people to sign up for the program. "They realize this is a good project and they want to help," she says.

A Marriage of Research Interests Benefiting the Elderly

The way Eric Dishman, general manager of product research and incubation at Intel's Digital Health Group, remembers it, the collaboration with OHSU began about seven years ago. That was shortly after he was hired.

"This was before there was a Digital Health Group here and before ORCATECH existed," he said.

But over time, the two entities moved from what Dishman calls "dating to full-on marriage," an arrangement that was more or less consummated with the $3 million BAIC grant.

Back in 2002, before the nuptials, Intel's Research Council awarded ORCATECH investigator Misha Pavel, an OHSU professor of biomedical engineering, a small seed grant to get things off the ground.

Pavel directs ORCATECH's Point of Care Lab, where many of these devices are developed and tested prior to their deployment in homes. He says refining devices such as games will help seniors maintain their cognitive abilities, much as physical exercise helps to maintain physical condition.

Dishman notes that while the studies are focused on seniors, other populations can benefit from the research.

"I get about 500 phone calls a month from families with autistic children who have seen prototypes from the research that we have done on people with Alzheimer's," he says. "And they say they need these same kinds of capabilities."

Dishman said the market potential for products to aid independent living is huge and growing fast.

"There are 600 million people on this earth who are over the age of 65 today," he says. "That will double to 1.2 billion by 2025, then double again in the next 20 years, so there is an enormous market opportunity because many people who are 65 and older have multiple chronic conditions.

"And the 80-year-old plus category is the fastest-growing worldwide.

Sadly, half of all 80 -year-olds will have some type of dementia by the time they are 85. There is an enormous potential for a home health platform that would better allow people to manage their own health and welfare as well as provide early warning systems through looking at behavioral and biological changes. It's a market worth potentially hundreds of billions of dollars."

But before any products can be sold, he says the underlying technologies need to be put through large-scale, longitudinal studies.

"The whole ORCATECH thing is about how we bring scale to this effort," he says. "We can't just test in dozens of households. We are testing in hundreds and then thousands of homes so we can look at statistical trends of both large populations and individuals.

"This effort will bring scientific rigor to the field of behavioral biomarkers. Genetic biomarkers show we might be biologically at risk for a condition. Behavioral biomarkers are ways of measuring and monitoring behavior using technology to show the early detection or onset of a disease."

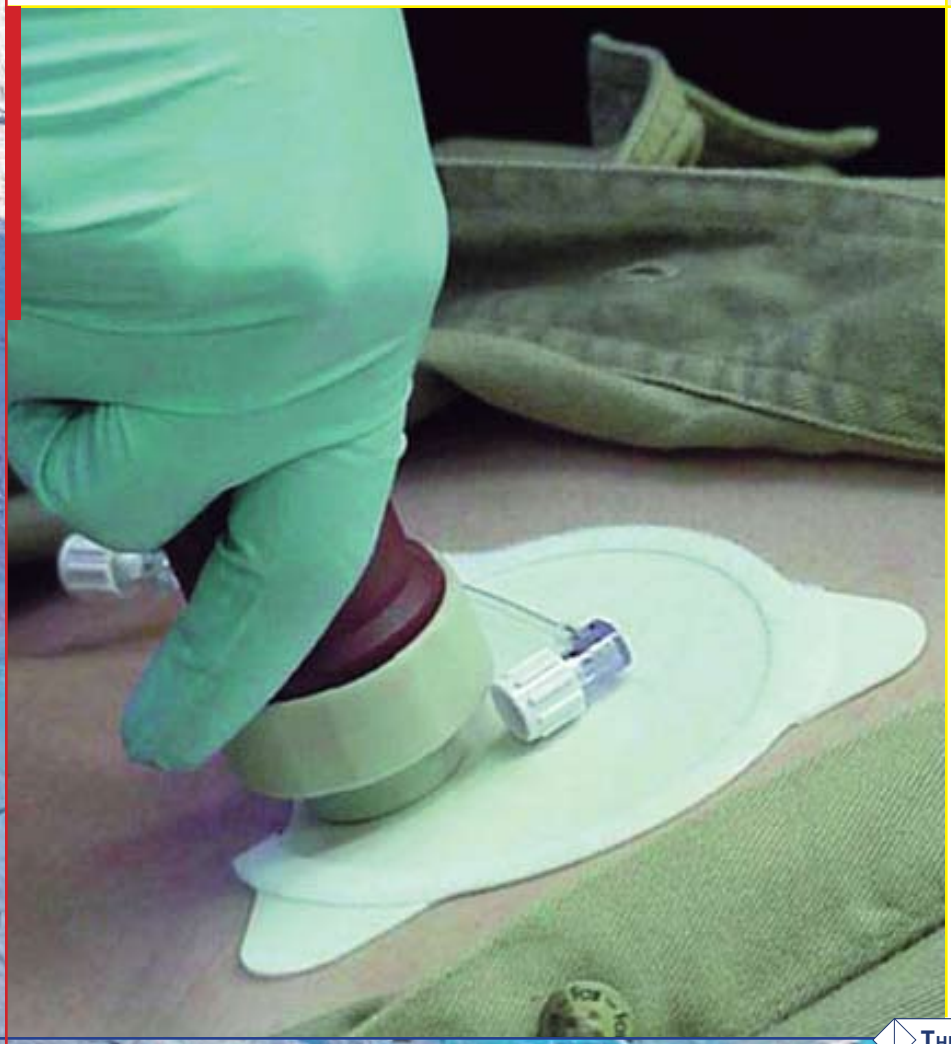
Dishman says the BAIC program will increase national attention around behavioral biomarkers, not just their medical counterparts.

"You combine the two and you can start to do some pretty powerful stuff," he says.

"If you have a genetic biomarker that says you are at risk for Alzheimer's and you combine it with behavioral biomarkers that look for subtle changes of everything from how you talk to how you walk, then you start to have a much better early warning system and even the ability to intervene before the disease unfolds fully."

Innovative Resuscitation System Saves Lives in Critical Patient Care

Chapter 17



The FAST1™ Intraosseous Infusion System, commercialized by Pyng Medical Corp., uses technology invented by Pyng Medical with the support of British Columbia Institute of Technology, to deliver drugs and fluids into the sternum in less than 30 seconds, much faster than traditional IV access.

The FAST1™ is only device able to provide access within seconds to get drugs and fluids to the heart of someone who is critically injured.

Seconds can mean the difference between life and death in medical emergencies. Trauma patients in car accidents, life-threatening situations at home, on battlefields, or on ambulance crash carts and in hospitals, need life-saving medicine and fluids, and they need them fast. But sometimes administering intravenous (IV) drugs and fluids rapidly and reliably is not possible.

When Veins Collapse

When patients receive serious injuries, or experience health emergencies such as cardiac arrest, the body starts to shut down and the person's veins become smaller and more difficult to access. Even with the most skilled provider, it can take precious time to thread a catheter into a peripheral vein in the arm or leg before the vein becomes flat and inaccessible. The FAST1™ technology, invented by Pyng Medical with the support of British Columbia Institute of Technology (BCIT), allows drugs and fluids to be administered directly into the sternum through the intraosseous (IO) space, which acts as a non-collapsible route to the heart. It is the only device able to provide access within seconds to get drugs and fluids to the heart of someone who is critically injured. For that reason the FAST1 is used in the battlefields of Iraq and Afghanistan when access to the peripheral veins is not a fast and efficient option.

Jason LeMoine, a fifth-generation firefighter and paramedic at a 21-station fire department in the San Francisco Bay area, and who also works as a registered nurse at a local medical emergency center says, "I have seen patients die when time was not on our side. It was frustrating when we couldn't get IV access to them faster."

But on one particular September day in the San Francisco Bay area, where fiery sunsets and wind-swept beaches are part of the landscape, something even more stunning appeared.

LeMoine, along with a team of firefighters, responded to a report that an 18-year-old was having a seizure. When they arrived, they found the patient was not having a seizure but he was in cardiac arrest. Two bystanders, who were performing CPR, reported that the downtime of the patient was between five and seven minutes. When the fire department arrived, the patient was unconscious and had "flat-lined." "He didn't have a heart rhythm," he says.

Never were the words "time is of the essence" more apparent. Instead of taking valuable time to use traditional IV access when the patient was pulseless, LeMoine, 36, used FAST1™ technology to administer life-saving medication to the patient. "We were able to revive him within five to six minutes," says LeMoine. "When the patient was transported to the hospital, he had a pulse."

Development of Intraosseous Access

While timing and technology saved the life of this patient, this is just one of many successful outcomes due to FAST1™. Numerous stories like this one can be attributed to research conducted by the Health Applied Research and Development group at British Columbia Institute of Technology (BCIT). Judy Findlay and David L. Johnson Ph.D., were the principal inventors of the technology. Technology transfer also was handled by the Health Applied Research and Development group led by Dr. Johnson. Findlay, now the director of BCIT's Health Technology Research Group, says, "This has been a successful collaboration between BCIT and Pyng Medical Corp. The company's flagship product, which has been adopted worldwide, has already saved many lives."

The collaboration between Pyng Medical Corp., based in Richmond, British Columbia, and BCIT began when Michael Jacobs, founder of Pyng, came to BCIT for assistance. Specifically, Pyng needed BCIT's scientific and engineering expertise in helping develop a product that could be used in medical emergencies when IV lines failed or peripheral IVs were difficult to access.

The FAST1™ allows drugs and fluids to be administered directly into the sternum.

Developing technology that can save lives takes an enormous amount of time, patience, and teamwork. FAST1™ development involved in-depth research of adult sternal and vascular anatomy as well in-depth research into the skills, attitudes, and training of users and the unique challenges of pre-hospital environments.

Findlay explains, "It is often assumed that an invention coming out of a university is ready to be manufactured, but that is seldom the case. The invention is really just step one. The solution needs a significant amount of development which may entail a huge risk for the company licensing the product. This is where professional product development comes into play — including developing and meeting design requirements, verification and validation testing, achieving regulatory approvals (in this case by the FDA and Health Canada), and eventually manufacturing, distribution and product launch."

