



DMS geneticist Mathieu Lupien, Ph.D., recently discovered a “pioneer” factor, called PBX1, that may lead to an understanding of how breast cancer tumors become resistant to therapies.

A glimmer of hope against a deadly disease

By the time pancreatic cancer causes symptoms, it’s often too advanced to treat, says DMS’s Stuart Gordon, M.D. The five-year survival rate for patients with metastatic pancreatic cancer is under 2%. But if the cancer is caught before it spreads, overall survival improves considerably. The problem is figuring out how to spot it early.

“There hasn’t been a very good screening test,” Gordon says. Ideally, he explains, a test to screen for a disease will be relatively inexpensive, noninvasive, safe, and highly specific and sensitive, meaning the results can be trusted to be accurate.

Test: Gordon recently collaborated with researchers at the University of Vermont to enroll 546 participants in a test of a screening protocol designed to catch pancreatic cancer early in people with an elevated risk of the disease. To be eligible, participants had to have either at least one close relative with pancreatic cancer or a genetic mutation that increases the risk of the disease.

The first step in the protocol is a blood test that looks at levels of an antigen called CA 19-9; high levels can be a sign

of pancreatic cancer. This test fits many of the criteria identified by Gordon: it’s not expensive or invasive and it is safe. However, a patient who tests negative for CA 19-9 could potentially still have pancreatic cancer, and one who tests positive might not have it. “But it’s probably the best serum marker we have,” Gordon says, which is why the team used it.

Detect: Participants with high levels of CA 19-9 then had endoscopic ultrasound (EUS) imaging. Gordon says EUS is an effective way to detect pancreatic cancer early in its development. But, he adds, it’s expensive and invasive and must be done under general anesthesia.

Of the participants, 27 had elevated CA 19-9 levels. All but one of the 27 underwent EUS imaging (one declined). Potentially cancerous growths were spotted in five participants, and in one the growth turned out to be pancreatic cancer. That person had surgery to remove the tumor and was still alive without a recurrence at the end of the study, over three years after having surgery. Two other participants had noncancerous growths serious enough to warrant surgical removal. The patients who did not have surgery were monitored to see if the findings became cause for concern.

Cost: Gordon says the test isn’t yet ready for widespread use. But he and his colleagues noted in *Gastrointestinal Endoscopy* that detecting the one cancer cost about \$41,000—which is comparable to mammography or colonoscopy.

It was easy to recruit patients for the study, he adds, because anyone who has had a family member with pancreatic cancer knows how devastating it can be. “Family members are pretty shook up about it,” he says. “They wanted to do something to help the cause.” That’s a goal Gordon shares as well. AMOS ESTY

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JON GILBERT FOX

Gordon studied a pancreatic cancer screening test.

Inflammation variation

Cortisol, often called “the stress hormone,” can be pro-inflammatory, anti-inflammatory, or neither, depending on its concentration in the blood. So found a recent study led by Dartmouth anesthesiologist Mark Yeager, M.D. In a variety of experiments, Yeager and his colleagues showed that baseline cortisol levels permit inflammatory immune responses, but moderate cortisol concentrations suppress inflammation and high concentrations are neither pro- nor anti-inflammatory. Cortisol regulation of human inflammation is both “dualistic” and “dynamic,” wrote the researchers in the journal *Dose-Response*. “It evolves over time.”



Adverse effects

Before 1971, millions of pregnant women took the drug diethylstilbestrol (DES), on the advice of their doctors, in hopes of preventing pregnancy complications. Instead, the drug proved dangerous for both mothers and babies. A new study coauthored by DMS’s Linda Titus-Ernstoff, Ph.D., adds to the list of dangers posed by DES. Women who were exposed to it in the womb are at a higher lifetime risk of infertility, preterm delivery, early menopause, and several other adverse health outcomes, according to the analysis, which was published in the *New England Journal of Medicine*.



For a **WEB EXTRA** with a link to audio laugh clips from Hudenko's study, see dartmed.dartmouth.edu/w11/we05.



