MIT CEHS NEWSLETTER

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CENTER FOR ENVIRONMENTAL HEALTH SCIENCES

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Bacteria May Readily Swap Beneficial Genes

Microbes have developed a quick and effective way to exchange genetic information coding for antibiotic resistance, other functions. Article by MIT News Office, Denise Brehm on Oct. 2011

Much as people can exchange information instantaneously in the digital age, bacteria associated with humans and their livestock appear to freely and rapidly exchange genetic material related to human disease and antibiotic resistance through a mechanism called horizontal gene transfer (HGT). In a paper appearing in *Nature* online October 30, 2011, researchers — led by Professor Eric Alm of MIT's Department of Civil and Environmental Engineering and Department of Biological Engineering — say they've found evidence of a massive network of recent gene exchange connecting bacteria from around the world: 10,000 unique genes flowing via HGT among 2,235 bacterial genomes.

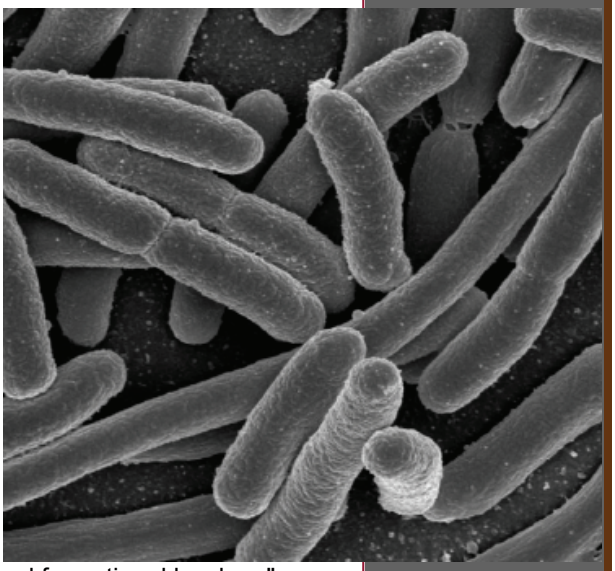
HGT is an ancient method for bacteria from different lineages to acquire and share useful genetic information they didn't inherit from their parents. Scientists have long known about HGT and known that when a transferred gene confers a desirable trait, such as antibiotic resistance or pathogenicity, that gene may undergo positive selection and be passed on to a bacterium's own progeny, sometimes to the detriment of humans. (For example, the proliferation of antibiotic-resistant strains of bacteria is a very real threat, as seen in the rise of so-called "superbugs.")

But until now, scientists didn't know just how much of this information was being exchanged, or how rapidly. The MIT team's work illustrates the vast scale and rapid speed with which genes can proliferate across bacterial lineages.

"We are finding [completely] identical genes in bacteria that are as divergent from each other as a human is to a yeast," says Alm, the Karl Van Tassel Associate Professor. "This shows that the transfer is recent; the gene hasn't had time to mutate." "We were surprised to find that 60 percent of transfers among human-associated bacteria include a gene for antibiotic resistance," adds computational systems biology graduate student Chris Smillie, one of the lead authors of the paper.

These resistance genes might be linked to the use of antibiotics in industrial agriculture: The researchers found 42 antibiotic-resistance genes that were shared between livestock-associated and human-associated bacteria, demonstrating a crucial link connecting pools of drug resistance in human and agricultural populations.

"Somehow, even though a billion years of genome evolution separate a bacterium living on a cow and a bacterium living on a human, both are accessing the same gene library," Professor Alm says. "It's powerful circumstantial evidence that genes are being transferred between food animals and humans."



Moreover, the team identified 43 independent cases of antibiotic-resistance genes crossing between nations. "This is a real international problem," says microbiology graduate student Mark Smith, another lead author of the study. "Once a trait enters the human-associated gene pool, it spreads quickly without regard for national borders."

The practice of adding prophylactic antibiotics to animal feed to promote growth and prevent the spread of disease in densely housed herds and flocks is widespread in the United States, but has been banned in many European countries. According to the Federal Drug Administration, more than 80 percent of the 33 million pounds of antibiotics sold in the United States in 2009 was for agricultural use, and 90 percent of that was administered sub-therapeutically through food and water. This includes antibiotics such as penicillins and tetracyclines commonly used to treat human illness.