The progression from research to product commercialization for FAST1™ had to do with its unique set of variables. A brilliant idea, as in the case of FAST1™, needs a significant amount

> "People don't often realize the amount of blood, sweat and tears it takes from research to commercialization of products."
>
> *David Christie, Pyng Medical Corp.*

of professional product development before it can be commercialized. With FAST1™, Findlay says, "The first invention that Pyng hoped to market met only five of about 20 necessary top-level design requirements. Once these had been established, BCIT worked with Pyng to develop a product that ultimately met all the necessary performance, safety and regulatory requirements."

Funding for the development of the technology came from Pyng's parent company, Pyng Technologies, from Canadian Federal Government funding sources and from the Science Council of British Columbia. In 1998, the first patent was assigned to Pyng for the "Apparatus for Intraosseous Infusion or Aspiration," followed by a 2004 patent for the "Method and Apparatus for the Intraosseous Introduction of a Device Such as an Infusion Tube."

Pyng's President and CEO David Christie comments, "It takes a bold vision to turn an invention into a business, and entrepreneurial energy and tenacity to get the idea to market. People don't often realize the amount of blood, sweat and tears it takes from research to commercialization of products. It took us more than seven years to develop the product, another three years to develop the market, and three more years to secure true profitability and a sustaining business." From the time Pyng came to BCIT in early 1993, it took until 2001 before the company sold its first product. Christie says, "Today, we have sold over 120,000 units. FAST1™ has likely saved tens of thousands of lives on the battlefield of Iraq and Afghanistan, in motor vehicle accidents, in cases of violent or accidental trauma, and in situations involving cardiac arrests." The company, which has eight patents in eight countries, has 17 employees and annual sales of $4.8 million.

Combat medics and the people they treat in Iraq and Afghanistan have benefited from the FAST1™ technology. Since the late 1970s, many American troops have worn the Kevlar flak vest which protects a person's "body core," that is, the heart, lungs and abdominal area. Battlefield injuries often involve the peripheral areas — a person's arms and legs. Many lives on battlefields have been saved thanks to FAST1™ rapid resuscitation access through the sternum.

Victims of civilian emergencies around the world are also benefiting from the FAST1™. Paramedic LeMoine, who has used FAST1™ with about 15 individuals over two years, says, "It is a fast way to get venous access. It only takes about 60 to 90 seconds to gain vascular access as opposed to standard IV access in a person's limb which typically takes three to 12 minutes, and that's if you even can get access."

IO devices like FAST1™ are now

> "The first few minutes during a medical emergency can mean the difference between life and death, which is why this is an excellent advancement in pre-hospital care."
>
> *Jason LeMoine, San Francisco firefighter and paramedic*

recognized as the first-in-line, safe and effective alternative when IV access is not an available route to deliver life-saving drugs and medicine. Recently, the American Heart Association made a historic recommendation when it revised its guidelines for Advanced Cardiac Life Support (ACLS) and recommended IO devices, which include FAST1™, as the first alternative for adults in cardiac arrest. At the same time the International Liaison Committee on Resuscitation (ILCOR) recommended IO access be used for adults and pediatric patients as a first alternative in life-threatening situations. Since FAST1™ was first developed, other IO devices have entered the marketplace.

Today, Pyng has started the development of the next generation of FAST1™, and complementary devices.

"In the face of the ever-changing role of emergency medical service and the evolution of our medical products, we anticipate an even broader use of FAST1™ technology," says Christie.

LeMoine adds, "FAST1™ has saved numerous lives and will save many more. The first few minutes during a medical emergency can mean the difference between life and death, which is why this is an excellent advancement in pre-hospital care."

Robotic Technology Helps Patients with Neurological Injuries Walk Again

Chapter 18

Using technology developed by researchers at the University of Zurich, Hocoma Co. created the Lokomat, the world's first robotic device that automates locomotion therapy on a treadmill and improves the efficiency of treadmill training.

Lokomat therapy of a spinal cord injury patient at the Swiss Paraplegic Center, Nottwil, Switzerland.

In her early days as a physical therapist, Candy Tefertiller says some patients were, figuratively, "left by the wayside."

That's because clinicians could not figure out a way to get patients upright and moving their legs on a treadmill without hurting themselves — or the therapist working with them.

That changed when her facility, the Shepherd Center in Atlanta, got a Lokomat — a robotic device that automates locomotor treadmill therapy. Patients essentially slip into an exoskeleton that supports their legs and off they go.

The device is made by a Swiss company called Hocoma. Appropriately, its motto is "We Move You."

Big Improvement Over Manual Training

"The biggest difference in having the Lokomat is knowing that no matter what the person's size is, within reason, or degree of debility or weakness, I will be able to get him or her upright and moving," says Tefertiller, who is the clinical program director for Beyond Therapy and Multiple Sclerosis at the Shepherd Center, which obtained a Lokomat around two years ago.

Prior to that, patients underwent rehabilitation training on a treadmill where they were supported in a sling and therapists manually assisted the clients in moving their legs in the appropriate walking pattern.

If the patients exhibited significant spasticity — involuntary contraction/movement of the legs — manual locomotor training can be difficult, and is often not a very good tool for these patients, says Tefertiller, a therapist for almost eight years.

"I'm very thankful to have the Lokomat," she says.

Beyond Therapy is a rigorous, activity-based program designed to help people with neurological disorders, including spinal cord injury, improve their lifelong health, minimize secondary complications and get the most out of any new neural links to their muscles.

"For many patients with stroke, traumatic brain or incomplete spinal cord injury, it's a great way to get them moving and attempt to reintegrate their nervous system," she says. "It helps them remember how to walk and goes through the same type of motor patterns that you and I do every day. It is essentially designed to re-teach their bodies to walk again."

A Promising New Technology and the Birth of a New Company

The Lokomat is the brainchild of Gery Colombo and two partners, fellow biomedical engineer Matthias Jörg and economist Peter Hostettler. Hocoma is a combination of the trio's nicknames. They came up with the moniker when they were undergraduates in the middle 1980s.

Colombo is an electrical engineer who focused on biomedical technology in his studies at the Federal Institute of Technology in Zurich. Working primarily with incomplete spinal cord injury patients who have some feeling and motor control below their injuries, he looked into ways to improve their therapies.

"It was around 1995, and my team had the idea to develop a robot that could do manual treadmill training automatically," says Colombo, the company's chief executive officer.

In manually assisted treadmill training, a patient is suspended in a harness over a treadmill and two physical therapists are moving the legs of the patient while he is doing the training to relearn how to walk.

"Being an engineer, I had the idea that this could be done by a robot instead of two physical therapists. The robot is an exoskeleton that is worn by the patient," says Colombo, who co-founded Hocoma with the two colleagues to fund the engineering work on the device.

"It was a dream back then," Colombo muses. "We had a small project idea and thought we were geniuses. Funny that 10 years later we were really able to create something and use that name."

Since its launch in 2000, Hocoma has sold 130 Lokomats for clinics in 28 countries at a cost of around $200,000 each. Hocoma now has approximately 70 employees in Zurich and at a subsidiary in the United States. Hocoma, Colombo notes, was launched as a private company in 1996, but the three founders worked for free for the next four years on its development. In 2000, it raised about $375,000 from private shareholders to hire staff and head down the commercialization road.

In one of the more recent developments, the company is adding feedback to measure the interaction of patients and the machine.

"We can then display how much the patient is participating during the training," Colombo says. "And to make it more interesting, because treadmill work can be boring, we are adding a virtual environment program. It could be a virtual forest, subway or train station, and the patient, with his activity in the machine, can control how he is moving through this virtual environment. If the patient pushes harder, he will walk faster."

Teaming up with Other Researchers

In addition to the Lokomat, which is for adults, Hocoma has a smaller version for children as well as another device that helps retrain severely weakened arms. The latter technology, for a device called Armeo, is the result of research led by David Reinkensmeyer, a professor in the mechanical and aerospace engineering department at the University of California, Irvine.

The key to the Armeo, Colombo says, is that it supports the arm with an exoskeleton featuring a spring mechanism that unloads the weight of the limb.

"For a healthy person, it's easy to lift the arm," he says. "But for a stroke patient, that weight (roughly 10 pounds) is already quite a challenge. If you can unload the arm from its own weight, then a patient can with much less force perform functional tasks.

"We also can measure the movements and give patients virtual feedback via a monitor. They can do

simple tasks or more complex ones in a virtual environment such as a shop and pick something off a shelf and put it in a basket."

Reinkensmeyer, who has been working with Hocoma for more than 18 months, says the collaboration has gone well and that he is looking forward to continuing it.

"I have been impressed with Hocoma's commitment to quality and good design. They listen well, and have built multiple collaborations to produce the best product possible," he says.

A Strong University-Business Partnership

Colombo describes the technology transfer process from the University of Zurich to his company as a straightforward, collaborative partnership.

"I think because I had worked there it was much easier," he says. "Not only was the transfer on paper, but it was also in the brain, so to speak. We continue to work closely with the university."

Herbert Reutimann, managing director at the University of Zurich technology transfer office, says backing for the Lokomat research and development came from the Swiss National Science Foundation and from CTI, the Commission for Technology and Innovation, a governmental institution that provides funding for joint research projects between universities and small- and medium-sized enterprises. Without this support and financial backing, the Lokomat's path to success likely would have been longer and more difficult.

Reutimann says the collaboration between the university and Hocoma went smoothly and continues to do so.

"People on both sides wanted to see this apparatus become reality," he explains. "Lokomat is a superb example to show the benefits which can result for patients and the society from the long-term collaboration between academia and an innovative company".

Reutimann said the licensing agreement features royalties to the university from the sale of devices using its technology. UC Irvine also will receive royalties from the sale of Armeo devices.

> "Lokomat is a superb example to show the benefits which can result for patients and the society from the long-term collaboration between academia and an innovative company."
>
> *Herbert Reutimann, University of Zurich*

"The people who developed this device are very close to the clinic and the patients, and had their interests at the forefront," says Reutimann. "Whatever they did, they had the needs of their patients and the therapists in mind from the beginning. It was created right beside the patients in close collaboration with the physicians and the therapists, and was continually evaluated to meet the patients' needs. I believe that is one of the key factors to its success."

Providing a Live View of the Cellular World

Chapter 19

Auburn University and Aetos Technologies team up to develop a tool that, for the first time, enables scientists to observe living cells in real time.

Vitaly Vodyanoy in the optical lab.