DMS's quantitative biology institute, its director Jason Moore, Ph.D., told *Nature*, is "training computational-biology students to speak multiple languages beyond bioinformatics."

Autism study is no laughing matter (or is it?)

There are many kinds of laughter, from hearty guffaws to polite chuckles. The distinction that interests William Hudenko, Ph.D., a DMS assistant professor of psychiatry, is between "voiced" and "unvoiced" laughter. A natural tendency of children with autism to produce voiced laughter could help them build stronger social connections, he says.

Voiced laughter, Hudenko explains, has a song-like quality. It's "what comes to mind when you think about laughter," he says. Snorts and chuckles, on the other hand, are examples of unvoiced laughter, which is usually atonal and does not involve the vocal chords.

Joke: "Unvoiced laughter is related to low-arousal, frequently social situations," Hudenko says. "For example, if I cracked a lame joke and you chuckled, it wouldn't be because you're really amused. You'd be doing so because you've learned that it's the appropriate social response."

As children grow, they typically use more unvoiced sounds. By adulthood, up to half of laughter is unvoiced. But much is still unknown about laughter in children, and less in children with autism.

In research he conducted before arriving at DMS this summer, Hudenko and colleagues at Ithaca College recorded

laugh samples of 30 children aged 8 to 10. Half were typically developing children, and the other half had a confirmed autistic disorder—mostly on the mild end of the autism spectrum.

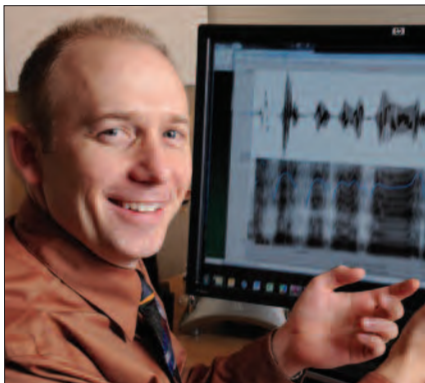
Block: The researchers made the children laugh with time-tested strategies such as knocking over block towers and popping bubbles. Their findings, published in the *Journal of Autism and Developmental Disorders*, show that the children with autism laughed in a sing-song, voiced fashion 98% of the time, while only 60% of the laughs in the typically developing group were voiced.

Hudenko and a colleague then recruited Ithaca undergraduates to rate how much they liked various laugh samples. These results, published in the journal *Autism*, reveal that subjects found the unguarded, voiced laughter of children with autism much more enjoyable. This was true even when subjects heard only voiced laughs from each group.

Genuine: "There's something about the laughter of children with autism that goes beyond voicing," Hudenko says. He thinks it may reflect a preference for what is genuine over what is forced. "Research has shown that we don't like it when people produce disingenuous expressions, because they're essentially trying to cheat us," he says. "I think as children with autism develop, they don't learn social laughter the way typical kids do. When they laugh, they're genuinely happy, and that's probably why we like hearing it."

Hudenko is excited by the idea that the work could aid children with autism. "Laughter helps build bonds between people," he says. "I'd like to help these kids find appropriate social contexts to express this laughter people enjoy hearing and connect more meaningfully with their families and peers." ALISSA POH

Voiced laughter, Hudenko explains, has a song-like quality.



JON GILBERT FOX

Laughter is all in a day's work for Hudenko.

A hole in "lifesaver" argument

It is conventional wisdom "that every screen-detected breast cancer survivor has had her 'life saved' because of screening," wrote DMS's H. Gilbert Welch, M.D., and Dartmouth senior Brittney Frankel in *Archives of Internal Medicine*. But they concluded that of the 230,000 women a year diagnosed with breast cancer after mammography, only about 4,000 to 18,000 actually benefit from the test. Many who survive would have been treated successfully even without mammography, while thousands of others are treated unnecessarily.



