



# IDEAS WITH A FUTURE

Projects by College of Medicine faculty members show how new discoveries at UVM can bring about improved treatments, techniques, and jobs.

by Jennifer Nachbur

In the center of the laptop screen lies the main attraction: an image of the human heart that rotates as colored waves of blue, green, yellow and red flow over it. Added to the neon display — pinpricks of light illuminate different regions. Across a segment of the right side of the screen run the familiar peaks and valleys of EKG lines. Guided by the computer's trackpad, a bright blue "wand" appears at the left of the screen, emitting a water ripple of color from each location on the heart that it touches. This is a representation of the heart, not the real, three-quarters-of-a-pound of muscle that beats relentlessly, one hopes, within your chest; but this image behaves exactly like the real thing.

With laptop open, cardiologist Peter Spector, M.D., demonstrates this new interactive teaching tool, a three-dimensional computational model called Visible EP (for "electrophysiology"), which he co-developed with Professor of Medicine and engineer Jason Bates, Ph.D. Their collaboration was a fortuitous mixture of knowledge and skillsets.

"Jason didn't know *what* he was programming and I didn't know *how* to program what we needed to make it do," says Spector. He likens their working relationship to two people riding on a unicycle, with one — Bates — blindfolded and pedaling, while the other — Spector — perched on the pedaler's shoulders, telling him which way to go.

A number of College of Medicine faculty have cultivated discoveries like Spector's, each at a different point along the road to commercialization. Growing support for these promising innovations — through the University's Office of Technology Commercialization (OTC) and efforts including the Department of Medicine's SPARKVT program — are bringing more and more faculty members' discoveries to light in the commercial marketplace. While some products now sit in spinoff companies like Spector's Visible

At left: Professor of Medicine Peter Spector, M.D., who worked with Professor of Medicine Jason Bates, Ph.D., to develop a computerized map of the electrical activity of the heart that can be used as a diagnostic and teaching tool.

Jeff Clarke



Above, left: Professor of Medicine Mercedes Rincon, Ph.D., holds a patent relating to a protein that can help predict a cancer cell's responsiveness to chemotherapy. Above, right: Professor of Psychiatry Thomas Simpatico, M.D., at left, with Chittenden County State's Attorney T.J. Donovan. Simpatico's web-based tools are being tested in a program to reduce recidivism.



Electrophysiology, others are still in the testing stages, or are transforming into new and expanded inventions.

Over the past several years, Vermont has gained national recognition for its innovative pursuits. An October 2012 *CNN Money* article listed Vermont among ten states with the most patent activity, with 3.5 patents per thousand residents. In early 2013, a Brookings Institute report ranked Burlington number two in the nation among the "20 most innovative cities in the U.S."

Often, the innovation first occurs in the lab, where a research discovery takes place. At that point, explains Corine Farewell, director of the OTC, the inventor, be they one person or a group, completes an Invention Disclosure Form and consults with the OTC on intellectual property (IP) strategies.

"Our goal is to steward the technology through the necessary intellectual property channels to make the product or service available for the public good," Farewell says.

Professor of Medicine Mercedes Rincon, Ph.D., has been on the OTC radar — and in their offices in the Given building — many times over the past seven years. She holds one patent and two licenses related to her work with MCJ, a protein that can help predict a cancer cell's responsiveness to chemotherapy.

Rincon and former graduate student Wendy Neveu, M.D.'11, Ph.D.'10, isolated an antibody that recognizes MCJ, and filed for the first patent for this diagnostic tool in February 2007. Nearly

six years later, it was granted in January 2013. Rincon opted to license the patent to Burlington, Vt.-based biomarker development company BioMosaics to market the antibody for use in testing breast and ovarian cancer patients.

Rincon's work has evolved from that initial discovery to broader applications that are drawing a lot of excitement. "There seems to be a connection between metabolism and cancer, and maybe MCJ is the missing link," says Rincon.

## Streamlining systems to link disadvantaged populations to appropriate care

Individuals suffering from substance abuse and mental health challenges often end up in the criminal justice system without ever having accessed the treatment that might have prevented their entry in the first place. That issue is at the heart of a novel web-based system, called MHISSION (Mental Health Intergovernmental Service System Interactive On-Line Network) that Professor of Psychiatry Thomas Simpatico, M.D., a former Metro Chicago Bureau Chief for the Illinois State Mental Health Authority, brought to UVM and Vermont in 2004.