When Vitaly Vodyanoy wanted to see something that had forever been invisible, he figured out a way to see it. Cobbling together glass lenses and playing with the angles of various light sources, he built a novel microscope that allowed him to see the miniscule workings of living cells in real time. It enables live cell images to be visualized for the first time. Like the inventors of the first microscopes, Vodyanoy has provided us with a new perspective on human life.

A professor of physiology and director of the Biosensor Lab at Auburn University in Auburn, Ala., Vodyanoy had been conducting research on biological membranes, and specifically, olfactory function. A biophysicist and biologist, he was intrigued by the molecular phenomenon of olfactory function — how the olfactory sensors interact with the receptors on neurons, and the multitude of biochemical events that provide us with the sense of smell.

He'd been searching for cilia under his microscope. Cilia are the delicate hairlike structures found in great numbers on the surface of a cell, and used, in many organisms, in locomotion. Vodyanoy was studying the cilia that are projected from olfactory sensory neurons.

"I wanted to look at cilia in the mucous of the olfactory, but they are very small, one billionth of a meter — only a few microns in length," he says. "All of the olfactory receptors are embedded in this structure, but they are essentially invisible. So I started looking around to find a way of doing this."

An "Illuminating" Discovery

As a physicist and biologist, Vodyanoy was a veteran user of microscopes, and he understood how they worked. Optical microscopes use refractive lenses, usually made of glass, to focus light into the eye or another light detector. Various wavelengths of light are used for special purposes — the study of biological tissue, for example. Today, biologists frequently use ultraviolet light combined with fluorescent tagging to make certain parts of an organism "glow" under the microscope, enabling the researcher to see those tagged components as distinguished from other parts.

Vodyanoy had visited Gaston Naessens, a scientist in Canada in the early 1990s and seen him use a microscope with a special kind of illumination system. Illumination is critical to microscopy because it gives an image a three-dimensional appearance and enables the user to see otherwise invisible features. According to Vodyanoy, this particular microscope had a light condenser that converted a beam of light into a cone, effectively illuminating the subject at a high resolution. Years later, when Vodyanoy was unable to see the olfactory cilia, he decided to create a better illumination system for his microscope.

"It's really an old kind of technology," he says, "but I made a special kind of illumination system, one that produces annular illumination. It's

a special structure that produces empty cones of light, which has advantages for looking at small particles. So it's a combination of old technology put together in one unit to produce new, higher resolution on smaller subjects."

Vodyanoy is not a microscopist. His main research interests are in cellular dynamics, chemical sensing and the physics of interaction. But he is also, according to those who know him, a renaissance man — someone who loves music and art, a good cook, a charmer.

"He is this wonderful man, a Russian scientist, who created this instrument because he couldn't see what he needed to see," says Jan Thornton, director of the technology transfer office at Auburn. "He is just the type who seeks knowledge and will do whatever it takes to find things out."

According to Thornton, her team had been invited to Vodyanoy's lab to see another discovery, when they happened upon the microscope. He had created it with his own money, and hadn't even thought of disclosing it. But after the technology transfer professionals had seen it, they disclosed the invention to the U.S. Department of Defense. The government, which has become more interested in highly sensitive tools for detection of disease agents in the wake of the 9/11 terrorist attacks, asked for a prototype.

Vodyanoy obliged.

The Start of a Collaborative Partnership

Around the same time, Thornton had begun meeting with a venture capitalist in Memphis. The investor, Thomas Lawrence, had experience bringing new inventions out of a university setting and into the marketplace. He'd been approached by Auburn University alumni to take a look at their technology transfer efforts and help them develop a sustainable model for bringing in licensing income in the era of declining government support.

Once Lawrence and his son Sam saw the microscope and the

prototype Vodyanoy had built for the government, they were impressed enough to work with Auburn to form a collaborative partnership. Together, they launched Aetos Technologies in 2003 to commercialize discoveries made at Auburn and other universities, and the first technology they wanted to bring to market was Vodyanoy's microscope.

"We immediately understood the importance of this," says Sam Lawrence. "This microscope gave us the ability to see live, real-time cellular interactions in a completely analog manner — just light and lenses, no software manipulation."

> "This is especially important in the study of infectious disease, where it's important to see how cells infect one another, or in the development of drug delivery tools, as it allows researchers to see how much of a chemical is entering a cell."

Lawrence brought in experts in microscopy, a variety of medical fields, nanotechnology and engineering to look at the tool and it met with excitement and enthusiasm.

"The base technology was really exciting," Lawrence says, noting, "The importance of this to basic research in biology and medicine was immediately recognized."

While the product had an enormous amount of potential, the company had to first invest time, money and energy into fitting the scope to the needs of the market. Researchers at Aetos and Auburn spent the next year collaborating to develop the product from a benchtop prototype to a device that could be compatible as an add-on component to the standard bench microscopes.

The first commercial product, called the CytoViva optical illuminator, was launched in 2004. It's an "add-on" that provides ultra high-resolution, high-contrast images. Less than two years later, the company developed the CytoViva Dual-Mode Florescence unit. This tool enables researchers to use fluorescent tagging in combination with high-resolution, high-contrast, real-time imaging. In the same year, 2006, Aetos launched CytoViva as a separate company.

Biologists use fluorescence to visualize intracellular interactions, marking portions of cells with fluorescent tags to better observe the biomechanics that are occurring. The dual-mode fluorescence unit allows users to combine morphological data with fluorescent data, making it possible to see all the structural data and all the dynamic data, and to switch back and forth between the two.

"Heretofore, researchers would have to take a picture of the cell with one technique, then take another picture of the other data, and nothing allowed them to look at both at the same time," says Sam Lawrence. "Now, they can do both and do it in real time."

The tool allows researchers to see the morphological structures of cells responding to and interacting with other cells. This is especially important in the study of infectious disease, where it's important to see how cells infect one another, or in the development of drug delivery tools, as it allows researchers to see how much of a chemical is entering a cell.

"We can offer a full system to scientists that allows for a robust qualitative and quantitative picture of their research," Lawrence says.

Continuing a Successful Track Record

Aetos Technologies and Auburn University have won several awards and accolades for the CytoViva

products, including being selected as one of the 100 most significant new products by R&D Magazine in 2006, and winning a Nano 50 award in 2006 and 2007. The company's products are being sold worldwide for applications ranging from cell biology to bio-informatics.

One customer, an oncologist, is using the microscope in a predictive, diagnostic way to understand the way cancer metastasizes inside a living human being. Next to the market: a scope with a CytoViva-compatible environmental chamber that will enable researchers to keep a sample alive for hours or days while it's being studied.

Even as CytoViva begins to sell its components and prepares for future product development, Vodyanoy says researchers in a variety of fields on the Auburn campus have been flocking to his lab to use his microscope. "We've had many visitors to our lab," he says. "We've seen nanotubes, the insides of cells, and we've visualized the transport of protein in blood vessels."

And yet he remains modest about his discovery.

"I don't look at this as an invention, it's really just a tool," Vodyanoy says. "It's a real workhorse."

The development of the first microscope in the 16th century revolutionized biology and today it remains an essential tool in science.

Oleg Pustovyy, Sam Lawrence, Chuck Ludwig, Vitaly Vodyanoy in the optical laboratory.

Vodyanoy's microscope might very well continue the revolution, as it provides scientists the first tool with which one can study both the qualitative and quantitative aspects of life at the smallest scale.

Tiny Devices That Protect, Entertain and Simplify

Chapter 20

Collaborative efforts bring a technology platform developed at Cornell University to the public.

Wafers are loaded for processing into Applied Materials' Etch Centura by Kionix senior engineer, Andy Minnick.

Have you ever dropped a laptop computer or cell phone?

Or have you ever heard of accident victims in isolated areas being quickly rescued?

In situations like these, people owe a debt of gratitude to researchers at Cornell University in Ithaca, N.Y. That's because they helped develop the tiny microelectromechanical motion sensors that play a critical role in locating victims and deploying assistance, or protecting data on hard drives that may be lost due to a hard jolt or a fall.

Microelectromechanical systems, or MEMS, technology isn't an easy concept to grasp. Fortunately, though, MEMS technology exists and it factors into many devices that we rely on every day. From lifesaving GPS assistance, to tilt-sensing game controllers and cell phones with gesture recognition, MEMS inertial sensors are the enabling component. The ability of such devices to detect motion and translate that motion into an electrical signal that ultimately protects a hard drive and the data it contains is attributable to MEMS technology. One thriving company called Kionix, Inc., located in Ithaca, N.Y., is taking that technology to new levels.

Kionix is recognized as a global leader in the design, engineering, and manufacture of high-performance, silicon-micromachined MEMS sensors. These tiny sensors are equipped to measure acceleration, rotation and free-fall. With the use of fabrication equipment standard to the semiconductor industry, the company constructs three-dimensional, moving silicon structures on the scale of modern microelectronics. Inertial-sensor innovations developed by Kionix are used today in a wide range of applications including hard disk drive protection, computer and video gaming, personal navigation, sports diagnostics and health-monitoring systems.

From Laboratory Inventions to a Vision for a Company

The work of Cornell University engineering professor Noel MacDonald, Ph.D., was especially significant in the development of MEMS technology. A leading researcher in the field of semiconductor fabrication, MacDonald pioneered the concept of using semiconductor manufacturing techniques, specifically reactive ion etching, to manufacture very small electromechanical devices in single crystal silicon wafers. Although prolific in the number of inventions he designed while at Cornell, MacDonald already had ample experience in commercializing his technologies and preferred to pursue teaching and academic research.

Many of MacDonald's inventions and designs did, however, land on the desk of licensing managers at Cornell's office of patents and licensing. Richard Cahoon, now director of the Cornell Center for Technology, Enterprise and Commercialization, was a manager at that time and recalls being intrigued by MacDonald's entire technology platform.

"His underlying invention involved the ability to do a certain kind of deep etching in single-crystal silicon. I realized this represented a funda-

mental breakthrough, and although a basic idea, it demonstrated a very powerful tool," says Cahoon. "We were looking at methods and devices that would be useful and relatively inexpensive for sensing and actuating. I began to create a vision around the platform of this technology and considered the business possibilities that could jump off from this platform."

Cahoon was willing to take the lead in creating a company and packaging its property portfolio to make it compelling enough to recruit investors, management and partners. Yet, he needed to find others with the background and the desire to start a company. He realized that this called for some innovative collaboration among knowledgeable colleagues.

