

Driving out HPV

Your teenaged daughter has begun to drive on her own. She's completed driver's education, passed her test, and signed a parent-teen contract to drive safely and carefully. You know she's a reasonably careful driver. But she's also human, and human beings make mistakes. Plus, she isn't the only driver on the road. Now imagine that three souped-up soy-beans could prevent her death in a head-on collision. Would it save her from all mistakes or protect her from every kind of accident? No, but it would eliminate one deadly possibility. Given that possibility, wouldn't you want her to swallow those tiny pieces of protein?

This illustration, albeit far-fetched, has an actual, clinical equivalent. Now available to adolescent girls and young women is a vaccine, engineered around a surface protein that blocks the spread of the human papillomavirus [HPV] in females. In protecting against four strains of HPV, Gardasil, marketed by Merck, has proven highly effective in eliminating the primary cause of cervical cancer, historically one of the deadliest cancers in women. Advanced cervical cancer still has no cure, and 10 women die in the United States every day of this cancer, with rates twice that high in Fulton County, Georgia. However, with approximately 70 million girls and women now vaccinated, the vaccine has sustained an almost 100% rate of efficacy over its five years of availability, with no serious side effects.

"As a cancer vaccine goes, this is the best we have," says Kevin Ault, associate professor of Gynecology and Obstetrics at Emory. "In four or five generations, we have gone from cervical cancer being the most common cause of cancer death in the United States for women to being a vaccine-preventable disease."

Ault has worked on the disease for more than a decade, culminating in development of the vaccine and his contribution to landmark papers on HPV in the *New England Journal of Medicine* in May and *Lancet* in June. His interest began during his tenure at the University of Iowa, when he heard of a possible link between the HPV and precancerous Pap smears.

As a clinical trial investigator, Ault found testing of the vaccine to be challenging on several fronts. First, HPV does

not grow easily in a lab. Then there were technical questions: how many injections would ensure the vaccine achieved its full effect, and how would investigators accommodate changing technology and guidelines for Pap smears? Beyond those difficulties were privacy issues of enrolling adolescents and college students in the study. To answer these challenges, the researchers tested and tracked a large experimental group, approximately 20,000 people.

The announcement of an effective HPV vaccine raised concerns in some circles that vaccinating girls amounted to handing them a license to have sex. Ault, the father of two daughters, responds to that concern with data from a study of teenagers who chose not to engage in sexual intercourse [Abma et al., 2004, *Vital and Health Statistics*, 23:24]. "You usually get the answers, as a parent, that you'd want to hear. It's against their morals. They haven't found the right person. They don't want to get pregnant. Those are usually the Top 3, and sexually transmitted infections are somewhere lower on the list. Given that, it's hard to believe they'd change their behavior if they're not thinking about them anyway."

According to the CDC, more than half of men and four-fifths of women will contract HPV during their lifetimes. Addressing the potentially devastating effects of the virus, the CDC recommends vaccination for females between the ages of 9 and 26. Although both men and women can, and do, become infected with the virus, more men than women seem to slough the virus without a problem. Those who come down with HPV may develop such serious symptoms as genital warts or precancerous lesions on the cervix, vulva, anus, or penis. Absence of active symptoms, however, does not necessarily indicate the absence of the virus. HPV can, often does, remain dormant for years before erupting into full-blown disease.

No current test will confirm the presence of the virus prior to the emergence of the disease's symptoms. Around the world each day, approximately 750 women die of cervical cancer. Through vaccination and continuing research on ways to prevent and treat HPV, the human papillomavirus could go the way of smallpox, eradicated globally.

Ault would celebrate HPV's disappearance. So would the daughters and sons of the women who live long enough to enjoy the ride. —Perky Daniel

Tea, turmeric, and Taxol for cancer prevention

Can green tea play a role in preventing head and neck cancer? How about curcumin, the principal ingredient in the Indian curry spice turmeric?

Emory's Winship Cancer Institute researchers are searching for the answers to these and other questions as they embark on four avenues of investigation in the prevention and treatment of head and neck cancers. The projects are part of a five-year, \$12.1 million Specialized Program of Research Excellence (SPORE) grant in head and neck cancer from the National Cancer Institute (NCI).

SPORE grants are large, highly competitive, multidisciplinary grants that fund scientific research to bring new laboratory findings quickly to the clinic. The first SPORE grant ever received in Georgia, this is one of only five head and neck cancer SPORE grants in the United States.

With an expected 40,000 new cases and 11,500 deaths in 2007, squamous cell carcinoma of the head and neck accounts for 4% to 5% of all newly diagnosed cancers in the United States. More than two-thirds of head and neck cancer patients have locally advanced disease before they are diagnosed, and consequently they have a poor five-year survival rate after treatment with surgery, radiation, or chemotherapy. According to the NCI, the Southeastern states rank among the highest in the nation in head and neck cancer incidence.



