MIT CEHS NEWSLETTER

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Massachusetts Institute of Technology
CENTER FOR ENVIRONMENTAL HEALTH SCIENCES

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ANNOUNCEMENT of new Center Director

Effective April 1, 2012, Professor John Essigmann will serve as the next Director of the Center for Environmental Health Sciences (CEHS). John is a long service and highly regarded faculty member in CEHS whose research is at the interface of chemistry, biology and public health, specializing on the mechanisms by which cells respond to DNA damage. Using synthetic methods, novel DNA damage products are prepared and then cloned into genomes of viruses. Following replication of the damaged viruses in cells, he is able to determine if the lesions studied will be mutagenic or toxic to the host. Over a hundred DNA lesions of relevance to environmental toxicology or drug development have been characterized in this system. He is on the editorial boards of six journals and had more than190 research publications, patents and books dealing with nucleic acid damage, repair, mutation and evolution. He serves on the advisory boards of six private companies and more than a dozen academic departments and centers. He is the co-founder and Scientific Advisory Board member of Koronis Pharmaceuticals.

He received his Ph.D. in Toxicology in 1976 from MIT, a pioneer in the field of toxicology. John is a member of the American Chemical Society, American Association for Cancer Research, and the Society of Toxicology. He received a prestigious MERIT Award from the National Cancer Institute in 2008 and the Thailand Gold Medal for research and teaching in the service of the developing world. He has chaired the NIH Chemical Pathology Study Section and has served on the governing councils of the Council of the National Institute of Environmental Health Sciences and of the Cancer Center of the National Cancer Institute.

In addition, John has a deep and abiding commitment to teaching and service. He has received the Graduate Student Council Teaching Award (twice), the School of Science Teaching Prize for Excellence in Undergraduate Education, the Arthur C Smith Award and is a Margaret MacVicar Faculty Fellow. In 2009, John was awarded a Martin Luther King, Jr., Leadership Award for his work with and support of underrepresented populations. John's breadth of experience and deep devotion to CEHS and MIT will serve him well in his new role.

IN THIS ISSUE

A New Look at Prolonged Radiation Exposure

MIT study suggests that at low dose-rate, radiation poses little risk to DNA
Article by MIT News Office, Anne Trafton on May 15, 2012

A new study from MIT scientists suggests that the guidelines governments use to determine when to evacuate people following a nuclear accident may be too conservative.

The study, led by Bevin Engelward and Jacquelyn Yanch and published in the journal *Environmental Health Perspectives*, found that when mice were exposed to radiation doses about 400 times greater than background levels for five weeks, no DNA damage could be detected.

Current U.S. regulations require that residents of any area that reaches radiation levels eight times higher than background should be evacuated. However, the financial and emotional cost of such relocation may not be worthwhile, the researchers say.

"There are no data that say that's a dangerous level," says Yanch, a senior lecturer in MIT's Department of Nuclear Science and Engineering. "This paper shows that you could go 400 times higher than average background levels and you're still not detecting genetic damage. It could potentially have a big impact on tens if not hundreds of thousands of people in the vicinity of a nuclear powerplant accident or a nuclear bomb detonation, if we figure out just when we should evacuate and when it's OK to stay where we are."

Continued on page 4

2012—2013 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:

- **Hadley Sikes**, Assistant Professor of Chemical Engineering, "*Methyl binding domain engineering to enable DNA epigenotyping of individual cells".*
- **Jennifer Calvo**, Research Scientist of CEHS, "*Studying Helicobacter pylori susceptibility in mice deficient for base excision repair and direct repair proteins".*
- **Gerald Wogan**, Emeritus of Biological Engineering, **James G. Fox**, Professor and Director of Division of Comparative Medicine (DCM), and **Robert Croy**, Research Scientist of Biological Engineering, *"Interactions between products of inflammatory cells and AFB1 in mutagenesis of hepatocytes and kupffer cells in gpt delta F344 rats".*
- **Andrei Tokmakoff**, Professor of Chemistry, *"Mutations and Tautomerism: using two-dimensional infrared spectroscopy to study DNA lesions generated from endogenous oxidative damages".*
- **Jonathan Runstadler**, Assistant Professor of Biological Engineering and Division of Comparative Medicine, *"Impact of the microbiome on influenza pathogenesis and immune response: a new, global approach to mitigating viral pathogenesis?".*

And Translational Pilot Projects award recipients and their project titles:

