Extracts

Device Ensures Patients Take Medication

Xhale Inc. CEO Richard Allen, left, and anesthesiology Professor Richard Melker are developing a breath monitor to track medication adherence.

Most of us have missed a dose of antibiotic or forgotten to take a daily vitamin. But when the stakes are higher — as they are for people with HIV/AIDS — a skipped pill could mean the difference between health and hazard for the entire population.

Now, a breath-monitoring device developed by scientists at the University of Florida and Xhale Inc. could help prevent the emergence of drug-resistant strains of HIV by monitoring medication adherence in high-risk individuals.

"For HIV, it's been shown that if you don't take a very high percentage of your medication, you may as well not take medication at all," said Richard Melker, a professor of anesthesiology at the UF College of Medicine and chief technology officer for Xhale.

Patients who take some but not all of their medication increase the likelihood the virus will mutate into a deadlier, drug-resistant form. Experts have tried literally hundreds, if not thousands, of ways to monitor drug adherence, ranging from daily log books to blister packs that record the time each pill is dispensed. Despite the money, time and effort devoted to these methods, Melker said only one works well: directly observed therapy, or DOT.

"If you have a disease that is deemed to be a public health risk, authorities can put you into a program where you have to come to the clinic every day and be observed putting the pill into your mouth and swallowing it," Melker said.

But that process is inconvenient for patients, as well as for clinic personnel who have to track them down when they fail to show up. A breath-monitoring device developed by UF scientists and Xhale could change that, allowing patients to participate in a type of virtual DOT from home.

"The machine sits in your home and when it's time for you to take your medication, it makes a beeping noise. If you don't hit a button after about five minutes, it's going to beep louder and louder until you come," Melker said. "If you don't come after a certain amount of time, the machine can call the clinical trial coordinator and indicate that subject or patient didn't take the medication as prescribed."

The device, which is slightly smaller than a shoebox, records the results of each breath test, allowing patients to bring a memory card or USB key to the clinic once a month and receive a printout of their results. Eventually, the researchers hope to reduce the size of their detection device to fit inside a cell phone. But for now, they're satisfied that the technology works.

"The doctor can see how often you took it and exactly what time. If it made the patient really sick or dizzy and they didn't take it, they can find out why," Melker said. "It's not just a question of did I or didn't I take it, but when you took it or why you didn't take it."

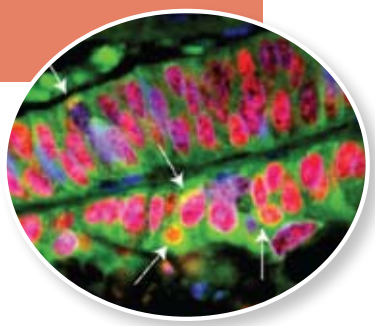
The researchers developed the adherence monitor by incorporating minute amounts of an alcohol into a gel capsule. The additive, called 2-butanol, is one of many GRAS — Generally Recognized as Safe — compounds approved by the Food and Drug Administration for use in foods.

"We wanted (patients) to swallow a chemical and have it transform into something else that's easy to monitor," said Matthew Booth, an assistant professor of anesthesiology at the UF College of Medicine and an investigator in the study. "When it hits the stomach lining and liver, an enzyme converts the alcohol to a gas that can be measured in the breath."

To determine how well the byproduct could be detected, six healthy volunteers swallowed empty pills in which the capsules contained trace amounts of 2-butanol. After five to 10 minutes, the scientists could measure the volatile byproduct in the volunteers' breath using a small detector. The scientists say their device could also be used to monitor medication adherence in patients with other communicable diseases, such as tuberculosis.

Ann Griswold

Vita Golubovskaya was part of a team that discovered that mutations in the tumor-suppressing p53 protein (red) lead to overabundance of a second protein called focal adhesion kinase, or FAK, (green) which makes cells resistant to radiation or chemotherapy.



Cancer Therapy Targets Identified

New therapies must target a key protein interaction to destroy aggressive cancer cells' protective force field, University of Florida scientists reported in April at the American Association for Cancer Research's annual meeting in San Diego.