The incidence of lung cancer and head and neck cancers will remain high for the next two to three decades, predicts hematologist/oncologist Dong Moon Shin, principal investigator of the grant. Although smoking has declined overall in the population, a large number of aging smokers and ex-smokers may still develop these diseases, says Shin.

Emory's SPORE program includes four translational research projects. The first uses a combination of polyphenon E (a chemical substance found in plants and extracted from green tea) and erlotinib (a growth factor inhibitor) to prevent advanced precancerous lesions of the head and neck. The second project is directed at developing therapies that block cellular pathways that allow cancer cells to metastasize and proliferate.

In the third project, Winship researchers have modified the chemical structure of curcumin to produce a more powerful analog than the original compound. Curcumin has shown anti-cancer activity in earlier studies, but its effects have been limited because it induces cell death not only in cancer cells but also in healthy cells.

In the final area, Winship and Georgia Tech investigators are working on development of a new class of biodegradable nanoparticles that will carry Taxol to targeted head and neck cancer cells, while avoiding unwanted side effects to normal cells.

Directions from Mars to Venus

Why and how do males and females solve spatial problems differently? That's what Rebecca Herman and Kim Wallen at the Yerkes National Primate Research Center wanted to know.

What they found is that the two sexes use different parts of the brain to navigate. For example, when finding a location, men generally use north and south coupled with distance estimates, suggests Herman, whereas women prefer physical cues such as street names, signs, and buildings.

In the April 2007 *Hormones and Behavior*, the researchers point to subtle hormonal changes that occur as the brain develops to explain these differences. They compared normal

female and male rhesus macaques with those that differed in prenatal exposure to male hormones.

The researchers arranged boxes baited with food, varying the consistency of food locations (spatial information) and the presence of colored markers (landmarks). Males and females performed the same when both markers were present, but the females performed better than the males in locating the food when only the landmark information was present. The male monkeys whose testosterone exposure was blocked early in gestation were better at using the landmarks than the control males.

A better understanding of sex differences in cognitive performance may shed light on why men and women experience disorders such as Alzheimer's disease and autism differently.

Training the trainers



Varsity high school players in Georgia benefit from the same athletic training services as the U.S. Soccer Federation. Both are supplied by Emory Sports Medicine through its certified athletic training program, which is helping develop national accreditation standards.

Forrest Pecha is no novice to international sports. As head athletic trainer for the U.S. men's alpine ski team, he watched the skiers take two silver medals in the 2002 winter Olympics. He has worked on rehabilitation and strength programs for Ruud van Nistelrooy from Real Madrid soccer team, and he served as an athletic trainer for the U.S. men's U-20 national soccer team in Panama in 2006. This July Pecha headed with the team to Canada to help keep the ath-

letes healthy during the youth world cup tournament.

Since 2005, Emory Sports Medicine—where Pecha serves as program manager and director for athletic training services—has provided athletic training services to the U.S. Soccer Federation (USSF) through its certified athletic trainer (AT) program. Emory ATs have worked with both the U.S. men's and women's national teams as well as the federation's youth national and development programs. "It's a way to give our ATs on-the-field experience at the highest levels and for U.S. soccer to get the highest level of care," says Pecha. "It's a good fit."

Certified athletic trainers are mid-level care providers. If an athlete gets hurt on the field, the AT is the first person to assess the injury, determining if the athlete needs rehabilitation or further consultation with the team doctor. Outside of game time, ATs concentrate on treating injured athletes and on conditioning programs to prevent injuries.

At Emory, the sports medicine program is raising the bar for certified ATs, offering advanced education through a one-year fellowship for four fellows each year. The third class of fellows graduated in July.

"We're preparing athletic trainers to support the orthopedic and sports medicine physician," Pecha says. At a minimum, applicants already must

hold masters' degrees, be board certified as an AT, have state licensure, and have traditional athletic training experience. During the fellowship, the ATs are immersed in all aspects of a clinical orthopedic practice. They gain scrub privileges to assist physicians in the operating room, each assisting with approximately 250 surgeries per year. They learn to interpret radiographic findings, and they complete a research project, such as a recent fellow's study on ACL injury prevention. They also travel with the national soccer teams, ski teams, or other high-level sports teams one month out of every four during the fellowship.

It's hard to beat that experience, says Pecha. "Our program is a flagship. In fact, we're working with the National Athletic Trainers Association to develop national accreditation standards for AT fellowship and residency programs."

In addition to affiliations with the USSF, Emory's ATs work with the Tour de Georgia cycling race, the U.S. Ski and Snowboard Association, the Southeast All Star Football Camp, collegiate athletics, and high school varsity and club sports teams.