The MIT researchers found that HGT occurs more frequently among bacteria that occupy the same body site, share the same oxygen tolerance or have the same pathogenicity, leading them to conclude that ecology — or environmental niche — is more important than either lineage or

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Upcoming Activities

Robert S. Harris Lecture to be held on March 8th 2012

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Gerald Wogan Lecture to be held on April 26th 2012

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CEHS Poster Session to be held on May 16th 2012

CEHS NEWS

2011—2012 Pilot Projects Awardees

CEHS allocates a significant portion of its NIEHS P30-ES002109 funding to support pilot projects that: provide initial support for investigators to establish new lines of research in environmental health, allow explorations of innovative new directions representing a significant departure from ongoing research for established investigators in environmental health sciences, and stimulate investigators from other fields to apply their expertise to environmental health research.

Current award recipients and their project titles are:

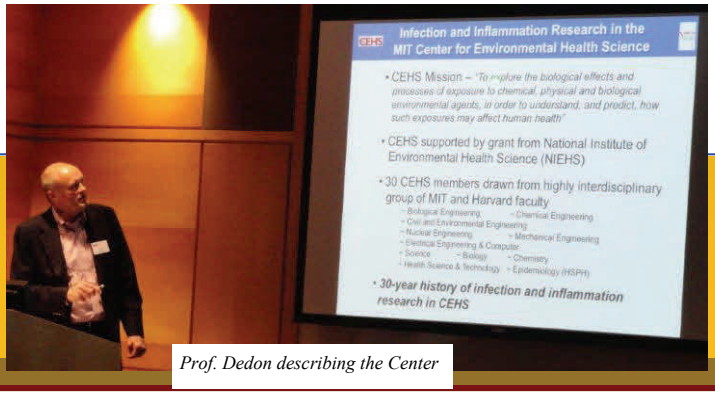
- **Susan Erdman**, Principal Research Scientist, Division of Comparative Medicine, along with **Eric Alm**, Associate Professor, Biological Engineering and Civil and Environmental Engineering, "*Targeting perinatal 'fast food' exposures and cancer risks later in life"*.
- **Jeff Gore**, Assistant Professor, Physics, "*Cooperation and cheating in the evolution of antibiotic resistance in bacteria"*.
- **Narendra Maheshri**, Assistant Professor, Chemical Engineering, *"An in vivo targeted mutagenesis system to examine that fate of clustered abasic sites".*
- **Elizabeth Nolan**, Assistant Professor, Chemistry, *"S100 proteins and zinc in epidermal repair".*
- **Katharina Ribbeck**, Assistant Professor, Biological Engineering, *"A study of mucosal colonization by Candida albicans".*

And this is the first year CEHS has funded a Translational Pilot Project.

- **Eric Alm**, Associate Professor, Biological Engineering and Civil and Environmental Engineering, along with **Stuart Levine**, co-Director of CEHS Genomics and Imaging Facilities Core, *"Tracking bacterial transmission in Fijian farming communities as a test case"*

2011 CEHS Translational Workshop

On October 27, 2011, the MIT Center for Environmental Health Sciences held its first Translational Open House with researchers from the Center for the Study of Inflammatory Bowel Disease at the Massachusetts General Hospital. The event was a great success in attracting over 100 clinicians, scientists, and students, all interested in the role of inflammation in human disease. In a mix of presentations and posters, the event facilitated discussions among MGH and MIT researchers and led to several new collaborations. Due to the overwhelmingly positive response to this first Translational Open House, the CEHS plans to host focused themes for future workshops in the areas such as the effects of DNA repair and infectious disease on environmental exposures. Please join us at our next workshop! Details to follow soon.



Prof. Dedon describing the Center

Linda Griffith

Elected in 2011 to the National Academy of Engineering

Linda G. Griffith, the MIT School of Engineering Professor of Teaching Innovation, who has dual appointments in the biological engineering and mechanical engineering departments, was honored for her contributions to the 3-D functional biomaterials, engineering hepatic tissues and cell transplant devices.