The barrier deflects damage from radiation or chemotherapy, making some cancer cells difficult to destroy, but researchers from UF and the University of North Carolina at Chapel Hill may have discovered why. Their study revealed that mutations in the tumor-suppressing p53 protein lead to overabundance of a second protein called focal adhesion kinase, or FAK, which makes the cells less vulnerable to attack.

"These findings are significant to future cancer research and the development of new therapies," said Vita Golubovskaya, an assistant professor in the UF Department of Surgery, who presented the findings. "The high correlation between these two markers is critical for predicting patient prognosis."

The next step will involve developing cancer therapies that target this interaction, Golubovskaya added.

Both p53 and FAK are found in low levels in normal, healthy cells. The p53 protein ensures that cells strike a wholesome balance between growth and death. In its normal state, p53 suppresses the FAK protein and weakens the molecular force field around cancer cells. But mutations in the p53 protein can interfere with this regulatory function.

Mutations in the p53 gene are commonly found in patients with cancer, and those with more aggressive forms of the disease boast particularly high levels of p53 and FAK. Most cancer therapies are largely ineffective against the resulting FAK force field, which has been identified in melanoma and most solid tumors of the breast, lung, brain, thyroid and colon.

Scientists are still unsure what causes mutations in p53 and why FAK binds to the damaged protein. But the study revealed that the interaction interferes with the signaling process that normally induces cell death, allowing cancer cells to grow unchecked.

The population-based study centered on 600 patients with breast cancer. UNC researchers, led by Kathleen Conway-Dorsey, an assistant professor of cancer epidemiology, analyzed p53 mutations in tumor tissue samples from the patients. UF researchers then identified the FAK protein in the breast cancer samples and performed a statistical analysis, finding that the p53 mutation is associated with overabundance of FAK.

"Basically, tumors of breast cancer patients with p53 had a higher probability of high expression of FAK," said Golubovskaya. "We have shown before that FAK overexpression will highly correlate with more aggressive breast cancers."

Results from the current study could help predict patient prognoses, researchers say. Many patients with mutant p53 and an overabundance of FAK don't fare well, but new therapies could change that by targeting the protein interaction. The next step will involve identifying the types of p53 mutations that contribute to an overabundance in FAK.

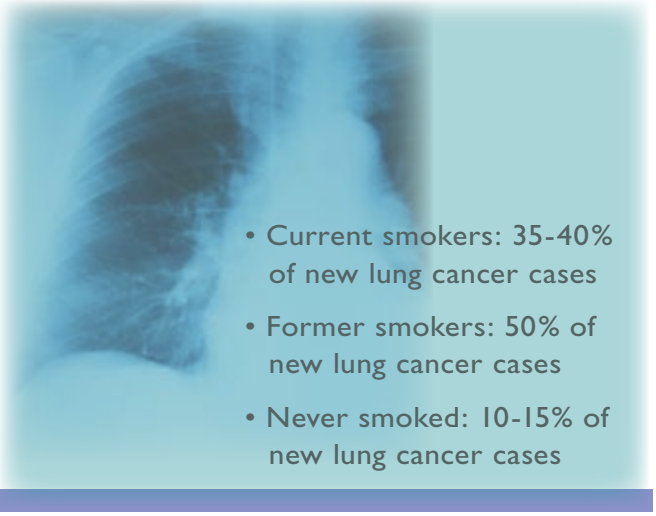
The research was supported by Golubovskaya's grant from Komen for the Cure and a National Institutes of Health grant held by surgical oncologist William Cance, chairman of the UF College of Medicine's Department of Surgery.

Jennifer Brindise

Extracts

Protein Shields Lung Cancer Cells

A protein that helps lung cancer cells thrive appears to do so by blocking healthy cells' ability to fix themselves when radiation or chemicals such as nicotine damage their DNA, according to a University of Florida study published in the journal *Molecular Cell*.



High levels of the protein, known as Bc12, are found in the cells of lung cancer patients who smoke.

Previous UF research has shown that nicotine activates the protein, which helps tumor cells live long past their natural lifespan and resist chemotherapy. The new findings explain how the protein enables cancer cells to circumvent the body's own efforts to change them back into healthy cells — or evade treatments designed to kill them.