"If you're going into the field of athletic training, you have to have a passion for athletics," Pecha says. "But more than that, you have to have a passion for making people healthy." —Rhonda Mullen

WEB CONNECTION To hear Emory sports medicine physician John Xerogeanes talk about ACL injuries in female athletes, visit emoryhealthcare.org/media/podcast/podcasts/New_Innovative_ACL_Treatment_Part_1.html

A genetic predictor of heart attack



Working with an international team, Emory researchers have found a common genetic variation is linked to a substantial increase in the risk of a heart attack. The variation

is found on chromosome 9p21 and is the first common variant that's linked to a substantial risk of heart attack in study groups of those of European descent. The findings were published last spring in the online and print editions of *Science*.

Researchers found that people with the variation have a 1.64-fold greater risk of suffering a heart attack and a 2.02-fold greater risk of suffering a heart attack early in life.

Approximately 21% of people of European descent carry two copies of the genetic variation (one from each parent).

Heart attacks are the leading cause of death in industrialized countries. Nearly half of men and one-third of women who reach the age of 40 will suffer a heart attack in their lifetime. If the genetic variation was absent in the general population, there could be 21% fewer heart attacks, according to researchers.

The study was led by the Icelandic genomics company deCODE Genetics, with researchers from Emory, Duke, and the University of Pennsylvania.

"The gene variant we have linked to heart attack points us to a major biological mechanism that substantially increases the risk," says Emory cardiologist Arshed Quyyumi, one of the study's authors. "Discoveries like this one greatly heighten our understanding of the role genetics plays in heart disease."

Milestones

■ **Emory physicians and scientists** are playing a leading national role in evaluating promising new vaccines and therapies for infectious diseases in adults and children as one of the newest members of a group of Vaccine and Treatment Evaluation Units, funding by the National Institute of Allergies and Infectious Diseases of the NIH. The designation includes a seven-year contract of approximately \$23.7 million, which will enhance the NIAID's ability to respond to emerging public health needs.

■ **The NIH** has awarded more than \$31 million over five years—one of the largest NIH grants in Georgia history—to a partnership of Atlanta academic, research, and health care institutions focused on accelerating the translation of laboratory discoveries into health care innovations for patients. Known as the Atlanta Clinical and Translational Science Institute, the partnership is led by Emory, along with Morehouse School of Medicine, Georgia Tech, and Children's Healthcare of Atlanta.

■ **Emory Crawford Long Hospital** is a 2006 Thompson 100 Top Hospitals Performance Improvement Leader, an award bestowed by Thompson Healthcare, which provides health care information and decision support data on clinical and business performance improvement.



Thompson Healthcare studied the performance of more than 2,800 U.S. hospitals in areas such as patient mortality and length of stay to choose the most improved from 2001 to 2005. Emory Crawford Long was also one of five organizations this year, and the only one in the Southeast, to win a national award from the Equal Employment Opportunity Commission for its program to train and hire high school graduates and adults with developmental disabilities and integrate them into a busy hospital workplace.

■ **A new Center for Systems Imaging** will open at Wesley Woods Center this winter. With 20,000 square feet dedicated to research, the center will house radiochemistry laboratories and a prototype MRI/PET scanner that Emory is testing.

■ **The Nell Hodgson Woodruff School of Nursing** received a pilot grant from the Robert Wood Johnson Foundation's Quality and Safety Education for Nurses project to create and implement a quality and safety curriculum to serve as a model for other nursing schools across the country. The school was one of 15 nursing schools around the nation chosen for this initiative.

■ **Emory University Hospital** was one of the top winners in the National Research Corporation's 2007-2008 Consumer Choice Awards. The award identifies hospitals that health care consumers have chosen as having the highest quality and image in more than 190 markets in the United States.



■ **Yerkes National Primate Research Center** has received a four-year, \$60,000 Nonhuman Primate Clinical Medicine Residency Program Training Grant for veterinarians, which will allow it to expand its two-year residency training program in partnership with Emory's Division of Animal Resources to three years.

Rioting feet

Emory's alliance with a company in the world's hot spot for genetics research led to a breakthrough for restless legs syndrome (RLS) this summer.

Collaborating with deCODE Genetics in Iceland, Emory neurologist David Rye helped track down a gene variant responsible for at least 50% of all RLS cases. Study results were published in the July 19 online and August 16 print edi-



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Rye has worked with deCODE scientists on several sleep-related research projects for nearly a decade. For the RLS study, Rye added clinical details from Emory RLS patients to data from Icelandic patients. deCODE processed DNA from blood samples for their genetic fingerprints and crunched the numbers. To confirm diagnoses of all the RLS patients in the study, Rye validated a novel tool that incorporated accelerom-

tions of the *New England Journal of Medicine*.

