In the 1970s, epidemiologists found that workers in factories using vinyl chloride, the key ingredient for PVC plastics, had unusually high rates of a rare form of liver cancer called angiosarcoma.

Biologists later identified a mutation that appears to be associated with this cancer, which originates in cells of the blood vessels that feed the liver. Now, using new sequencing technology that enables large-scale analysis of DNA damage-associated mutations, MIT researchers have pinpointed the specific type of DNA damage that may be responsible for this mutation.

With this knowledge, scientists could develop tests to monitor workers who might be exposed to vinyl chloride, because it has been previously shown that this type of DNA damage can be detected as a biomarker in urine samples. This could alert factories that they need to improve their safety practices if their workers are being exposed to too much vinyl chloride.

The research also lays the groundwork for applying this technology to identify other types of DNA damage, also called DNA lesions or adducts, that may be responsible for certain types of cancers. The initiation of many cancers may arise from the mutations generated by DNA lesions that are produced by natural processes such as inflammation, or by exposure to environmental agents such as vinyl chloride. These processes generate a variety of DNA lesions, making the identification of the most significant lesion a challenging task.

“I can think of a dozen different lesions this technology could be applied to,” says John Essigmann, the William R. and Betsy P. Leitch Professor of chemistry and a professor of toxicology and biological engineering. “Unfortunately there are a lot of things in the environment that are potentially associated with disease, and many of them do so by damaging nucleic acids.”

Essigmann, director of MIT’s Center for Environmental Health Sciences, is the senior author of this study, which was published in the April 1 issue of the journal *Nucleic Acids Research*. The paper’s lead author is Shiou-chi (Steven) Chang, a graduate student in biological engineering.

**Figure 1.** An X-gal indicator plate is traditionally used to determine the mutation frequency of DNA damage (also called DNA adducts). The blue dots indicate a mutation, and different mutations produce plaques with different colors on the plate. With advanced sequencing, X-gal indicator plates are no longer necessary for determining the mutation frequency, but are still used to cheaply verify if the experiments are going according to plan. **Photo:** Jose-Luis Olivares/MIT

**Rapid analysis**

Vinyl chloride is believed to cause many different types of DNA damage, but until now scientists had been unsure which of those lesions were most likely to produce cancers such as hepatic angiosarcoma. These lesions are formed when metabolic byproducts of vinyl chloride react chemically with the bases that encode the genetic information in DNA.

Scientists studying this type of cancer narrowed the suspects down to a group of lesions called etheno adducts, which contain an extraneous carbon-carbon double bond added to the regular DNA bases. There are four different versions of etheno adducts: One that forms on the DNA base adenine, one that involves cytosine, and...
MIT chemists have devised an inexpensive, portable sensor that can detect gases emitted by rotting meat, allowing consumers to determine whether the meat in their grocery store or refrigerator is safe to eat.

The sensor, which consists of chemically modified carbon nanotubes, could be deployed in “smart packaging” that would offer much more accurate safety information than the expiration date on the package, says Timothy Swager, the John D. MacArthur Professor of Chemistry at MIT.

It could also cut down on food waste, he adds. “People are constantly throwing things out that probably aren’t bad,” says Swager, who is the senior author of a paper describing the new sensor this week in the journal *Angewandte Chemie*.

The paper’s lead author is graduate student Sophie Liu. Other authors are former lab technician Alexander Petty and postdoc Graham Sazama.

The sensor is similar to other carbon nanotube devices that Swager’s lab has developed in recent years, including one that detects the ripeness of fruit. All of these devices work on the same principle: Carbon nanotubes can be chemically modified so that their ability to carry an electric current changes in the presence of a particular gas.

In this case, the researchers modified the carbon nanotubes with metal-containing compounds called metalloporphyrins, which contain a central metal atom bound to several nitrogen-containing rings. Hemoglobin, which carries oxygen in the blood, is a metalloporphyrin with iron as the central atom.