Cancer is frequently associated with the accumulation of genetic aberrations in cells' chromosomes. If these damaged cells can't access their built-in repair system and subsequently survive long enough to divide and multiply, they pass along their mutations.

"If a cell experiences DNA damage, often that DNA can be repaired. But we found that Bc12 can block the DNA repair mechanism, which promotes tumor formation and genetic instability," said Xingming Deng, an assistant professor in UF's College of Medicine who is affiliated with the UF Shands Cancer Center. "This is a very important fundamental mechanism that explains why this protein has (a cancer-forming) function."

Researchers say just one cell that develops a genetic mutation and is unable to repair itself could be enough for a full-blown tumor to develop.

"Lung cancer is the No. 1 killer of all cancer types; it is the most dangerous," Deng said. "We wanted to find a way to treat lung cancer, how to prevent lung cancer, because lung cancer prognosis is very poor."

Nearly 162,000 people will die from lung cancer in 2008, accounting for about 29 percent of all cancer deaths, according to the American Cancer Society. More people die of lung cancer than of colon, breast and prostate cancers combined.

In the study, UF scientists performed a series of laboratory experiments on lung cancer cells in culture that illuminated the molecular chain of events that allows Bc12 to disrupt DNA repair.

Deng also plans to explore the possibility that nicotine-induced activation of Bc12 can be blocked to increase chemotherapy's effectiveness.

"This will probably help us in the future find ways to prevent tumors," said Deng, adding that the protein could be a target for drug development. "We can target this mechanism and somehow find a way to prevent tumor formation."

The research was funded by about $1.2 million in grants from the National Institutes of Health and the Flight Attendant Medical Research Institute. FAMRI was established in 1997 as a result of a $300 million settlement between airline flight attendants and the tobacco industry. The nonprofit organization awards grants for research focusing on smoking-related illnesses.

Melanie Fridl Ross

Termite Damage Cuts Insulation Values

Termites aren't just out to eat the wood in your home. A new University of Florida study shows the voracious insects like to feast on your home's insulation, too — making it nearly 75 percent less effective.

In tests measuring how termites damage the thermal properties or insulation in homes and other buildings, three types of widely used construction materials — 2-by-4 boards, five-ply plywood and foam board insulation — were exposed to the pest for eight weeks by entomologists at UF's Institute of Food and Agricultural Sciences.

"All three building construction materials were damaged by termites, but the pest caused more damage to insulation than to either the wooden 2-by-4 or plywood samples," said Phil Koehler, an entomology professor who supervised the study by graduate student Cynthia Tucker and research associate Roberto Pereira. Their findings were published in the April issue of the journal *Sociobiology*.

The thermal imaging tests, which measured heat transfer through the three building materials, focused on damage caused by a species of subterranean termite, *Reticulitermes flavipes*, that's well-known in North America.

Tucker, who is completing work on her doctoral degree in entomology at UF's College of Agricultural and Life Sciences, said they were surprised to find that rigid foam board insulation was most heavily damaged by termites, with 12 percent of the material being removed by termites in eight weeks, causing a 27-percent loss in insulation values.

"Most types of insulation are composed of plastic that's not a source of food for termites, but the soft texture of insulation allows termites to build extensive tunnels and consume paper that lines the outside surface," Tucker said. "In fact, the insulation materials are an almost ideal habitat because they protect the pest from cold temperatures."

She said tests showed that plywood was the most resistant to heat flow, but once termites damaged the plywood, temperature changes were significant. After termites ate just 3.1 percent of the wood, insulation values dropped 74 percent.

When the pest attacked 2-by-4 boards, consuming 6.7 percent of the wood by tunneling along the fibers and within softer spring wood, there was a 35-percent drop in insulation values.

"Until recently, changes in the thermal properties of a structure caused by termites — especially for buildings in areas where temperature extremes require lots of heating or air conditioning — have been overlooked," Tucker said.

Phil Koehler, pgk@ufl.edu

Chuck Woods

Thomas Wright

Entomology graduate student Cynthia Tucker, left, and Roberto Pereira, a UF research associate, use a thermal imaging camera to measure heat transfer through building materials damaged by termites. Materials damaged by termites were shown to be less energy efficient, resulting in higher heating and cooling bills.