COEC News

Science School for Judges

MIT and the Broad Institute open their doors to the judicial community for a workshop at the intersection of science and the law. *Article by MIT News Office, Emily Finn on Sept. 2011* *http://web.mit.edu/newsoffice/2011/science-for-judges-0920.html*

Last week, tucked away in a second-floor teaching space at the MIT Museum known as "the cell," students huddled together in a dark corner of the room labeled "nucleus," where they laboriously snapped together LEGOs — in this case representing nucleotides — to match a long chain of genetic material in front of them. Then, clutching their strands of messenger RNA, they were ushered toward the center of the room by their instructor, Kathy Vandiver, who sat them at small tables marked "ribosome" and set them off building proteins out of additional toy bricks. But these weren't primary school students. They were judges from all over the country who had come to MIT for Judges' Science School, a crash course in scientific information and methods for legal professionals. Sponsored by the Advanced Science and Technology Adjudication Resource Ctr. (ASTAR), a professional organization funded by the U.S. Dept. of Justice, Judges' Science School convenes six to eight workshops each year with participants selected by chief justices in 47 U.S. jurisdictions. This session, the first ever held at MIT, was on "Gene-Environment Interaction in Health and Disease." That's where the LEGO came in. "We wanted to make the session very hands-on," says Vandiver, the outreach director for MIT's CEHS, which hosted the event along with the MIT Museum and the Broad Institute. The activity was intended to help judges visualize DNA's structure and function, so they could better understand how mutations in the molecule lead to cancer and other diseases. Scientists are increasingly answering the decades-old question of "nature versus nurture" — that is, whether our health and behavior are determined by our genes or our surroundings — with a resounding "both." New discoveries show that the risk of everything from criminal activity to skin cancer is mediated by the complex interplay between a person's environment and his or her genetic predispositions. But this interaction makes it difficult to establish true causation, something that's critical in the courtroom. "If I experience adverse radiation exposure at a certain site and I develop cancer, whose fault is that? Is anyone to blame? Who pays?" asks Franklin Zweig, a senior fellow at ASTAR and director of the event.

The 'X' factor

The consensus among the CEHS presenters — Leona Samson, the Uncas (1923) and Helen Whitaker Professor of Toxicology and Biological Engineering and CEHS director; and Bevin Engelward, an associate professor of biological engineering and CEHS co-director of CEHS COEC — was that for any given individual, those questions are very difficult to answer. Radiation and other environmental toxins cause mutations in DNA, which are known to lead to cancer — sometimes. But mutations can be caused by a number of other factors we wouldn't ordinarily consider toxic, and they also occur spontaneously over the natural lifetime of a cell. On top of that, some individuals are genetically blessed with an increased capacity to repair their DNA, meaning that two people exposed to the same quantity of radiation over the same period of time may be at different risks of developing cancer. Over the three-day workshop, the judges gained an appreciation for this tangled web of cause and effect. "It's obviously very difficult to say with any degree of certainty that factor 'X' was the causative one — that without it, the disease wouldn't have happened," says Paul Kapalko, a civil court judge in New Jersey. Of course, judges aren't left to make those calls entirely on their own; most cases that hinge on scientific or medical evidence invoke the testimony of expert witnesses. But just who qualifies as an expert? Judges need a basic knowledge of science so they can sniff out testimony that seems based on flawed research, or out of line with what's generally accepted by the scientific community. Kapalko describes this role as the "gatekeeper" of information in the courtroom. "All we can do is help ensure that something that's not truly science doesn't get in front of the jury," he says. "Our job here is to understand the science better so we can perform that duty."

Getting things right

To that end, much of the event was devoted to giving judges tools to evaluate scientists' methods and conclusions. They got a chance to learn firsthand how scientists correlate genetic mutations with specific diseases by donning gloves and pipetting samples of DNA into gel for separation in the teaching lab of Megan Rokop, the Broad's outreach director. Jane Beckering, a judge on the Michigan Court of Appeals, called the program "absolutely fabulous." "Science is developing at an incredible rate, and we need to do our best to keep up. This is the kind of evidence we're going to see in years to come," she says, adding that she'd had two recent cases — one involving toxic mold, the other an overdose of radiation in a cancer patient — in which she felt she would have benefited from a better understanding of genetics and environmental health factors. Zweig says the best way for judges to stay current is through direct interaction with scientists themselves, who appreciate both the complexity of the work and what's at stake in applying it to real-world cases. "The justice system depends on the ability of the court to get things right, and the ability to get things right depends on objective, even-handed information," Zweig said. "So we go to places that have [that information] and can dispense it." For their part, the MIT and Broad researchers were eager to do just that. "At CEHS, [an event like this] is part of our will and obligation," Samson says. Engelward adds that she was impressed with the judges' receptiveness and the quality of their questions. She says she also appreciates how this type of training can benefit society as a whole: "As judges, they have such influence, so this was an efficient way to touch a much larger population." Timothy Henderson, a district judge in Wichita, KS, echoes that sentiment. There were 32 judges at the MIT session of Science School — very few, considering that 28 million cases were filed in the U.S. legal system last year alone. But Henderson says the participants will share their new scientific knowledge with their colleagues. "We don't live in an ivory tower in the courtroom," he says, adding that he has regular interaction with other judges, legislators and lawyers through his state bar and his service on various committees. Building on a concept he'd learned earlier that day — through LEGOs — Henderson offers a metaphor: "Maybe we are the mutation within the judicial community."