"We've got a slam-dunk," answers Rye to those who have questioned whether RLS is a legitimate disorder. "But more work will be required to translate these findings into improved patient care."

Those with severe RLS have trouble sitting still

eters to measure the number of times a person's legs twitch during the night.

After an RLS diagnosis was confirmed, nurses recruited and then interviewed extended family members about signs and symptoms of RLS. Patients were, in many cases, overjoyed that someone recognized their problem and offered treatment options. (Dopamine agonists, used to treat Parkinson's disease, often work well.)

"These people were in dreadful shape," says Rye. "RLS is a real problem if you have it. To those who are unfamiliar with the disorder, it sounds trivial, even fanciful or ridiculous."

Coming up with a term in Icelandic for RLS was a challenging first step. "We had to introduce a new word to Icelanders for newspaper ads to attract study participants. 'Fótaóeirð' literally translates as 'a foot with no rest,' which doesn't resonate to someone without RLS. Icelanders unaffected by RLS might interpret this word as a 'riot' in one's foot."

A new method of analyzing large amounts of genetic information helped the researchers pinpoint the RLS gene variant. Referred to as genome-wide association, the technique allows scientists to probe for gene variants in more than 300,000 single nucleotides of the genome.

Iceland has more sheer capacity for genome processing than anywhere else in the world, and Emory scientists are collaborating with deCODE by providing clinical expertise and access to the diverse genetic profiles of Americans, says Rye.

deCODE's mission is to conduct population-wide genetic studies to uncover major genetic contributors to common diseases. Translating these discoveries in human genetics into new drugs and diagnostic tools is deCODE's forte. The uniformity of the Icelandic population, totaling only about 300,000, helps researchers isolate and connect genes with clusters of disease.

In 2002, Emory and deCODE signed a formal "strategic alliance" and continue to collaborate on a variety of genetic studies, primarily in cardiovascular disease and the neurosciences. —Valerie Gregg

WEB CONNECTION To view a slideshow about RLS, visit <http://www.whsc.emory.edu/rls.htm>

Public health places

In less than 12 years after the Rollins School of Public Health moved into its first home, the school has maxed out the room for growth in its current facility. With a

Haley and Emerson Rollins show off an early model of the second public health building, which will be named in honor of their great-great-grandmother.



tripling of the number of students, faculty, and research dollars, the school's classrooms, offices, and laboratories now extend to five buildings scattered across the Emory campus. However, those satellite locations are about to be brought together in a newly planned building that will add more than 160,000 square feet of space to the school.

As with the first Grace Crum Rollins Public Health Building, this second building is made possible by a commit-

ment from the O. Wayne Rollins family, for whom the school is named. Not only will the \$50 million gift enable the school to double its physical size but also it will be instrumental in attracting the highest caliber of faculty and students.

Named for Claudia Nance Rollins, Wayne's mother, the new building will be a multi-use facility, including more laboratory space, technologically sophisticated classrooms, conference spaces, and an auditorium. New conference capabilities will enhance specialized training, distance learning, and professional exchange programs that spread public health solutions around the world. The schematic design phase is nearing completion, with construction scheduled to begin next summer. When it opens in 2010, the new structure will link to the current building through a pedestrian bridge.

The Rollins family's contributions to the school include major funding toward the Grace Crum Rollins Building, significant endowment and faculty recruitment gifts, and creation of the Center for Public Health Preparedness and Research. With the naming of the new building, five generations of the Rollins family are now recognized at the school.

Cutting ribbons and breaking ground

The Emory School of Medicine opened its new \$58.3 million education building in August, empowering it to train the next generation of doctors to provide 21st-century patient-centered care. The state-of-the-art building enables implementation of a new curriculum that integrates basic and clinical sciences and allows students to acquire clinical experience through interaction with real and simulated patients.

The curriculum teaches the fundamentals of science within clinical settings and immerses students in clinical experiences from their first week on campus. With 160,000 square feet of space, including auditoriums, seminar rooms, and classrooms, the entirely wireless building has allowed a 15% increase in the size of the entering freshmen class to 133 students.

The 1915 Society is one of the groups supporting the new building with a brick engraving program. Named in honor of the year the medical school first moved to the Emory campus,

the society offers membership to those who donate \$1,915 to the medical school for scholarships. In turn, first-time members are eligible to name a paver around the foundation of the building.

So far, more than 150 people have become members of the 1915 society, and the first tier of 133 pavers was in place for reunion weekend and dedication of the building in August. The second tier of named bricks will be installed this winter.

To participate in the program, contact Heather Pharris, director of alumni relations and development for the Emory School of Medicine, at 404-727-5932, or hpharri@emory.edu.