For this sensor, the researchers used a metalloporphyrin with cobalt at its center. Metalloporphyrins are very good at binding to nitrogen-containing compounds called amines. Of particular interest to the researchers were the so-called biogenic amines, such as putrescine and cadaverine, which are produced by decaying meat.

When the cobalt-containing porphyrin binds to any of these amines, it increases the electrical resistance of the carbon nanotube, which can be easily measured.

“We use these porphyrins to fabricate a very simple device where we apply a potential across the device and then monitor the current. When the device encounters amines, which are markers of decaying meat, the current of the device will become lower,” Liu says.

In this study, the researchers tested the sensor on four types of meat: pork, chicken, cod, and salmon. They found that when refrigerated, all four types stayed fresh over four days. Left unrefrigerated, the samples all decayed, but at varying rates.

There are other sensors that can detect the signs of decaying meat, but they are usually large and expensive instruments that require expertise to operate. “The advantage we have is these are the cheapest, smallest, easiest-to-manufacture sensors,” Swager says.

“There are several potential advantages in having an inexpensive sensor for measuring, in real time, the freshness of meat and fish products, including preventing food-borne illness, increasing overall customer satisfaction, and reducing food waste at grocery stores and in consumers’ homes,” says Roberto Forloni, a senior science fellow at Sealed Air, a major supplier of food packaging, who was not part of the research team.

The new device also requires very little power and could be incorporated into a wireless platform Swager’s lab recently developed that allows a regular smartphone to read output from carbon nanotube sensors such as this one.

If you would like to read this article on the MIT News website, please visit http://newsoffice.mit.edu/2015/sensor-detects-spoiled-meat-0415.
Welcome new Faculty Members

We are pleased to announce the new Center Faculty Members.

Colette Heald, Associate Professor of Civil and Environmental Engineering and Earth, Atmospheric and Planetary Sciences, who’s research interest are global atmospheric composition and chemistry, and interactions of these with the biosphere and climate system. This includes the study of both particles and gases in the troposphere, their sources, sinks, transformations, long range transport and environmental impacts. Please visit her website for further information of her research and publications [http://web.mit.edu/heald/www/](http://web.mit.edu/heald/www/).

Matthew Shoulders, Assistant Professor of Chemistry, who’s research interest is focused on integrating the tools of chemistry and biology to elucidate the complex pathways responsible for maintaining cellular protein homeostasis. Please visit his websites for further information of his research and publications [http://shoulderslab.mit.edu/](http://shoulderslab.mit.edu/).

We are delighted to introduce Ms. Lany Leung. Lany manages all of the CEHS events and seminars. Lany can be located in the CEHS Headquarters (Room 56-669) and can be reached via email lany@mit.edu or by phone 617-452-2072. Please feel free to introduce yourself if you have not done so already!

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Congratulations to Professor Eric Alm for receiving the 2014 Cozzarelli Prize in Biomedical Sciences. This Prize acknowledges papers that reflect scientific excellence and originality.

Professor Alm won for paper Transfer of noncoding DNA drives regulatory rewiring in bacteria by Yaara Oren, Mark B. Smith, Nathan I. Johns, Millie Kaplan Zeeli, Dvora Biran, Eliora Z. Ron, Jukka Corander, Harris H. Wang, Eric J. Alm, and Tal Pupko.

A commentary accompanying this article is available.

Promotional Milestones

Congratulations to Professor Catherine Drennan named as one of the 2015 MacVicar Fellows, in recognition of her exceptional contributions to education at MIT.


Congratulations to Professors Jacquin Niles and Colette Heald who have been promoted to Associate Professor with Tenure.
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. For more information about the CEHS Pilot Project Program, please visit our website http://cehs.mit.edu/research/pilot-project-program.

Current award recipients and their project titles:

- **Colette Heald**, Associate Professor of Civil and Environmental Engineering and Earth, Atmospheric and Planetary Sciences. “Basic Science: Health Implications of the Ozone Climate Penalty”.
- **Jongyoon Han**, Professor of Biological Engineering and Electrical Engineering and Computer Science and **Katharina Ribbeck**, Assistant Professor of Biological Engineering. “Translational Research: A Microfluidic Airway Model to Study the Role of Mucus in Asthma Pathogenesis”.