Extracts

Microgreens Get Florida Farmers Thinking Small

Dubbed one of 2008's culinary buzzwords by National Public Radio, microgreens — vegetables harvested soon after sprouting — are expected to be one of this summer's hottest food trends, as well as a boon to many small specialty farms that provide them to restaurants and farmers' markets.

Experts at the University of Florida's Institute of Food and Agricultural Sciences are helping farmers take advantage of the phenomenon.

"This interest in microgreens is a tremendous opportunity for a lot of the small farmers in Florida," said Robert Hochmuth, an extension agent at IFAS' North Florida Research and Education Center in Suwannee. "But it's not the same as growing regular crops. There's a learning curve involved."

Microgreens aren't the same as "sprouts" or regular young vegetables. Only certain vegetables can be grown as microgreens, such as arugula, radishes and kale.

They are grown under carefully controlled greenhouse conditions on specially textured fabric mats or other growing medium. Irrigation has to be meticulously measured, and harvesting perfectly timed.

The result is a tender, colorful vegetable packed with flavor as well as nutrients. In the restaurant world, those qualities make them ideal ingredients for "designer salads" that give diners a unique culinary experience — especially during the summer months when salads typically become more popular.

"It's so easy for salad to be boring," said Anthony Sicignano, executive chef of The Breakers Palm Beach. "There are the typical vegetable ingredients that form the base. People try to dress those up with toppings like cheese or meats or dressings — things that often aren't what a person looks for in a salad.

"If you can add vegetables that add a zest of flavor and texture, though, you can create a salad that tastes different and wonderful, but without violating the salad's basic identity," he added.

Robert Hochmuth

Malabar spinach

While it's possible to grow microgreens in small, personal batches, like many home chefs do with herbs, restaurant chefs like Sicignano depend on small farmers for large quantities and variety.

"It can be a tricky business," said Denise Francis, who runs the Twinn Bridges Farm in Macclenny, Fla., with her husband, Scott. The couple have been working with Hochmuth for the last three years to develop a microgreen growing program.

"The timing is everything," she said. "Parsley is usually perfect at 25 days, while radishes usually only take five. Meanwhile, you have to plan everything out so that the chefs get the mixes of microgreens that they like."

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Stu Hutson

Advertisers, Scientists Track Emotions In Brain

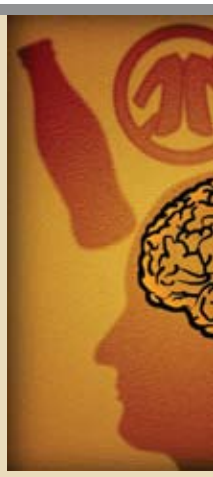
First came direct marketing, then focus groups. Now, advertisers, with the help of neuroscientists, are closing in on the holy grail: mind reading.

At least, that's what is suggested in a paper published in February in the journal *Human Brain Mapping* authored by a group of professors in advertising and communication and neuroscience at the University of Florida.

The seven researchers used sophisticated brain-scanning technology to record how subjects' brains responded to television advertisements, while simultaneously collecting the subjects' reported impressions of the ads. By comparing the two resulting data sets, they say, they pinned down specific locations in the brain as the seat of many familiar emotions that ripple throughout it. The feat is another step toward gauging how people feel directly through functional magnetic resonance imaging, or fMRI, and other brain-scanning technology — without relying on what they claim to be feeling, the researchers say.

"We are getting to the heart of the matter by really showing this process in the brain, and how it works," said Jon Morris, a professor of advertising and communications and lead author of the article.

Using MRI or fMRI — the former creates internal images of the brain, while the latter tracks blood flow within the brain — to test consumers' responses to advertisements or other stimuli is not new. But according to the study, much of the previous research has found that, for example, responses to pleasant or unpleasant stimuli occurred throughout many regions of the brain, rather than in one specific location. As a result, the technique seemed of limited usefulness: Analysts could gauge only general response activity, not specific emotions.



"There was no real key happiness center, no key sad center, no key love center," Morris said. "What you got was brain activity, in general."