What resulted was a "protoboard," or a mix of business, technology, and not-for-profit people, and even some ambitious engineering students from MacDonald's lab. The group was united by their experience in the worlds of technology and business. Cahoon recalls how they all brought to the table some key solutions for laying the groundwork of what would eventually become Kionix.

Yet they still needed to identify the right CEO for the company, a born leader who would be energized by the challenge. Greg Galvin, Ph.D., fit the bill. After earning his doctorate in materials science, as well as an M.B.A. from Cornell University, Galvin served for more than five years as deputy director of the Cornell Nanofabrication Facility. He also worked as director of Corporate Research Relations at Cornell, an experience that undoubtedly served him well as president and CEO of Kionix.

Galvin took a sizeable risk in starting the company in 1993, according to Jeanette Shady, director of external communications for Kionix. Along with co-founder Timothy Davis, Ph.D., who now serves as executive vice president and chief technical officer, they initially funded the venture with a modest $25,000 in personal financing and investments from family and friends. The two also faced the challenge of being located in upstate New York, a region relatively isolated from mainstream venture capital.

Until Kionix completed its first silicon wafer fabrication facility five years later, it continued to rely on Cornell's infrastructure and rented use of the Cornell Nanofabrication Facility. It wasn't until late in 1998 that the company had its own fabrication facility, built from the ground up, located in the Cornell Business and Technology Park. In 2001 a new production facility was built to support Kionix's production requirements, which now stand at more than 40 million MEMS inertial sensors per year and are growing rapidly.

Galvin's appreciation of the Cornell Nanofabrication Facility and the seminal MEMS research pioneered by MacDonald still runs deep. He says it was one of the key ingredients of the overall collaborative effort that eventually yielded the birth of Kionix. "If it wasn't for MacDonald's background and the research capabilities available here at Cornell, the creation of Kionix probably would not have happened," says Galvin.

A Plethora of Intellectual Property

As Kionix technologies took off, so too did the intellectual property coming out of Cornell University. The company secured its first license for its plasma micromachining technology in 1994, and the original license granted through Cornell was amended to allow for the incorporation of new discoveries into the company's portfolio. Scott Macfarlane, a senior licensing manager with the Cornell Center for Technology Enterprise and Commercialization, serves as liaison between Kionix and Cornell and says that more than 200 patents now protect Kionix products and manufacturing processes.

The industrious company has realized many successes since its founding, including acquisition by Calient Networks of San Jose, Calif., in 2000. Given Calient's focus on fiber-optic systems, the company was eager to acquire Kionix's optical business, specifically its MEMS micro-mirror array technology. Prior to the transaction, a new Kionix was spun off to investors to pursue inertial sensor and microfluidic business opportunities. As Galvin points out, in the end each company was able to focus on related, yet different, MEMS applications, and Kionix shareholders benefitted by the acquisition.

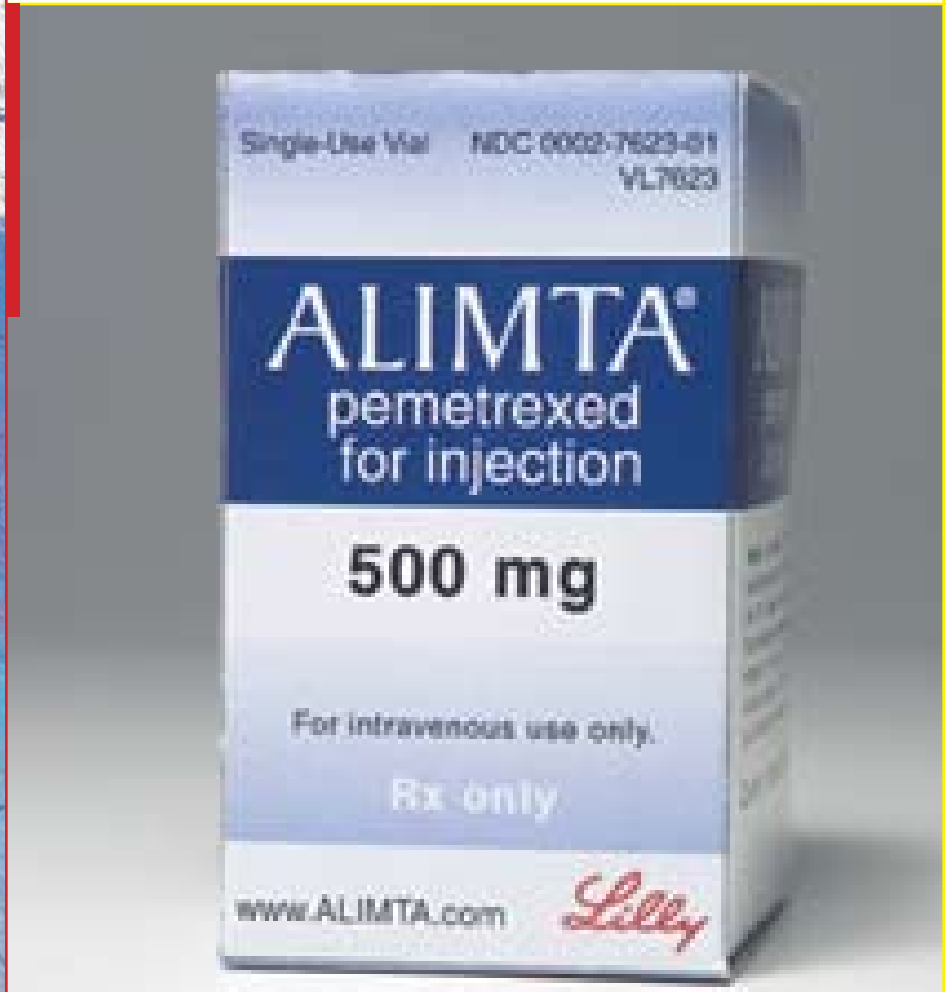
Almost 15 years ago when Galvin accepted the challenge of leading a new company, he couldn't possibly have predicted the technological explosion that would fuel the demand for MEMS products. By 2006, Kionix achieved annual sales of greater than $10 million with a compounded annual growth rate in excess of 100 percent. Continued and rapid growth is expected over the next several years as advances in technology and demand for inertial sensors continues to rise.

Kionix now employs more than 100 people and remains a privately held company with shareholders that include both individuals and organizations. Having come a long way from the initial $25,000 investment by friends and family, Kionix has to date raised more than $70 million from both individuals and institutional investors. A close collaboration with the Ithaca-based Cayuga Venture Fund has helped mitigate the difficulty of raising capital far from the traditional centers of venture investors.

Collaborations have played and will continue to play a significant role in the success of Kionix. Galvin places great importance on customer collaborations and the unparalleled customer service provided by his company. "The company's global sales team does more than insure sales success," he says. "Each operation is supported with a technical expert who can respond rapidly to questions and work in tandem on new applications." According to Galvin, this capability propelled Kionix to its leadership position in the markets it serves. As for the teamwork among researchers at Cornell that ultimately led to the creation of Kionix, they continue to spark new partnerships. Today, Kionix is involved in new collaborations with researchers at Cornell, and other related parties, in completely new areas of technology. Galvin is confident such relationships will lead to a new company and another great success.

Partnership Forged in Trust Yields Revolutionary Cancer Drug

Chapter 21



An anticancer drug first launched in the United States in 2004, Alimta® inhibits the growth of tumor cells with manageable toxicity, giving hope to millions of cancer patients worldwide. If not for the collaboration, foresight and perseverance of researchers at Princeton University and Eli Lilly and Co., the drug might never have been developed.

Developed through a collaboration between researchers at Princeton University and Eli Lilly and Co., Alimta® is used to treat a cancer often associated with exposure to asbestos, as well as non-small cell lung cancer.

Photo courtesy of Eli Lilly and Co.

The brimstone butterfly adorns the business cards of Edward C. Taylor, Ph.D. A fitting homage to his life's work, the butterfly symbolizes Taylor's inspiration to develop the anticancer drug Alimta® (pemetrexed).

Alimta® is currently approved in the United States to treat recurrent, or second-line, non-small cell lung cancer, the most common form of lung cancer. It is also approved in combination with another drug called cisplatin for the treatment of malignant pleural mesothelioma, a cancer often associated with exposure to asbestos.

The development of Alimta dates back to 1946 when Taylor, now a retired distinguished professor and organic chemist at Princeton University in Princeton, N.J., entered graduate school and was looking for a thesis topic. He came across an article describing the discovery of a compound found in human liver that, bizarrely, possessed a structure of which a portion was identical to the structure of pigments in the wings of butterflies. Taylor's curiosity about this unexpected discovery eventually led him to make a major advancement in the fight against cancer.

The compound from the liver was later determined to be folic acid, a vitamin that plays an essential role in making cell division possible. "It was found that folic acid is essential for all forms of life," says Taylor.

It was then he saw the potential for an anticancer agent. Like all cells, tumor cells need folic acid, or folates, to divide and multiply, allowing the tumor to grow. "If you could inhibit it, you would have a good way of arresting the growth of tumors," he says. "The challenge was to inhibit the growth of the tumor and not healthy human cells. People tried for years, but no one succeeded."

Inspired by the discovery of folic acid, Edward C. Taylor, Ph.D., worked for decades to develop a drug that arrested the growth of tumors without affecting healthy tissue.

Photo courtesy of Princeton University

Trust is Essential to Success

In the 1970s Taylor resumed work on an antifolic agent that might selectively target tumor cells. After years of work, he came up with a promising compound called Dideazatetrahydrolic acid (DDATHF). But he knew his work could only be carried so far at Princeton, and he needed help. "I needed facilities and expertise that Princeton didn't have," he says. "If I wanted this compound thoroughly looked at, who would do it?"

Taylor enlisted the help of Eli Lilly and Co. in Indianapolis. At the time, Taylor had already been consulting with Lilly for years, and had established close relationships with the company, so in the early 1980s he sent DDATHF to them.

"It turned out to be one of the most

effective antitumor agents they had seen," he recalls.

Knowing they might be on the brink of a major breakthrough, Taylor (through Princeton) and Lilly in the mid-1980s set up a collaborative effort to explore the potential of what appeared to be an extremely promising new area of cancer research. During the following four years, approximately 800 new drug candidates were synthesized and evaluated through this collaboration. DDATHF, the original lead, eventually failed clinically because of toxicity, but another compound finally emerged that proved to be the compound of choice for development, and that compound became the drug named Alimta®.