The CEHS Bioanalytical Core facilities have recently purchased an Agilent ICP-MS 7900 instrument with the Milestone UltraWave microwave sample digestion system. This instrument will be installed and operational by mid-July the latest. The Milestone UltraWave microwave sample digestion system is the newest and top-of-the-line digestion system, which is capable of digesting all kind of samples including geological samples.

Students and Postdocs must be trained by Dr. Koli Taghizadeh to use the ICP-MS system along with the sample preparation. Once they have completed this training, they will be able to perform the analysis by themselves. Of course, Dr. Koli Taghizadeh will be available for consultation and troubleshooting if needed.

A three-day training course with an Agilent engineer representative to use the Agilent ICP-MS instrument along with a day of sample preparation training by the Milestone representative has been scheduled. Research groups who plan to use the ICP-MS instrument should attend both training. We kindly ask Principal Investigators to identify members from their labs who would like to attend both training courses to contact Dr. Koli Taghizadeh by emailing her at KOLIT@MIT.EDU.
The Center for Environmental Health Sciences (CEHS) at MIT held its annual poster session on May 13, 2015 at the Morss Hall, Walker Memorial Building (50-140). The session highlighted the work of the environmental health research communities of MIT and some of our sister institutions. Over sixty posters were presented from the science and engineering laboratories affiliated with the Center. We would like to thank all of the poster presenters for participating in this event.

The CEHS has an overall mission to study the biological effects of exposure to environmental agents in order to understand, and predict, how such exposures affect human health. Moreover, by uncovering the chemical, biochemical and genetic bases for environmental disease, sometimes we are able to leverage that understanding to delay or even prevent the development of disease in human populations. To that end, the center brings together 39 MIT faculty members from a total of nine MIT departments (in both the School of Science and the School of Engineering) plus one Harvard faculty member from the Harvard School of Public Health (HSPH).

This year’s CEHS cash prizes are awarded in two categories, graduate students and postdoctoral scholars. The cash prizes were made possible by the Myriam Marcelle Znaty Research Fund, which was established nearly 30 years ago to support the research of young scientists at MIT.

Graduate Students, Postdoctoral Scholars, and Research staff presented the results of their research at MIT’s Morss Hall. The CEHS 2015 Poster Winners are mentioned below.

[Image: Graduate student winners (from left to right): Marianna Sofman (3rd place), Fei Chen (2nd place), and Amy Rabideau (1st place). Photo: Aran Parillo]

Ms. Amy Rabideau from Professor Bradley Pentelute’s lab won first place in the graduate student category. Amy presented her work on the “delivery of polypeptides and antibody mimics into cells using anthrax toxin.” In second place is Mr. Fei Chen, from Professor Edward Boyden’s lab, presented his work on “expansion microscopy.” Finally, in third place is Ms. Marianna Sofman, from Professor Linda Griffith’s lab, presented her work on “engineering angiogenesis: a materials approach to vascularizing tissue.”

In the postdoctoral scholar category, first place went to Dr. Kelly W.L. Chen, from Professor Douglas Lauffenburger’s lab, presented her work on “multivariate analysis of intestinal epithelial cell and immune cell crosstalk in normal and inflammatory conditions.” Second place went to Dr. Kathryn B. Smith-Dupont, from Professor Katharina Ribbeck’s lab, who presented her work on “biophysical tools for understanding the barrier properties of mucus: cervical mucus as a case study.” And lastly, Dr. Uthpala Seneviratne, from Professor Steven Tannenbaum’s lab, took third place after presenting his work on “decoding the S-nitroso proteome in a mouse model of Alzheimer’s by SNOTRAP and mass spectrometry–clues for altered signaling pathways.”