A number of funding streams — including grants from the Vermont Department of Health, the Veteran's Administration (VA), and the U.S. Health

and Human Services' Substance Abuse and Mental Service Administration — facilitated MHISSION's evolution to a system targeting the veteran population, focusing particularly on veteran jail diversion, in addition to other criminal justice-related populations.

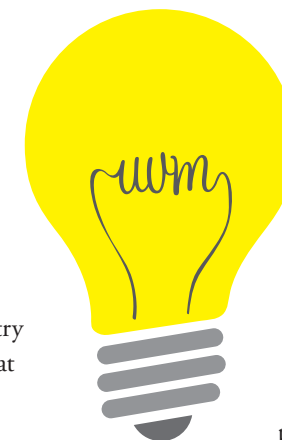
Sometimes, Farewell says, "The technology is so new that licensing to a startup company is the most desirable way to bring the invention to the market." Such was the case with MHISSION. With the OTC's support, Simpatico established MHISSION Translational

Systems (MTS) in 2012. "Having a spinoff allows us to be more agile in responding to the needs of a growing array of clients, while still maintaining a connection to UVM," says Simpatico.

Hailed by Vermont Governor Peter Shumlin as "a model for a more effective and humane approach to drug-related crime," Simpatico's most active current project is a pilot program with Chittenden County's Rapid Intervention

Community Court (RICC). Developed in partnership with Chittenden County State's Attorney T.J. Donovan, RICC's original aim was to reduce recidivism; with MHISSION's support, offenders with untreated addiction or mental illness get help, eliminating the need for incarceration.

"The MHISSION system effectively links populations to a wide array of





services,” Simpatico says. “That can apply to the homeless population, persons with mental illness and/or substance abuse, veterans, etc. Providing a connection with health care and human service delivery is really the essence of what it does.”

According to Donovan, the time is ripe for criminal justice system reform, and a web-based technological tool like MHISSION is just the ticket to facilitate that change. “We have traditionally looked to address substance abuse and mental illness issues through the lens of public safety with a focus on punishment,” he says. “In the partnership I have developed with Dr. Simpatico, we believe we can enhance our public safety by addressing these issues through the lens of public health.”

### Improving outcomes through personalized care pathways

The process of choosing a disease treatment option can often overwhelm a patient already dealing with the shock of a diagnosis. Having to consider length of hospital stay, invasiveness and recovery time, along with potential risks and cost issues, can be overwhelming.

Health economist Christopher Jones, Ph.D., says his methodology — called ForMyOdds — gives patients a helping hand in determining which treatment is best for their personal circumstances.

“ForMyOdds is all about predictive analytics, improving outcomes, reducing costs, and creating personalized care pathways,” says Jones, an assistant

professor of surgery and director of global health economics in the College of Medicine’s Center for Clinical and Translational Science (CCTS).

“Take the example of a patient with an unruptured aortic aneurysm,” says Jones, who is collaborating with vascular surgeon Andrew Stanley, M.D., on developing the ForMyOdds algorithm for that condition. “Relying on data we’ve analyzed, we can tell a patient — to a very granular level of detail — the most efficient and most optimized pathway for their unique circumstances.”

ForMyOdds uses data from patients and published study results — including individual circumstances, diagnoses, treatments, and outcomes — and applies a variety of mathematically-based analytical techniques that feed into each patient’s optimal pathway determination.

“We take great care to scour the literature and test our models,” says Jones, who has several collaborators on the project at UVM.

Insurance plans are Jones’ target market. He envisions a ForMyOdds “package” for physicians and patients that insurance companies pay for on a per-member, per-month basis. In a take-home-friendly portable form — think iPad, laptop or even Google Glass — a patient could engage via a portal to test for what Jones calls “alternatives” — alternatives based on consequences — for their particular medical treatment circumstances.

As one of several investigators funded through the Vermont Center on Behavior and Health’s Center of Biomedical Research Excellence award,



Top: Christopher Jones, Ph.D., with his ForMyOdds program, accessible by iPad, or even Google Glass. Above: Markus Meyer, M.D. presents at a recent SPARKVT pilot grant program.

a major effort over the next five years will be incentivizing patients using the ForMyOdds platform.