This was also a pioneering time for technology transfer at Princeton. By this time, Princeton had a well-organized technology transfer arm, but at the time of the project's initiation, the partnership was forged out of mutual trust.

The Princeton-Lilly joint research project that culminated in the discovery of Alimta® "was the first big collaboration that Princeton had undertaken, and it proved to be a major success because there was complete trust and integrity on both sides," according to Taylor.

Partnership, Perseverance Overcome Obstacles

As a pharmaceutical company, Lilly focused on understanding how the compounds behaved in humans. "Our role was to conduct evaluations and animal studies to determine which compounds were candidates for clinical trial," says Joe Shih, Ph.D., a distinguished research fellow at Lilly.

A key part of Lilly's role was to understand the compounds' toxicity in humans and how to mitigate it. That turned out to be a crucial element. Early clinical trials with Alimta® were plagued by unpredictable toxicity issues. Although the majority of patients in the trials responded well, some experienced serious, life-threatening side effects. While the drug's clinical benefits were clear, these problems threatened to end the project. That's when another member of Lilly's team saved the project.

Clet Niyikiza, Ph.D., at the time a statistician and mathematician with Lilly, stepped forward to solve the problem. "He said, 'Give me three weeks,'" recalls Taylor, "and he would solve the problem."

Scouring the clinical data to find the common thread among patients who experienced the side effects, Niyikiza, determined that the patients who experienced side effects had a pre-existing folic acid deficiency. Researchers had not anticipated this problem, since they were attempting to inhibit folic acid activity. But Niyikiza's work led to changing the protocol to co-administering folic acid and vitamin B-12 to patients, and this amended treatment saved the drug.

"It tipped the balance critically," says Taylor.

"Alimta® is a single compound that targets the utilization of many folate-based processes essential for the

growth of tumor cells," Taylor explains. "Other cancer drugs usually can target only one specific biological process, making it attractive for patients to receive a 'cocktail' of several drugs. But this strategy also means that the patient is subject to the combined toxicities of each component of this cocktail.

"Since Alimta® is a single drug that has multiple targets, it is harder for tumors to develop resistance to it," he continues. "That is part of the reason Alimta is one of the least toxic cancer drugs known."

Since its approval in the U.S., Alimta has gone on to be approved by regulatory authorities in more than 85 countries. Unlike most chemotherapy treatments for cancer, Alimta is easy to administer, requiring only a 10-minute infusion every three weeks.

Collaboration is the Cornerstone

Alimta's development is the result of decades of work and partnership between Taylor and the research team at Lilly, without which the drug would have never made it to initial trials.

"The attrition rate in drug development is enormous," says Taylor, citing that only one out of every 5,000 to 10,000 potential candidates ever becomes a drug. "It's a discouraging and extraordinarily expensive process."

He added that Lilly's agreement to collaborate with Princeton, and to help develop the drug, demonstrated Lilly's trust in Taylor and in the promise the early compounds held.

From Taylor's perspective, the partnership with Lilly and its evaluations of drug candidates, gave him, as well as his Lilly colleagues, the feedback needed to continue research in the direction that eventually led to the discovery of Alimta®.

"In drug development, you have to evaluate constantly what you are making so you don't go in the wrong direction," he explains. "Such feedback is not available in an organic synthesis lab."

It was the willingness of Lilly to perform extensive biological testing that made Alimta® possible.

Shih views the development of Alimta® as a model of how a pharmaceutical company and a university can work together.

"The science is being conducted all over the world at top research institutions like Princeton," he says. "Big pharmaceutical companies don't have the resources to conduct research at that scale. These institutions help us to identify interesting discoveries that can lead to new drugs."

Lilly is working with many institutions worldwide in the research and development of drugs for oncology, diabetes and neuroscience.

Summing up the importance of partnerships between research institutions and the private sector, Shih comments, "Collaboration is a cornerstone of this process."

Taylor says Lilly's help was invaluable. "Without this kind of collaboration, Alimta would still be a curious compound sitting on a shelf in my lab."

Campath: Collaborations Across Continents Prove Successful

Chapter 22

A long and winding road of research and development led to a promising drug that offers great hope to cancer patients and others.

The collaboration of these three scientists resulted in the development of the lifesaving therapeutic molecule Campath®. Shown from left to right: professor Herman Waldmann, Dr. Mike Clark and professor Geoff Hale.

Photo courtesy of Greg Smolonski, Photovibe

It is fitting that the promising cancer therapy called Campath® begins with the letter "C" — the same letter that starts the word "collaboration" (not to mention "continents" and "commitment.") For the story behind Campath is characterized by collaborative efforts that span several countries and involve hundreds of committed individuals.

Backed by several decades of research and development and then subjected to a dizzying series of mergers and acquisitions during its commercialization, Campath's history is both long and winding. Yet in the end, the personal stories like those of Juliana Oliveri, a chronic lymphocytic leukemia (CLL) patient successfully treated with Campath, are what matter the most.

One Grateful Patient's Story

The last thing a busy professional like Oliveri had time for in her life was a chronic disease. A former society singer and performer in major cities across the U.S., she had since switched the focus of her career and was working 16-hour days for the luxury goods industry in New York City. When a routine physical by her internist revealed an alarmingly high white blood cell count five years ago, Oliveri had no intention of slowing down, especially since she felt physically fine. Additional tests indicated that although asymptomatic, Oliveri had CLL, the most common form of adult leukemia.

Her doctors adopted a "watch and monitor" approach, and for the next three years Oliveri continued to work long hours, travel, and cater to demanding celebrity clients. The symptoms struck quite suddenly on her 49th birthday in July 2005, and they were serious enough to warrant admission to the hospital and the initiation of therapy. At the time she was first diagnosed, Oliveri had learned about a promising CLL therapy called Campath, and she took a proactive approach in helping her physicians formulate a treatment plan. Campath was the therapy she felt she needed, and fortunately that is what she received.

For six months Oliveri checked into the hospital three mornings a week as an outpatient. There she would endure routine blood work, followed by intravenous administration of Campath, and after an hour of close monitoring, she would leave the hospital to begin a full day of work "tending to the rich and famous." Recalls Oliveri, "I had no side effects during treatment – it was amazing." She has remained in full remission since completing Campath therapy in January 2006 and continues to lead a life as busy and demanding as ever.

Oliveri's experience with CLL has taught her many valuable lessons such as the importance of teaming up with health care specialists who understand cutting edge treatments. But overall, she credits her health to the availability of Campath. "Knowing I had Campath to go to when the time came for treatment was the best thing that could have happened to me," she says.

A Long and Winding History

The discovery of Campath, a monoclonal antibody that targets cancerous blood cells, began in the 1970s in the laboratory of Herman Waldmann, Ph.D., at the University of Cambridge in Cambridge, England. Waldmann, a pioneer in the field of monoclonal antibody production, first sought to develop the proteins to treat problems associated with bone marrow transplantation. Through Britain's Medical Research Council (MRC), money was raised to establish research projects along these lines. Joining him in those efforts in the early 1980s were two ambitious researchers in Cambridge's department of pathology — Mike Clark, Ph.D., and Geoff Hale, Ph.D.

The team of scientists spent years searching for monoclonal antibodies effective in targeting human immune cells. Eventually, they successfully discovered several. One of the next critical steps involved gaining the technical expertise to use the antibodies in human patients. With the help of colleague Greg Winter, Ph.D., they learned how to humanize antibodies, and in 1988, they successfully treated their very first lymphoma patient using the humanized antibody. The promising molecule, which binds to a specific target called CD52 on cell surfaces and directs the body's immune system to destroy those CD52-bearing cells, was named Campath, for Cambridge University Department of Pathology.

The commercialization potential of Campath had meanwhile generated discussion between Cambridge and the British government's technology transfer arm, the National Research and Development Corporation (now renamed the British Technology Group, or BTG). Richard Jennings, Ph.D., director of technology transfer and consultancy at the University of Cambridge, was involved in the negotiations at that stage and recalls that they represented a rather complex nexus of interest between different people and different organizations.

"It was a really fascinating project to work on, and it was driven by fantastic enthusiasm on the part of the academic inventors who showed a long-standing motivation to get new types of therapies to market for patients," says Jennings. "They remained driven, and this impressed us."

Campath molecule

When Clark recounts the early phases in Campath's development, the power of collaboration is what stands out above and beyond everything else. "We had already established that the antibody worked clinically, but we now needed to convince those involved that it was a commercially viable product," he says. "That initial direct collaboration between researchers and clinicians has been the key to the success of this entire project."

Through the work of Jennings'

office and the BTG the Campath team connected with The Wellcome Foundation (which became Glaxo-Wellcome and is now part of GlaxoSmithKline). Campath was licensed to the company in 1985 and efforts to commercialize it for use in the treatment of lymphoma and leukemia, as well as an immunosuppressive agent in rheumatoid arthritis patients, began in earnest. By the mid-1990s Phase II trial results were demonstrating that Campath showed potential for treatment of lymphoma and CLL patients.

The results of rheumatoid arthritis clinical trials however were unimpressive. Thus began the rollercoaster ride for Campath and its inventors. In 1995, around the time that Wellcome was considering a merger with pharmaceutical company Glaxo, it announced it was abandoning the project.

Yet the strength of scientific connections served to rescue the faltering project. Waldmann contacted Harvard University pathologist Timothy Springer, Ph.D., a colleague whose path he had first crossed when the two were learning monoclonal antibody technology in the MRC laboratory of Nobel Laureate scientist César Milstein, Ph.D. Springer had since returned to the U.S. and had founded a startup company, LeukoSite, in the Boston area. LeukoSite, it turned out, was in a position to license the rights to Campath from BTG.

By 1997 LeukoSite had negotiated a new licensing deal for Campath and clinical trials designed to test the therapy in CLL patients were back on track. Yet again the route of Campath was altered by a series of commercial mergers and acquisitions. Within two years LeukoSite announced its merger with another Boston area company, Millennium Pharmaceuticals, Inc. While the company quickly gained Food and Drug Administration (FDA) approval of Campath for the treatment of B-cell CLL patients who fail conventional chemotherapy, Millennium eventually transferred the rights to ILEX Oncology, Inc. In 2004 Genzyme Oncology, Inc. acquired ILEX and gained the production rights to Campath. While Campath's history with ILEX was short-lived, it was beneficial, as Genzyme investors recognized the therapy's potential at a time when it was looking to expand its prognostic and diagnostic portfolio in the treatment of hematological cancers.