If you would like to read this article on the MIT News website, please visit [http://newsoffice.mit.edu/2015/center-environmental-health-sciences-poster-winners-0519](http://newsoffice.mit.edu/2015/center-environmental-health-sciences-poster-winners-0519).
Getting students interested and excited about science is a key step to increasing the number of youth who will pursue future careers in science, technology, engineering, and math (STEM) fields. To generate interest in STEM at the international level, Dr. Kathleen Vandiver, Director of the Community Outreach Education and Engagement Core within the Center for Environmental Health Sciences (CEHS) at the Massachusetts Institute of Technology, packed up her environmental health teaching tools and traveled to Cambodia to participate in the first-ever Cambodian Science and Engineering Festival (CSEF). This festival was a national initiative to advance STEM education and inspire the next generation of Cambodian scientists and engineers.

About 10,000 youth attended the festival, which was held March 12-15, 2015 in Phnom Penh, Cambodia. Festival organizers initially expected about 3,000 people to attend the event, but the strong social media campaign with promotional videos generated excitement and drew large crowds. “The enormous success of the event was a tribute to the organizers and to the support of the Ministry of Education, but also to the Cambodian youth who demonstrated their eagerness to learn about careers in science and technology when given an opportunity to do so,” noted Dr. Vandiver.

The event was geared towards 11-17 year old students, which the CSEF was built on the belief that the best way for students to learn science is by having fun. Dr. Vandiver saw the CSEF as an opportunity to take her hands-on “Atoms and Molecules Kits” overseas to teach Cambodian youth about hard-to-grasp scientific concepts. The kits have different colored LEGO® bricks represent elements with atoms that students can snap together to build molecules. Guided by shapes outlined on activity placemats, students can model a chemical reaction by first building the reactant molecules and then reassembling the same atoms into new molecules, the products.

“When students reconstruct the chemical products from the reactants using the bricks as atoms, the students grasp the essential concept in a moment of self-discovery. This is a powerful way to learn,” explained Dr. Vandiver, who began developing and using these kits during her 16 years as a middle school science teacher.

Dr. Vandiver has created different lessons utilizing the same Atoms and Molecules Kits to teach a number of abstract scientific concepts, including photosynthesis, but at her CSEF booth she primarily used the “Understanding Air” lesson to help students make the connection between fuel combustion and environmental health issues of air pollution and climate change. To help bridge the language gap, she teamed up with seven volunteers from surrounding Cambodian universities who helped translate to the students who visited her booth. She also had all the “Understanding Air” instructional print materials translated into Khmer, the official language of Cambodia.

During the closing ceremony of the festival, Dr. Vandiver received a Certificate for Appreciation from the Kingdom of Cambodia, signed and awarded by the Cambodian Minister of Education to the Center for Environmental Health Sciences at MIT.

To encourage continued STEM learning after the festival, the CEHS donated two classroom sets of the Atoms and Molecules Kits to local schools. Dr. Vandiver knew that in order for the kits to be a useful gift, she would need to train the teachers on how to use them. Therefore, she organized and conducted a half-day workshop to train the teachers at the recipient schools. According to Dr. Vandiver, her teaching methods were seen as quite novel among the Cambodian science teachers, who rarely have access to such hand-on activities in the classroom.

If you would like to read the article in the PEPH Newsletter, please click here [http://tools.niehs.nih.gov/pephnews/lists/currentissue.cfm](http://tools.niehs.nih.gov/pephnews/lists/currentissue.cfm).
The MIT CEHS COE²C Outreach Benefits from 120,000 Visitors at the MIT Museum Annually

The MIT Museum, which serves more than 120,000 people each year, is an ideal venue for connecting the public with the work of MIT scientists and engineers. The CEHS Community Outreach Education and Engagement Core (COE²C) began a partnership with the MIT Museum with the design of the participatory gallery, called Learning Lab: the Cell in 2005. The COE²C’s latest collaboration came to fruition last November, when an exhibit about a CEHS Professor Bevin Engelward's CometChip technology was placed in the MIT Sampling Gallery. This exhibit is one component on the large main floor gallery that showcases samples of ongoing research at MIT.