“Now that we know what the optimal care pathways will be, how can we incentivize those patients to, for example, give up smoking around the time of surgery?” asks Jones, who aims to build in an algorithm that identifies not only the optimal incentive for a given patient to stop smoking, but the best means to alert that patient regarding their receipt of the incentive or, even, he considers, a disincentive.

### Teach One, See One, Do One

As a professor of medicine and director of electrophysiology at Fletcher Allen

Health Care, Peter Spector wears all the hats available at an academic medical center — patient care provider, teacher and researcher. To this he has added another title: founder and director at his spinoff company, Visible Electrophysiology, LLC. “What makes this all workable is the fact that these are all faces of the same thing: trying to deeply understand how the heart works,” Spector admits. “We’ve incorporated the things that we’ve learned in the clinical space and in the research arena into Visible EP.”

The software technology that he and Bates co-developed is remarkable in what it does — modeling the electrical behavior of the human heart — and the minute detailing it brings to that modeling.

“We’ve made, essentially, a living, breathing, interactive human heart,” Spector marvels. “It will sit there and beat in what would be the equivalent of a normal rhythm; you can induce every sort of abnormal heart rhythm that you can imagine that a patient could have, and it’s all happening on a computer screen.”

Also notable is the model’s capacity for providing unpredictable responses, a phenomenon called emergent behavior. While the parts of the heart and the rules of interaction have been programmed into the system, the computational heart model’s reaction is entirely emergent, says Spector. And that feature makes Visible EP an attractive tool for medical education, as well as research applications. Because it can’t be readily seen, electrophysiology has been regarded as a particularly difficult specialty to teach; the field was waiting for just such a teaching tool as Visible EP. Spector and Bates were recognized with an award for licensing Visible EP at the 2013 Vermont Invention to Venture conference, an annual day-long event co-organized by the OTC.

The model wasn’t originally developed to be a teaching tool. Bates and Spector created it in an attempt to figure out how to cure the most common abnormal heart rhythm, atrial fibrillation (AF). Despite the large number of patients afflicted with AF — more than five million in the U.S. alone — treatment has been less than adequate. In addition to Spector and Bates, the

arrhythmia research team consists of three biomedical engineering doctoral students and a postdoctoral M.D. research fellow. Using their computer model, combined with studies of the real human heart, the arrhythmia research team has proposed a new approach to analyzing an individual patient’s electrical activity and to using this information to guide a new type of ablation. The group has developed a new catheter, signal processing algorithms and a mapping approach for treatment of AF. This work has been sponsored by a grant from the Eyslin Foundation and has led to the submission of eight patent applications.

### Supporting innovation through SPARKVT

The SPARKvt pilot grant program was launched in 2012 by Department of Medicine Chair Polly Parsons, M.D., to examine proposals for innovative and novel project ideas ripe for rapid advancement to the bedside. Parsons invited investigators in her department to submit a wide range of discoveries. Five were accepted for presentation in May 2013 to SPARKVT’s consultant panel — a collection of business leaders with extensive experience in the pharmaceutical, business, legal, and commercialization sector.

Markus Meyer, M.D., a cardiologist and assistant professor of medicine, had met with the OTC regarding the patentability of his concept for a simple, handheld heart function monitor. The device was among the ten projects presented and one of two faculty projects selected to receive one of SPARKVT’s initial \$50,000 seed grants. This past February, Meyer delivered a project progress report to the consultant panel. Rincon, who

co-leads the program’s organizing committee, said the panel members, who participated both in-person and via videoconferencing, expressed enthusiastic continued support for his project.

“The follow-up presentation was really helpful,” says Meyer. “You get to deal with people who have a completely different background and they have very good ideas. It’s simple — you get an answer right away.”

Meyer’s idea for the monitor grew out of an observation — and frustration — in his clinical practice.

“This device would basically make things much less expensive and faster,” he says. “Instead of waiting a few hours for results, you would see an immediate result, at a fraction of the cost.”

With idea in hand, he met with the OTC staff, who drafted patent protection for the monitor, and then moved to the next step — research — and building a team of co-investigators. Martin LeWinter, M.D., professor of medicine, serves as the team’s scientific advisor, assisting with grant proposals; Stephen Bell, a senior researcher in the cardiovascular research laboratory, is chief technician/engineer; Bradley Palmer, Ph.D., assistant professor of molecular physiology and biophysics, focuses on data analysis and software.