Photo—Graphic: Christine Daniloff

CEHS Featured Article continued

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geographical proximity in determining if a transferred gene will be incorporated into a bacterium's DNA and passed on to its descendants.

"This gives us a rulebook for understanding the forces that govern gene exchange," Prof. Alm says. The team applied these rules to find genes associated with the ability to cause meningitis and other diseases, with the hope that transferred traits and the genes encoding those traits might make especially promising targets for future drug therapies.

"This is a very interesting piece of work that really shows how the increasing databases of complete genome sequences, together with detailed environmental information, can be used to discover large-scale evolutionary patterns," says Rob Knight, associate professor of chemistry and biochemistry at the University of Colorado at Boulder, who says he agrees with the authors' findings. "The availability of vast datasets with excellent environmental characterization will give us an unprecedented view of microbes across the planet."

Continuing the work, the researchers are now comparing rates of exchange among bacteria living in separate sites on the same person and among bacteria living on or in people with the same disease. They're also studying an environmentally contaminated site to see which swapped genes might facilitate microbial cleanup by metal-reducing bacteria. Other co-authors of the Nature paper are graduate student Jonathan Friedman, postdoc Otto Cordero and former graduate student Lawrence David, now at Harvard University.

The work is part of the National Institutes of Health's Human Microbiome Project. It was funded by the Department of Energy's ENIGMA Scientific Focus Area and the National Science Foundation.

http://web.mit.edu/newsoffice/2011/hgt-bacteria-1031.html

SECOND FEATURED ARTICLE

Slimy Science

Biological Engineering Assistant Professor says mucus is cooler than you think.

Article by MIT News Maeve Cullinane on December 2011.

The word slime doesn't exactly bring to mind the idea of fun. It's pretty safe to say that most of us would go out of our way to avoid any situation where we might get slimed — except maybe if it got us on a nationally broadcasted Nickelodeon show.

But, for Katharina Ribbeck — the Eugene Bell Career Development Assistant Professor in the Department of Biological Engineering — slime is not only fun, it's educational. Prof. Ribbeck, a visiting scholar living in Simmons Hall, runs a lab that exclusively researches slime — or mucus, as it might be more scientifically known. Aside from her research responsibilities, Professor Ribbeck, along with Asst. Housemaster Steve Hall, organizes the weekly residential scholar events for Simmons Hall. She has organized a student event based around a group discussion about the movie "The Departed" with MIT Chief of Police and former State Police Superintendent John DiFava; a swing dancing lesson with the MIT Ballroom Dance Team; a yoga class; and many other student-focused activities. That's how Prof. Ribbeck found herself hosting an event this past fall, that was near and dear to her — a celebration of slime.

Professor Ribbeck brought along three graduate students from her lab to help her execute a comical and educational presentation that involved a puppet show about the protective functions of mucus in the body, a pool noodle demonstration of mucus-coated cilia trapping particles in the lungs, and an interpretation of the way mucus helps us relieve ourselves by using a PVC tube and a broom handle.

Assistant Professor Katharina Ribbeck

Professor Ribbeck emphasized how mucus is not only vital to humans, but to other animals as well. One of the biggest gross-out highlight of the presentation was when she showed a video of a hagfish — a fish that secretes a giant wave of mucus to make it harder to grasp when it's under attack.

She concluded her presentation with a bang — dumping a bucket of actual slime on the head of one of her graduate students while playing a slimy sequence from "Ghostbusters" in the background. With slime still dripping off of his head, Professor Ribbeck's graduate student joined his lab mates to take questions from the audience. The researchers explained how their work relates to everyday problems and that one of their areas of focus is the role mucus plays in cystic fibrosis — a genetic disease that causes an excess production of mucus in the lungs and digestive track and usually leads to early death.

http://web.mit.edu/newsoffice/2011/slimy-science-mucus-research.html