Booze cues

Drinking references in song lyrics are nothing new—think Willie Nelson's "Whiskey River"—but they may be more frequent and influential for today's teens. "The average U.S. adolescent is exposed to 34 references to alcohol in popular music daily," said a paper coauthored by DMS pediatrician James Sargent, M.D. Sargent and researchers at the University of Pittsburgh found that one in five songs that U.S. adolescents listen to contains explicit references to alcohol, often a specific brand. "These alcohol brand appearances are associated commonly with a luxury life-style characterized by wealth, sex, partying, and other drugs," they wrote in the journal *Addiction*.





DH is taking part in a clinical trial to treat stroke victims with a chemical found in bat saliva; it can be used up to nine hours after the stroke—an important benefit in a rural area.

A new way to app-raise seniors' health

Using “apps,” applications created for smartphones, it’s possible to count calories, interpret a baby’s cry, or whistle for a dog. Now, DMS researchers are developing an app to monitor the health of senior citizens.

The standard way to evaluate physical and mental well-being is through surveys. But self-evaluations are subject to bias from patients’ imperfect memories and from their desire to give favorable responses, says epidemiologist Ethan Berke, M.D. So he set out to create a better way.

In 2005, while at the University of Washington, Berke teamed up with Tanzeem Choudhury, Ph.D., a specialist in designing machines that measure physical and social behaviors. Their first attempt resulted in a fanny pack filled with sensors and batteries. By 2009, Berke and Choudhury, by then both at DMS, had developed a less obtrusive device—a two-inch-by-two-inch mobile sensor—that they tested in a pilot study.

Sensors: For 10 days, eight residents of a local retirement community wore sensors clipped to their waists. The sensors recorded subjects’ activity level, including the time they spent walking or running, as well as their social interactions, including

the number of conversations they engaged in and the pitch and volume of the participants’ voices (the actual conversations were not recorded). Then the researchers compared the data gathered by the sensors to the subjects’ responses on surveys of their physical and mental health.

Social: The results, published in the *Annals of Family Medicine*, were compelling. On measures of social and mental well-being, the data from the sensors correlated closely with the survey results. Subjects who spent the most time talking to others—as measured by the sensors—reported on the surveys being happier and more socially connected.

On measures of physical activity, the sensor data didn’t correlate quite as closely with the survey results. A likely explanation, Berke says, is that subjects had trouble recalling past physical activity.

But with the general relationship established, Berke and Choudhury began seeking a way to incorporate the sensors into smartphones. With help from Dartmouth computer scientist Andrew Campbell, Ph.D., they created an app called BeWell that monitors physical activity, voice acoustics, and sleep patterns. It runs on Android phones and gives real-time “well-being scores.” The app proved 80% accurate in a pilot study. Before making it available to the public, Berke plans to test it on 100 older adults at a health center in Manchester, N.H.

Avert: He envisions a day when the app can help avert physical and mental health problems. Often, he says, patients are given mental-health surveys only after they show symptoms of severe depression. “If people were wearing these devices, we might have the ability to detect changes in mental-health status,” he says, “which could result in earlier diagnosis and . . . treatment.”

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It runs on Android phones and was 80% accurate in a pilot.

Home truth

Too many older adults with serious mental illness reside in nursing homes when they could be living in less-restrictive settings. So suggests a study by members of the DMS Department of Psychiatry, published in the *Journal of Aging and Social Policy*. “The appropriateness of nursing homes for individuals with serious mental illness remains a controversial issue in long-term care policy,” they wrote, “more than a decade since [a landmark Supreme Court decision], which affirmed the rights of persons with disabilities to live in their communities.”



Motion potion

Getting adolescents off the couch and in motion may have lasting benefits not just for their waistlines but also for their brains. In a study conducted by a DMS neuroscientist and two students, rats that exercised regularly during adolescence demonstrated better memory function in adulthood than rats that had not. They also had higher levels of an important protein called brain-derived neurotrophic factor. “Exercising during adolescence may capitalize on the peak of neural plasticity that occurs during this developmental stage,” the researchers wrote in the journal *Neuroscience*, “and lead to more durable effects on cognitive function compared to exercising during adulthood.” ■



MARK WASHBURN

Berke hopes his phone app will safeguard seniors.