- **Peter C. Dedon**, Professor of Biological Engineering, *"RNA modification systems as environmental sensors and regulators in cancer growth*
- **Bevin P. Engelward**, Associate Professor of Biological Engineering and **Scott Floyd**, Clinical Investigator of MIT Koch Institute for Integrative Cancer Research, *"High-throughput approach for measuring DNA damage and repair kinetics in glial cells and gliomas"*
- **Stacey A. Missmer**, Assistant Professor of Epidemiology at Harvard School of Public Health, *"Pilot investigation of air pollution and endometriosis"*
- **Steven R. Tannenbaum**, Professor of Biological Engineering, Chemistry, and Toxicology, **James G. Fox**, Professor and Director of MIT DCM, and **Kun Lu**, Postdoc in Biological Engineering, *"Interactions between gut microbiomes and arsenic exposure"*

CEHS Genomics and Imaging Facilities Core

To address the increased demand for computational analysis of environmental health data, the Genomics and Imaging Facilities Core has recently expanded its bioinformatics staff. The team now includes three PhD bioinformatics scientists, Dr. Huiming Ding, Dr. Ryan Abo, and Dr. Vincent Butty as well as Stephen Goldman who supports the IT needs of the Core. The informatics team, led by Dr. Stuart Levine, is available to CEHS members for consultation and to assist them in analyzing their data.

Dr. Huiming Ding has significant experience in deriving interaction networks and in creating statistical scoring algorithms and databases. His current collaborative projects involve the study of functional interaction networks from time course data and generation of genome-scale metabolic pathway models.

Dr. Ryan Abo is a PhD who has a strong background in genetic and genomic analysis. He has been involved in a range of projects including Chip-seq motif finding, *de novo* mutation identification, and the role of transcription at enhancer sites.

Dr. Vincent Butty is an MD/PhD with a strong background in RNA sequencing methodologies and immunology. Dr. Butty is currently involved in the analysis of long non-coding RNAs, the role of chromatin in development and the response to genotoxic and infectious stresses.

In addition to the informatics team, the core has significantly expanded its computational infrastructure to handle the enormous storage and analytical requirements associated with "omic scale" data. This effort has been managed by Stephen Goldman.

The informatics staff (located in 68-317) are available for consultations on data analysis or your computational needs. If you have any questions or wish to discuss a project, our email is biomicro@mit.edu.

NEWS

2012 CEHS Poster Session

The Center for Environmental Health Sciences (CEHS) at MIT held its annual poster session on May 16, 2012 at the Media Lab E14-674. The session highlighted the work of the environmental health research communities of MIT and some from our sister institutions. There were more than 60 posters presented from the science and engineering laboratories affiliated with the Center.

Center Director: John Essigmann

An important theme of the Center is the study of 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 35 MIT faculty members from a total of seven MIT departments (in both the School of Science and the School of Engineering) plus four Harvard faculty members; from the Harvard School of Public Health (HSPH) and the Harvard Medical School affiliated hospitals (Massachusetts General Hospital and Brigham and Women's Hospital).

The CEHS cash prizes were split into two categories, graduate students and postdoctoral scholars. For each category, the prize for first-place was $500 cash, second-place prize was $100 cash, and the third-place prize is a CEHS polo, tumbler, notebook, and lanyard. 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.

(left to right): Ujjal Sarkar (1st place postdoc poster winner (tie)), Michelle R. Sukup Jackson (1st place graduate student poster winner), and Bogdan Fedeles (1st place postdoc poster winner (tie))

Michelle R. Sukup Jackson of Professor Bevin P. Engelward's lab won first place in the graduate student category. Michelle presented her work on "Visualizing Homologous Recombination and Illustrating DNA Repair Pathway Interaction *In Vivo* with Recombomice." Second place went to Vasileios Dendroulakis of Professors Peter C. Dedon and William Deen labs, who presented his work on "Oxanine and Xanthosine most Abundant Products of NO induced RNA Deamination." Lastly, third place went to Loreena Buck of Professor Linda Griffith's lab who presented her work on "Influence of Extracellular Matrix and Oxygen Tension on Mouse Hepatocyte Differentiation."

Vasileios Dendroulakis (2nd place graduate student poster winner)

Loreena Buck (3rd place graduate student poster winner)

In the postdoctoral scholar category, first place was a tie. Bogdan Fedeles of Professor John M. Essigmann's lab presented his work on "Unleashing the Mitochondrial Fire: A Novel Aniline Mustard Antitumor Agent that Targets the Mitochondrial Electron Transport Chain." Ujjal Sarkar of Professor Steven R. Tannenbaum's lab presented his work on "Development of Active Serine Hydrolase Profiling Tools and Their Applications." Third place went to Zachary Nagel of Professor Leona D. Samson's lab who presented his work on "High-Throughput Assay to Assess the Global DNA Repair Capacity of Human Cells."