According to Terry Murdock, Genzyme senior vice president and general product manager of Campath, the gain of Campath as a therapy in the treatment of CLL was the perfect platform for the company in which to leverage a diagnostic tool and a targeted therapy. "In hematological malignancies like CLL, the need to eradicate residual disease in patients is important as relapses are often related to the residual nature of the disease," says Murdock.

The merging of ILEX and Genzyme was ideal as the strengths and directions of the two companies complemented one another. "ILEX had a strong clinical operating route

and a strong base of experience in getting clinical trials completed. It also had a solid track record of getting drugs developed," says Murdock. "Genzyme has a strong academic and clinical physician base, as well as experience with regulatory approval and manufacturing. Putting those two things together, we provide a solid base to move forward with Campath."

A Bright Future Ahead

Under the protection of Genzyme, Campath remains the first and only monoclonal antibody approved by the FDA for the treatment of patients with B-cell CLL. In the fall of 2007 the FDA granted a label expansion and approved Campath as a first-line treatment for the disease. Along with Bayer Healthcare Pharmaceuticals, which markets Campath, Genzyme is also developing the therapy as a treatment for multiple sclerosis. The latest news reports successful results in Phase II trials of Campath for multiple sclerosis patients; Phase III trials are now underway.

Reflecting on the long history and sometimes uncertain future of the therapeutic protein to which Clark has devoted much of his life, he recognizes certain recurrent themes. Most significant he claims were the collaborations that existed between clinicians and university research groups that provided the dedicated Campath researchers with the confidence necessary to push for its commercialization.

Hale echoes those sentiments and points to the unusually strong tie between himself, Clark and Waldmann — the original three behind the discovery of Campath.

"One of the greatest things about this project is that while the three of us have been working on it going back to the early 1980s, we've all remained very close," says Hale. "And there have been hundreds of other scientists, clinicians and patients who have helped along the way and made this project successful. Everyone has been very loyal every step of the way."

> "...it was driven by fantastic enthusiasm on the part of the academic inventors who showed a long-standing motivation to get new types of therapies to market for patient."
>
> *Richard Jennings, Ph.D., University of Cambridge*

Software Program Gets to the Heart of Electrocardiogram (ECG) Results

Chapter 23

Professor Peter Macfarlane, a trailblazer in the field of computerized electrocardiography, initiated the development of the University of Glasgow ECG Interpretation Algorithm more than 30 years ago. Today, it remains a significant tool in intelligently interpreting electrocardiograms (ECGs).

The Burdick Atria 6100 by Cardiac Science

Back in the late 1960s, a University of Glasgow professor sat down with a piece of blank paper and a pencil to begin developing software for electrocardiogram (ECG) analysis.

"No equipment whatsoever," chuckles Peter Macfarlane, who still works at the Glasgow Royal Infirmary. His title is professor of electrocardiology, which is the study of the electrical activity in the heart.

Electrocardiography — the branch of electrocardiology dealing with displaying and interpreting electrical signals the heart generates — is a starting point for detecting many cardiac problems. Some of these cardiac problems include irregular heartbeats, heart attack and some congenital heart conditions. The electrocardiogram is used routinely in physical examinations and for monitoring a patient's condition during and after surgery, as well as in the intensive care setting.

It is the basic measurement used in exercise tolerance tests and is also used to evaluate symptoms such as chest pain, shortness of breath and palpitations.

Professor Peter Macfarlane

Forty years ago, Macfarlane says, there were only two places in North America that were developing methods for ECG analysis.

"A cardiology professor in Glasgow at that time thought it would be interesting to do something along the same lines in Scotland," he says. "That's how it all started."

Eventually, his team got a small lab computer so he and his colleagues didn't have to deal with the university's cumbersome KDF9 computer, which Macfarlane jokingly says was so big it occupied about half a soccer field.

"As things moved on from there, we obtained some support from the Scottish government in the 1970s," he says. "Eventually, by the late 70s, they gave us a large grant and said we'd have to go out and find commercial partners. And that's what we did around 1981."

The university hooked up with a prominent German electronics manufacturer, which signed an agreement with the university to use Macfarlane's algorithm in the ECG equipment it was developing in its Swedish plant. Since then, through a series of acquisitions, a license to use the technology has been granted several times to different medical equipment manufacturers. The Glasgow software is now incorporated into ECG machines made by Burdick, a division of Seattle-based Cardiac Science.

The Glasgow ECG Interpretation Algorithm has been continuously improved since its initial development, allowing it to stay abreast of the latest

advancements in electrocardiographic research, company officials say.

"The faculty of medicine in Glasgow is at the forefront of new technology and we are continually working with our partners to improve health care throughout the world," Macfarlane says.

While other products use only age and gender to a limited extent, Macfarlane says the University of Glasgow ECG Interpretation Algorithm — a set of diagnostic rules sometimes involving complex math built into a software program — uses five clinically significant variables. They are gender, age, race, medication and clinical history.

This is critical because ECG patterns for patients of various ages from different ethnic backgrounds and with differing medical conditions can vary greatly, he says.

Macfarlane collaborates with Cardiac Science and travels regularly to the Deerfield, Wis., facility where Burdick ECG machines are manufactured. The University of Glasgow receives royalties for each machine sold that includes his algorithm.

Alex Castro, director of international marketing for Cardiac Science (Nasdaq symbol: CSCX), says his company is indebted to Macfarlane for his time, research and entrepreneurial spirit.

"Peter is the renowned authority in electrocardiology and Cardiac Science is thrilled to partner with him," says Castro. "We've woven Peter's algorithm into several generations of Burdick ECG devices and we regularly work with him on new product development."

Helping Different Age Groups

Macfarlane says the algorithm and software have evolved over time.

"It started off initially as an adult program," he says. "But by the late 1980s, we got money to look at ECGs in newborn babies and children."

Researchers then developed a pediatric ECG database in Glasgow that eventually had 1,750 healthy youngsters' ECGs, all recorded with the permission of the children's parents. By the early 1990s, they had added to the analysis program the ability to analyze ECGs from children as well as adults.

"The ECG of a baby is quite, quite different compared to the ECG of an adult," he says. "Children are not small adults. There is a continuing change from birth right through to adolescence. And as individuals get older the electrical activity diminishes a little bit and the size of the wave forms (on the ECG graph) decreases with increasing age. Also, men tend to have higher signals than women. And that has to be built into the program, too."

After the work with babies, they added the capability to compare ECGs over time.

"If you had an ECG from the minute you entered the hospital with chest pain, you could automatically compare it with an ECG on the second day," he says. "It's quite important to be able to compare ECGs recorded on different days, different hours in fact."

Ethnic Considerations

Macfarlane also has worked with researchers in Taiwan to get a database of ECGs from Chinese patients, which allowed him to put ethnic considerations into the program. He says researchers at the University of Glasgow are now recording ECGs from different ethnic groups, and so he hopes to further enhance the software with newer criteria.

Macfarlane says his algorithm offers two kinds of output for physicians to help them interpret the ECG data.

"One is a little bit more verbose in providing some reasons as to why the diagnosis was made," he says. "That one is really for family practitioners. We also have a shorter interpretation that we would expect to be used in the hospital environment by physicians who are more familiar with ECGs."

Macfarlane also says he believes his algorithm places more emphasis on the age and gender of patients than those of other vendors.

"As far as I know, no other manufacturer has access to a database of 1,750 ECGs from healthy children like the one we gathered that allowed us to develop our criteria for newborn babies and children.

"We are always looking for ways to improve interpretations based on experience," he says. "Believe it or not, the definition of a heart attack keeps changing from a clinical point of view as new biomarkers like troponin (a complex of three proteins integral to muscle contraction in cardiac muscle) have become available to indicate damage to the heart muscle."

He says his work has resulted in some new ECG criteria for acute heart attack. These criteria are being adopted by international bodies, such as the European Society of Cardiology as well as the American College of Cardiology and the American Heart Association and have very recently been published in the relevant cardiology journals.

> "We are always looking for ways to improve interpretations based on experience. Believe it or not, the definition of a heart attack keeps changing from a clinical point of view..."
>
> *Peter Macfarlane, Glasgow Royal Infirmary*

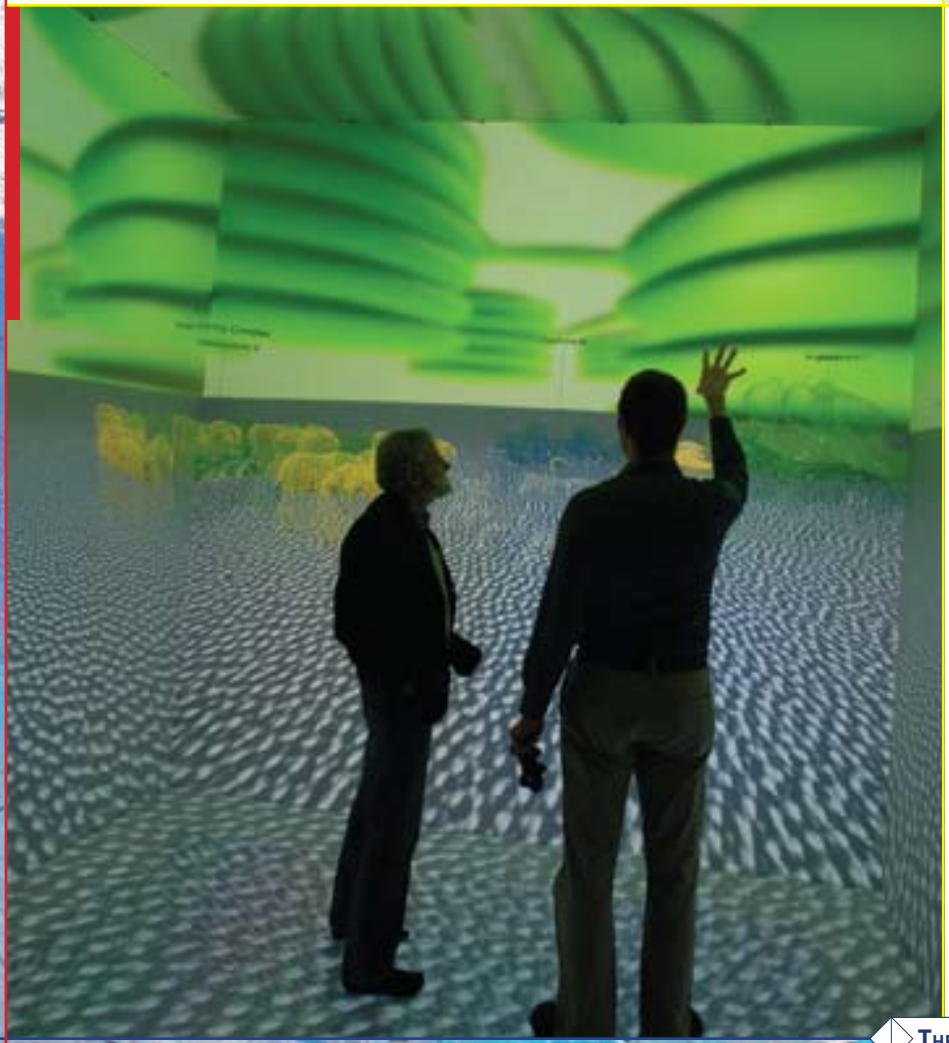
"These criteria will include some of the things we have been shouting about for quite some time, including the differences in ECGs of women and men," he says. "This criteria update is based solely on our efforts here in Glasgow to point out these things to the international community".