The CometChip exhibit is a particular anchor for some of the Museum’s volunteers who engage with families and adult visitors. Museum volunteers use molecular models to demonstrate what DNA is and how it can be studied, and readily make connections to the CEHS research by engaging students, families and adults.

For the past seven years, the MIT Museum’s classroom has served as a venue for the CEHS COE²C’s educational workshops for middle and high school students. The CometChip exhibit provides an excellent stimulus to think critically about how DNA damage can be detected with a technology developed at MIT. By interacting with this exhibit, it helps them see how they can apply the knowledge they have just gained to real world problems, such as the optimization of cancer treatments for individuals. The CometChip technology increases the efficiency of sample throughput, which is sensitive enough to provide single cell readings. This technique works because the cells with damaged DNA contain small DNA fragments that can be recognized as a “comet tail”-like structure in a gel when the sample is exposed to an electronic field.

The adjacent figure from the exhibit shows the comet chip in action. In this animation, the smaller fragments of DNA (purple) form the shape of a comet’s tail.

The following photos show some of the features of the CometChip Exhibit.

For more information about this exhibit, please visit [http://web.mit.edu/museum/exhibitions/samplingmit/cometchip.html](http://web/mit.edu/museum/exhibitions/samplingmit/cometchip.html).
two different versions that involve guanine.

About 10 years ago, Essigmann’s lab published a paper analyzing the mutagenic potential of ethenoadenine and ethenocytosine. For that study, they had to introduce the lesions into cells one by one and analyze each sample individually, which is a very time-consuming process.

In the past few years, the MIT team, led by Chang, adopted and improved a previously described next-generation sequencing approach, which allows for simultaneous analysis of many DNA strands. With the new system, “just by doing one sequencing reaction, you can get all of the data that might have taken weeks or months in the past,” Chang says.

Using this system, the researchers have completed the study of all four etheno adducts, using E. coli that vary in their DNA repair and replication abilities.

“With this method, you can study several DNA lesions all at the same time. You’re able to make a side-by-side comparison, which is always better than measuring one thing, and measuring another thing a few months later, and then another one after that,” Essigmann says. “We can do them all at once but get exactly the same high-quality information.”

The researchers found that one of the ethenoguanine lesions, known as N²,3-ethenoguanine, cannot be repaired by an enzyme known as AlkB, unlike the other three etheno adducts. This could explain why this particular DNA damage is the most prevalent etheno lesion and remains in cells for a long time. When the damaged DNA is copied, enzymes responsible for copying DNA may insert the wrong nucleotide opposite the lesion, which causes a guanine to adenine mutation.

Previous work has shown that this type of mutation, when it occurs in a specific stretch of a cancer-promoting gene known as K-ras, is associated with hepatic angiosarcoma.

“This is exciting new data that has redefined the role of etheno DNA adducts in mutagenesis and carcinogenesis,” says Ian Blair, director of the Center for Cancer Pharmacology at the University of Pennsylvania School of Medicine, who was not part of the research team.

The findings should stimulate new interest in analyzing urinary concentrations of etheno DNA adducts in human populations, he adds.

From bacteria to humans

Although these studies were done in E. coli cells, all of the enzymes studied, such as AlkB and the enzymes that introduce errors while copying damaged DNA, have human homologs. “Understanding how it works in E. coli, although it’s not human cells, may be a good model for understanding what may happen in humans,” Chang says.

The researchers are now analyzing other types of DNA lesions, including those caused by butadiene, a carcinogenic chemical found in tobacco and gasoline. They are also working on ways to adapt the system to study mammalian cells. Using the CRISPR/Cas9 gene-editing system, the team hopes to test what happens to particular DNA lesions in mammalian cells that differ in their DNA repair enzymes and DNA-copying enzymes.

This article can be found online at http://newsoffice.mit.edu/2015/vinyl-chloride-liver-cancer-0401.