Zachary Nagel (3rd place postdoc poster winner)

CEHS Featured Article continued

Continued from page 1

Until now, very few studies have measured the effects of low doses of radiation delivered over a long period of time. This study is the first to measure the genetic damage seen at a level as low as 400 times background (0.0002 centigray per minute, or 105 cGy in a year).

"Almost all radiation studies are done with one quick hit of radiation. That would cause a totally different biological outcome compared to long-term conditions," says Engelward, an associate professor of biological engineering at MIT.

How much is too much?

Background radiation comes from cosmic radiation and natural radioactive isotopes in the environment. These sources add up to about 0.3 cGy per year per person, on average.

"Exposure to low-dose-rate radiation is natural, and some people may even say essential for life. The question is, how high does the rate need to get before we need to worry about ill effects on our health?" Yanch says.

Previous studies have shown that a radiation level of 10.5 cGy, the total dose used in this study, does produce DNA damage if given all at once. However, for this study, the researchers spread the dose out over five weeks, using radioactive iodine as a source. The radiation emitted by the radioactive iodine is similar to that emitted by the damaged Fukushima reactor in Japan.

At the end of five weeks, the researchers tested for several types of DNA damage, using the most sensitive techniques available. Those types of damage fall into two major classes: base lesions, in which the structure of the DNA base (nucleotide) is altered, and breaks in the DNA strand. They found no significant increases in either type.

DNA damage occurs spontaneously even at background radiation levels, conservatively at a rate of about 10,000 changes per cell per day. Most of that damage is fixed by DNA repair systems within each cell. The researchers estimate that the amount of radiation used in this study produces an additional dozen lesions per cell per day, all of which appear to have been repaired. Though the study ended after five weeks, Engelward believes the results would be the same for longer exposures. "My take on this is that this amount of radiation is not creating very many lesions to begin with, and you already have good DNA repair systems. My guess is that you could probably leave the mice there indefinitely and the damage wouldn't be significant," she says.

Doug Boreham, a professor of medical physics and applied radiation sciences at McMaster University, says the study adds to growing evidence that low doses of radiation are not as harmful as people often fear. "Now, it's believed that all radiation is bad for you, and any time you get a little bit of radiation, it adds up and your risk of cancer goes up," says Boreham, who was not involved in this study. "There's now evidence building that that is not the case."

Conservative estimates

Most of the radiation studies on which evacuation guidelines have been based were originally done to establish safe levels for radiation in the workplace, Yanch says - meaning they are very conservative. In workplace cases, this makes sense because the employer can pay for shielding for all of their employees at once, which lowers the cost, she says. However, "when you've got a contaminated environment, then the source is no longer controlled, and every citizen has to pay for their own dose avoidance," Yanch says. "They have to leave their home or their community, maybe even forever. They often lose their jobs, like you saw in Fukushima. And there you really want to call into question how conservative in your analysis of the radiation effect you want to be. Instead of being conservative, it makes more sense to look at a best estimate of how hazardous radiation really is."

Those conservative estimates are based on acute radiation exposures, and then extrapolating what might happen at lower doses and lower dose-rates, Engelward says. "Basically you're using a data set collected based on an acute high dose exposure to make predictions about what's happening at very low doses over a long period of time, and you don't really have any direct data. It's guesswork," she says. "People argue constantly about how to predict what is happening at lower doses and lower dose-rates." However, the researchers say that more studies are needed before evacuation guidelines can be revised.

"Clearly these studies had to be done in animals rather than people, but many studies show that mice and humans share similar responses to radiation. This work therefore provides a framework for additional research and careful evaluation of our current guidelines," Engelward says.

"It is interesting that, despite the evacuation of roughly 100,000 residents, the Japanese government was criticized for not imposing evacuations for even more people. From our studies, we would predict that the population that was left behind would not show excess DNA damage - this is something we can test using technologies recently developed in our laboratory," she adds.

The first author on these studies is former MIT postdoc Werner Olipitz, and the work was done in collaboration with Department of Biological Engineering faculty Leona Samson and Peter Dedon. These studies were supported by the DOE and by MIT's Center for Environmental Health Sciences.

http://web.mit.edu/newsoffice/2012/prolonged-radiation-exposure-0515.html