"That," he says, "is satisfying."

"It's also been very good to have such a good collaboration with Burdick over the years," he adds. "They are certainly a leader in the field."

Scientific Visualization Leads to the CAVE™

Chapter 24



In 1991, University of Illinois at Chicago researchers conceived of and built the first life-sized, projection-based, four-sided display technology used for a wide variety of applications, including product manufacturing, health care and training.

Experiencing a Virtual Cell application (partially funded by National Science Foundation grants) in the 100 megapixel C6 immersive room at Iowa State University / Virtual Reality Applications Center

Imagine being able to stand inside a human heart and watch blood flow around you. Or, imagine test-driving a car, *before* it actually has been built.

Through the wonders of the CAVE (Cave Automatic Virtual Environment), the first technology to widely exploit immersive virtual reality (VR) environments, people can do just that. The "wow" technology was pioneered at the University of Illinois at Chicago's (UIC) Electronic Visualization Laboratory (EVL). CAVE is a trademark of the Board of Trustees of the University of Illinois.

EVL is an interdisciplinary graduate research laboratory that combines art and computer science with advanced networked visualization and collaboration tools and technologies. Since the early 1970s, the lab has been recognized for its leadership in computer graphics. EVL, a unique collaboration between UIC's College of Engineering and the School of Art and Design, is one of the oldest formal interdisciplinary efforts between art and engineering in the U.S. Through its combination of the two disciplines — engineering and art — EVL serves as an excellent example of collaborative university research.

CAVE Adaptations

From the CAVE's development at EVL, other products and services have emerged, ranging from immersive virtual rooms, to software libraries to desktop/office-sized displays to anatomical teaching devices for medicine. Its success in the marketplace is due to its unique collaborative components — science, coupled with vision, design and computational steering. Together they are helping solve complex problems. The CAVE name was first commercialized and licensed to Pyramid Systems and is currently licensed to Mechdyne Corp. of Marshalltown, Iowa.

In immersive CAVE environments, people walk inside a room surrounded by large wall-size projection screens, wearing special glasses that allow the CAVE 3-D graphics to be seen with three-dimensional depth. The glasses are synchronized with the projectors so the images appear to be in front of their eyes. People then can walk around virtual objects, see objects float by, as well as peer inside a world where reality and illusion come together. The ImmersaDesk®, which was developed in 1995 at EVL, is a derivative of the CAVE system. This system uses one screen, positioned at an angle, like a drafting table — people look forward and down instead of all around. The system was less expensive than the original CAVE since it didn't require building a room within a room. Pyramid Systems commercialized the ImmersaDesk system, which also followed through to Mechdyne Corp.

Software Solutions

Researchers at the University of Calgary's Sun Center of Excellence for Visual Genomics have taken CAVE technology in a new direction. Viewers who study the Sun Center's life-sized,

human model called CAVEman, are looking at a marvel of visual reality technology. The anatomical digital atlas offers students, scientists and medical personnel a high-resolution view inside the human body. The technology has been used at the University of Calgary since 2002.

Christoph Sensen, Ph.D., professor at the Centre for Advanced Technologies, University of Calgary Faculty of Medicine, says, "We are developing a Java 3D™-based human body model for research, education and clinical applications." The final result of the virtual reality development will be a next generation 4-D (designating space and time) visual window that will show genetic components of diseases like cancer, diabetes and Alzheimer's.

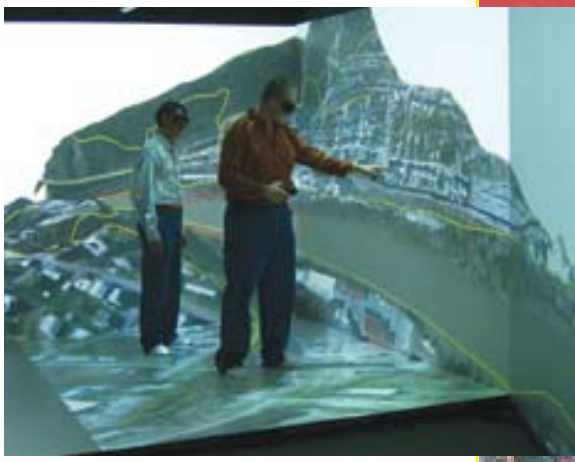
Sensen says, "Using our CAVE models, we will soon be able to simulate diseases for which we have no examples here in Alberta and teach our students how to treat them."

CAVE technology is also used to treat various phobias, including the fear of heights and spiders. Since people absorb most of their information through visual stimuli, a CAVE experience, which is being used in multiple ways in industry, can be a phenomenal way to impart information. An in-depth CAVE experience, for example, involves a basic four-screen (three walls and a floor) immersive room and a small graphics computing cluster.

Jeff Brum, vice president of marketing and business development at Mechdyne Corp., says, "While the costs can go into the millions of dollars for complex, six-sided, high- resolution rooms, the result in any CAVE is a compelling experience. When we have navigated to the edge of a virtual building or stood on the virtual space station looking down at Earth, many first-time CAVE users experience a real sense of vertigo."

Virtual Manufacturing

The CAVE's virtual applications allow people to address a wide range of challenges like creating better crops for improved harvests and better safety features on cars.



Google Earth Pro images displaying in real-time from the Internet into a reconfigurable virtual environment.

Image courtesy the GeoVirtual Lab at West Virginia University

"That's due to the fact that designers can sit in life-sized vehicles and create better sight-lines and other safety components," says Brum. Additionally, it allows manufacturers to "see" production lines before the products are rolled out so potential changes can be built in early in the planning process.

Car companies have incorporated these features by developing virtual

prototypes that help get the products into the marketplace sooner. The technology is also a cost benefit since virtual prototypes give companies an excellent alternative to building expensive physical prototypes.

Conceiving the World's First Projection-Based Technology with Walls and a Floor

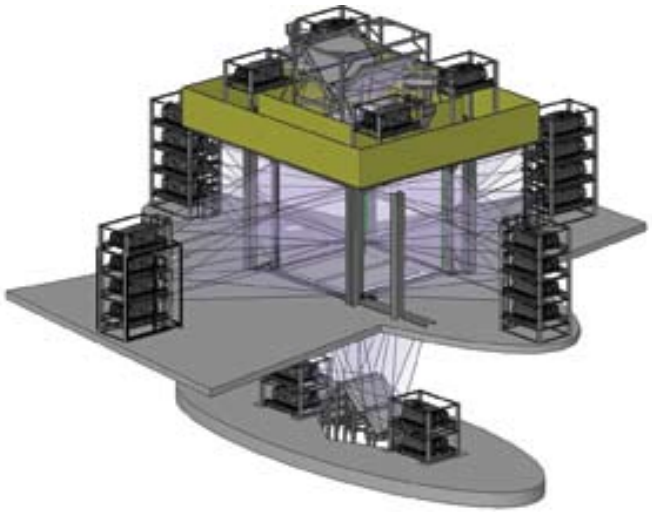
It was a long journey from the development at EVL in the 1990s to the wonders of today's virtual reality applications. Tom DeFanti, Ph.D., a distinguished professor emeritus at UIC now a research scientist at the University of California, San Diego's California Institute of Telecommunications and Information Technology (Calit2), co-conceived the CAVE system in 1991 with fellow UIC researcher and art professor Daniel Sandin. Carolina Cruz-Neira, an EVL Ph.D. student at the time, wrote the initial versions of the CAVE software library, and shares credit for the invention of the CAVE system.

"Dan and I conceived of the CAVE hardware; I named it; we built prototypes, and Carolina and other students wrote software drivers and applications for it," DeFanti explains.

In describing how CAVE has helped make the world a better place, Sandin says, "It is the first technology that provides a life-sized improvement in visualization since viewer-centered perspective was developed in paintings in the Renaissance. This is especially true with images on the floor, which gives users a true sense of presence like they are standing in, and are surrounded by, a virtual world."

CAVE Paves the Way for Numerous VR Applications

When one of Mechdyne's predecessor companies, Pyramid Systems, first learned of the work at UIC, it licensed the CAVE technology for commercialization. Next on the agenda was collaboration between research and industry. "Pyramid and UIC jointly promoted the CAVE at conferences and trade shows, supporting each other's research and development efforts," says Brum.



Design drawing of the world's highest resolution (100 megapixel) six-sided virtual reality room including 24 projectors, six sides/screens and structure.

Photo courtesy of Mechdyne Corporation

In 1994, three years after the technology was developed, Pyramid licensed the CAVE name and began commercializing the immersive environment concept. Five years later, Fakespace Systems acquired Pyramid and was subsequently acquired by Mechdyne. In 2006, Mechdyne acquired VRCO, a software company that licensed the original CAVE software library called CAVELib from UIC, putting all of the original CAVE components in one company.

DeFanti points out that CAVE technology originating at UIC has paved the way for a number of virtual reality offshoots.

"All of the subsequent technologies use concepts that are derivative in some sense of the original CAVE," DeFanti explains. "The success of the CAVE technology can be evidenced by Mechdyne's growth."