“Without the SPARK program, it wouldn’t be where it is right now,” Meyer says. “That allowed us to further develop the idea.”



From left: Sanchit Maruti, M.D., William Cats-Baril, Ph.D., Isabelle Desjardins, M.D., and Robert Althoff, M.D., worked together on the creation of a suicide risk assessment tool for hospitals.

## Replicating the expert decision-making process

The field of psychiatry contends with a highly regulated environment that can shift attention from patient care to paperwork. One requirement in particular — The Joint Commission-mandated suicide risk assessment for hospital-based patients — provided an excellent opportunity for a research project to determine a solution to a system severely lacking in uniformity. Fourth-year psychiatry resident Sanchit Maruti, M.D.'10, and his mentor Isabelle Desjardins, M.D., associate professor of psychiatry, launched the project in 2011.

"There are 800 suicides in hospitals in the U.S. each year," says Maruti. "This requirement came out of a necessity to address an issue," adds Desjardins.

He and Desjardins discussed the issue with experts in the field, reviewed literature and though they found a number of tools that are utilized, none of them could replicate the "gold standard" for suicide risk assessment — the psychiatrist's evaluation of the patient.

However, says Maruti, "The resources just do not exist to make that possible."

Desjardins describes the psychiatrist's critical thinking process as multidimensional. Suicide risk assessments, she says, evaluate risk in different timeframes — from immediate, to a few days out, to over a lifetime. She and Maruti more closely surveyed the literature on the cognitive process that leads a psychiatrist to determine a patient's level of risk, but nothing had been published.

Aiming to co-develop a tool that could replicate expert decision-making, be clinically beneficial, meet regulatory requirements, and could interface with the electronic medical record, Maruti and Desjardins reached out to a wide range of experts for advice, helped by William Cats-Baril, Ph.D., of UVM's School of Business Administration.

Among the questions considered, says Desjardins, were "What is really happening in your minds when you are evaluating suicide risk? How do you weigh these factors? What do you take into consideration?"

The information gathered during this process was distilled into a list of the tool's primary features: questions, levels of risk, and levels of intervention. The process would be directed by an electronic algorithm similar to the one Jones employs in his ForMyOdds model, and accessed on an electronic platform — an iPad.

Fletcher Allen's Jeffords Institute for Quality and Operational Effectiveness

**"What drives us is that it's ultimately about the patient ... if there's a process that can help improve the care of the patients, address an unmet need, anything that can have a positive effect on their health, that's our goal."**

— Sanchit Maruti, M.D.'10,  
Fourth-year psychiatry resident

provided them with \$20,000 in funding to develop the system in 2011 and following a demonstration of the prototype, Desjardins received a \$50,000 Investigator-Initiated Research Award from the UVM Medical Group in late 2012.

Collaborators have been key to shuttling the project along to its current status. In addition to partners in Fletcher Allen's PRISM electronic health record office, faculty members Robert Althoff, M.D., associate professor of psychiatry, and Kaley Freeman, M.D., Ph.D., assistant professor of surgery and emergency medicine physician, as well as Diantha Howard, M.S., biomedical informatics specialist in the Center for Clinical and

Translational Science, have provided enormous support to Maruti and Desjardins.

In the past year and a half, the team conducted research to measure how well their algorithm simulates the psychiatrist's cognitive process, and examined the feasibility of using the tool in a clinical setting. Freeman has led testing with more than 250 patients in the emergency department in conjunction with his UVM undergraduate Emergency Medicine Research Associate Program. Local psychiatry faculty, like Althoff and others, conduct comparative evaluations of the cognitive process of the system.

"We are at the very early stages, but it's promising," says Desjardins.

Maruti and Desjardins are also considering applications outside of the hospital in such institutional environments as prisons, in the Veterans Administration, and in colleges and universities, which could also benefit from the new tool.

This spirit of sharing new knowledge speaks to the role and mission of an institution of higher learning. It's no surprise that the latest innovations generated by UVM College of Medicine faculty have a strong public health and health system improvement bent — these inventions, whether laboratory-, computer-, or device-based, share a common objective to improve health among the population as a whole.

Maruti sums up what could be the guiding ethic of all College of

Medicine faculty seeking to commercialize their innovations. "What

drives us is that it's ultimately about the patient," he says. "If there's a process that can help improve the care of the patients, address an unmet need, anything that can have a positive effect on their health, that's our goal." **VM**