Sarah Carey

Dr. David Freeman with Livello

Imaging Solves Brazilian Horse's Sinus Headache

After surviving an odyssey of complicated medical problems and difficult surgeries, a Brazilian Olympic dressage horse named Livello is recuperating back in his home country, thanks to University of Florida veterinarians.

This is a horse that came all the way from Brazil because we had the technology to treat him," said UF equine surgeon David Freeman.

Freeman said Livello's case illustrated the importance of powerful imaging equipment such as UF's MRI unit in guiding effective medical treatment.

"Livello actually came here because the owners were aware we had CT and thought that could be used to help him, but it turned out that the MRI was a better imaging tool for his problem," Freeman said.

Livello's story began in Brazil last October with a bad tooth. A tooth extraction procedure damaged the horse's tear duct and intraorbital nerve, veterinarians said.

"Tears were coming down his face, and he had nerve damage that was causing him to rub his face and sneeze," Freeman said, adding that a subsequent procedure did not resolve the problem. "The surgeries went well, but never cleared up the infection Livello had developed in his sinuses."

Because of the infection, Livello subsequently developed facial swelling and a malodorous nasal discharge.

Livello's owners and their veterinarians had heard of Freeman and UF's imaging capability and decided to bring the horse to Gainesville. In February, owner Jorge de la Rocha, who also has ridden Livello as part of the Brazilian Olympic dressage team, flew the horse and veterinarian Patricia Brossi to UF's Alec P. and Louise H. Courtelis Equine Hospital.

"We had some idea based on Livello's history and clinical signs that there was probably some necrotic bone that needed to be removed," Freeman said. "But we didn't know the exact location or extent of it, and that is where both the CT and our new MRI unit came in."

An initial surgery resulted in the removal of a lot of dead bone and tissue, but Livello's sinus drainage continued, as did the nasal discharge.

"So we did another MRI on him about three weeks later and then another surgery after that," Freeman said. "The MRI images helped us find the sites where we needed to go, and the site was not an easy area to gain access to."

Within weeks of the third surgery, however, Livello's nasal discharge had vanished.

"Every now and then we get cases that test us and test our general ability to handle very serious veterinary challenges, and this was one of them," Freeman said.

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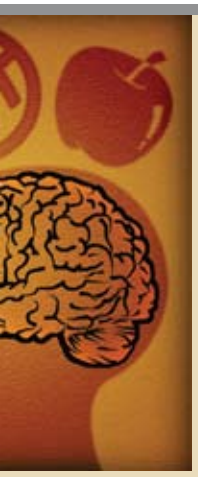
Sarah Carey



The UF team used an elaborate experimental system, currently under consideration for a patent, to try to narrow the search.

Because metallic or magnetic material can cause fMRI machines to malfunction, no television or sound equipment was allowed in the cylinderlike fMRI machines into which people are inserted. As a result, the researchers deployed a series of projections and mirrors to allow subjects to watch commercials. Sound reached them via tiny plastic pipes, similar to headphones once common on airplanes, rather than wires.

The 12 subjects also had hand-held devices that enabled them to report their feelings via a system called "Attitude Self Assessment Manikins." The "AdSAM" system lets viewers describe how they are feeling and the strength of those feelings by clicking on projections of people-like icons, a process that Morris characterized as more direct than translating feelings into words.

Researchers showed the subjects three television commercials advertising Coke, Evian and Gatorade, respectively, as well as an anti-fur commercial and an ad promoting teaching.

The researchers compared the activity in the subjects' brains as recorded by the fMRI machines to their reported responses on the AdSAM system. With several of the ads, they found the fMRI data and response converged on two of three measures — pleasure-displeasure and excitement-calm. Under the AdSAM system, these "bipolar dimensions" — as well as a third, dominance-submissiveness — form the foundation for more specific emotions.

Where the researchers compared the AdSAM data on pleasure-displeasure and excitement-calm to the fMRI data, they found simultaneous spikes in four different and highly localized areas of the brain. According to the article, the findings suggest "that human emotions are multidimensional, and that self-report techniques correspond to a specific task but different functional regions of the brain."

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