Mechdyne's 120 employees are spread out among its headquarters in Marshalltown, Iowa, an Ontario, Canada office, a software development office in Virginia Beach, Va., a Houston office, and an office in Leicestershire, England, which is spearheading growth in Europe.

By the late 1990s, with less than 100 immersive rooms in the world, some organizations found that the cost to set up supercomputers to drive a dedicated CAVE display was too cost-prohibitive. Users needed more flexibility to expand and justify the use of fully immersive environments.

"The idea to allow the side walls to push outward to create angled and flat wall screens, came from that feedback," says Brum.

This display, known as FLEX, is sold by Mechdyne and is now the largest configuration for immersive displays that the company sells. Brum points out that FLEX is a successful design component, but it has not replaced the immersive experience of CAVE systems.

"We regularly sell CAVEs to those who only want the experience of being surrounded by virtual imagery," he says.

Since the early 1990s when the CAVE concept was developed, it has gone through several advances based on performance and need. Digital projector technology, introduced in 2000, is even more astounding. The digital projections on each screen now have a resolution of 1400 x 1050 or about 6 million pixels on four screens. Compound that with the fact that CAVE has evolved to five- and six-sided systems. The higher resolution of the images and the additional sides in these enhanced CAVE environments provide a more realistic virtual environment, offering a vivid display of spatial relationships and improved information discovery.

> "CAVE's advanced technology has changed the way people work and learn by showcasing new ideas in a virtual environment."

"We have begun tiling high resolution projectors on each wall, which has led to our building the

two highest resolution virtual reality environments in the world," says Brum.

One of these enhanced systems is at Los Alamos National Laboratories in Los Alamos, N.M. Possessing five sides and amazing 43 million-pixel resolution, "La Cueva Grande" at Los Alamos has been used for a range of research projects since February 2006. The Los Alamos immersive environment can simulate everything from high energy explosions to the "dinosaur-killer" comet believed to have caused the mass extinction of dinosaurs 65 million years ago.

The highest resolution virtual reality environment is located in the Virtual Reality Applications Center at Iowa State University in Ames, Iowa. Originally built in 2000 by Mechdyne, Iowa State's C6 was North America's first six-sided immersive CAVE-like environment. In 2007, its resolution was upgraded to 100 million pixels, offering the highest resolution of imagery in any CAVE-like environment in the world — about 16 times the resolution of a typical immersive room. The enhanced C6 system can be used for showing students how photosynthesis works, giving researchers magnified views of 22,000 different genes, or for training soldiers for combat.

DeFanti and colleague, Greg Dawe, who designed and built the ImmersaDesk and the production model CAVEs at EVL, recently finished the StarCAVE in UCSD's Atkinson Hall. It is a 17-screen, 34-megapixel/eye pentagonal-shaped CAVE with excellent polarizing-preserving rear projection and a floor. It features the use of inexpensive lightweight circular polarized glasses that feel more like sunglasses than goggles.

CAVE's advanced technology has changed the way people work and learn by showcasing new ideas in a virtual environment. Imagination and innovation, hallmarks of CAVE, continue to play a giant role in opening the way to new collaborations in industry, science and education.

Chapter 25

Diaphonics: Giving Biometrics a "Voice"

A Canadian company called Diaphonics has worked with University of New Brunswick scientists to create voice identification products for use in banking and law enforcement. Their research also has uses in the fight against terrorism.

University of New Brunswick (UNB) professor Kevin Englehart, who has designed state-of-the-art artificial limb control systems, has helped develop voice-authentication systems for Diaphonics.

Starting in the early 1990s, University of New Brunswick (UNB) Professor Kevin Englehart began designing state-of-the-art control systems for artificial limbs in his role as associate director of the university's Institute of Biomedical Engineering.

But when a company called Diaphonics approached him and UNB to develop a voice-authentication system about four years ago, he and his team smoothly switched gears. The project is an offshoot of biometrics, the science of identifying people by particular biological measurements. In this case, rather than a fingerprint or a retinal scan, it's the person's voice that is used as an identification marker.

The technology, proponents say, has far-reaching implications in fighting organized crime, identity theft and terrorism.

They also believe that speaker recognition technology is well-positioned to capture a sizable share of the overall biometrics market, which is projected to grow to nearly $6 billion by 2010, because it is the only type of biometrics technology that does not require a specialized scanner, just a telephone.

Englehart, who is located at UNB in Fredericton, New Brunswick, said he had already done some research in speaker recognition, though it was not his main focus.

"Though it might not seem obvious, the problem of controlling an artificial limb isn't that much different than voice biometrics," he says. "You still need to analyze incoming signals, do some intelligent processing and then decide what to do. If you draw big boxes around it, the mechanics of the problem for controlling a limb is not that much different than recognizing who said what.

"In the case of artificial limbs, it's the electricity from muscles and basically smart, embedded computers that reside inside a limb that learn what the patterns look like, and then relaying these patterns to a robotic limb.

"With speech it's the distinctive patterns of a person's voice. The kind of computing and signal processing technology behind both problems is surprisingly similar."

A Collaborative Beginning

The collaboration between UNB and Diaphonics started in 2003 with a small grant from Canada's National Research Council (NRC) for Englehart to lay out the design for building a voice identification system from the ground up for Diaphonics, a privately held firm backed by a number of venture capital firms.

"Everything looked good in the initial work," says Englehart. "And about a year after that, they landed a large federal grant from the Atlantic Innovation Fund to build the system.

"We then entered into a three-year collaborative research and development agreement to build the system that expanded to include another professor, a post-doc researcher, plus three engineers and a software architect to set up a

development shop in Fredericton in the NRC building."

Englehart says the system that has been developed is more sensitive than the human ear.

"Could you fake a voice and fool the system?" he asks rhetorically.

"It's highly unlikely because the software is actually more capable of distinguishing voices than you or I could."

In fact, most impersonation is based largely on mannerisms. Even just the tiniest little nuances of how a person articulates certain phonemes, one of the basics elements of speech, are picked up to build a template, he says.

By measuring pitch, frequency, intonation, and how long it takes a person to say certain words or phrases, the system creates a unique profile or template that is virtually impossible to duplicate, even for a talented impersonator.

"So the person with the closest template would be the individual identified as speaking, not the imposter," Englehart explains.

"You would have a very specific template and so would everyone else in the system."

In addition to a person using his or her unique voice to gain, for example, access to a bank account, additional technology created by Englehart's team can be used to discover a person's identity through audio surveillance.

Computer representation of human speech.

"There are applications in forensics where you might want to know if the voice clip you have really is Osama bin Laden," says Englehart. "A voiceprint is like a fingerprint. If you are tracking someone, or monitoring a phone call, our software can be running in the background. It has obvious applications for intelligence work."

Englehart calls the collaboration between UNB and Diaphonics "a fantastic two-way exchange of information and productivity."

"The guys who formed Diaphonics came out of the telecom industry in Atlantic Canada and were very knowledgeable about the market, but realized they needed engineering help to build their system." he says. "So they looked to us. And there are a lot of incentives and political reasons for industry to work with universities in Canada."

Andy Osburn, CEO of Diaphonics, says his company and Englehart's team were a good fit. Osburn — whose specialty was acoustics during a 20-year Canadian Navy stint — was Diaphonics' chief technology officer when the arrangements were set up with UNB.

"We are the kind of company that needs to pursue leading-edge speech technologies," he says. "We have a

strong technology team at Diaphonics, but we are working at capacity. It is quite common for a firm like ours to seek an academic partner that has a lot of depth and breadth in a particular field, in parallel with what the company is doing."

In addition to the appropriate research background, Osburn says the "human component" clicked with the UNB researchers, too.

"You have to land on a group that you think you can work with," he says. "It is obviously a collaborative team arrangement. We got started four years ago with a bit of collaborative research that was sponsored by the NRC, and it took off from there."

He says the three-year research and development project finished in the fall of 2007.

"But we will continue to work with and have ties to Kevin's group," he says. "There are always going to be new things to do as we move ahead.

He says he was pleased that the 36 months of collaboration identified technologies the company wanted to pursue.

"We also had time to see where the market was going as well," notes Osburn. "As a result, we have been able to produce and commercialize several products."

It is now in beta testing by existing customers, including banks, correctional institutions and the military.

David Foord, director of Intellectual Property at UNB, agrees that the partnership between Diaphonics and his university went well.

"We see all sorts of similar efforts in the research office here at the university. This is one that was excellent, in part because they took the right steps to make sure first there was chemistry and then moved into a larger project so they had a good statement of work and budget and vision for what was going to be done.

"The management team at Diaphonics is an impressive group who know what they want to do and know the market," says Foord, who notes that the university will receive royalties for its work on the voice biometric products.

"We're also pleased there will be ongoing research and development work," he says. "That wasn't something that we really planned for, it just happened because of the way we structured the legal agreement that allowed for this ongoing collaboration."

> "It is quite common for a firm like ours to seek an academic partner that has a lot of depth and breadth in a particular field, in parallel with what the company is doing."
>
> *Andy Osburn, Diaphonics*

Collaboration is a vital component of technology transfer.

Whether among researchers, departments or between university offices and the business community, local and national governments or nonprofit organizations, it is these working partnerships that cultivate great ideas and transform them into them into technologies that benefit society.

The 2008 *Better World Report* celebrates real world examples of technologies that were born from collaboration—partnerships that, in some cases, spanned years.

You'll read about technology that vastly improves the speed at which drugs and fluids can be administered in an emergency, how what started as a "curious compound" now provides hope to millions battling cancer, and how a researcher working on artificial limbs helped develop voice identification technology that may one day help fight terrorism.

You'll read about researchers who didn't let setbacks, mergers or geography stop them from making sure their work helped make this a better world.

Here are a few examples of the 25 successful collaborations profiled in this book and the products that may never have materialized if not for academic research and the transfer of these discoveries to the marketplace:

- Tiny microelectromechanical motion sensors that play a critical role in locating victims and deploying assistance
- Nanoscale iron products for toxic and hazardous environmental remediation
- Work that provides hope for a vaccine against amebic dysentery
- Technology that efficiently converts ammonia into hydrogen to produce inexpensive fuel
- The next generation of children's books.

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

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2008 Edition
www.betterworldproject.net

ISBN 0-9778444-5-5