MIT CEHS NEWSLETTER

Supported by NIH NIEHS Center Core Grant P30-ES002109

Massachusetts Institute of Technology
Center for Environmental Health Sciences

Spring 2013

Keeping an Eye on Bird Flu

MIT studies of two influenza viruses reveal genetic mutations that could result in pandemic flu

CEHS Director's Prelude:

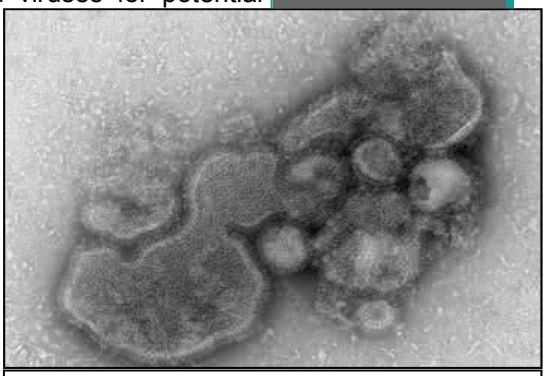
In late 2005, Ram Sasisekharan and I participated in a meeting held in Bangkok sponsored by the World Health Organization and the United Nations Development Program. The focus of the meeting was on emerging and current challenges in environmental health. Among the speakers was John Clemens who was on leave at that time from Johns Hopkins University to head the International Vaccine Institute, which is based in Korea. Clemens set a somber tone for the meeting. Many of the attendees, me included, studied chronic diseases such as cancer, which are potentiated in some still not well understood way by a complex interplay between environmental chemicals and infectious agents. This interplay of infection and chemicals kills millions, but slowly. The agents Clemens described have the capacity to kill millions, or tens of millions, quickly in fast moving pandemics. One of the most sobering messages to come from this session was the reality that the capacity and turn-around time of the worldwide vaccine industry may be insufficient to protect the world from fast moving, and fast mutating, viruses such as those from the influenza categories. At the time of the Bangkok meeting, there was a major bird flu (specifically H5N1) epidemic in Southeast Asia and Sasisekharan began to wonder what type of mutational combinatorics could result in the "jumping" of H5N1 to humans. Ram started to think of ways that his expertise in functional glycomics might be brought to bear to provide new approaches to understanding the evolution of host-viral interactions, interactions that typically involve binding between glycoproteins of the virus with those of the human (or animal) host. Since that meeting, Sasisekharan has mobilized a large effort that spans the gap between basic science and public health. The two *Cell* papers described in this newsletter represent the latest thinking and results from his laboratory on how epidemics emerge and, perhaps, how we might be able to use modern tools to intervene.

John M. Essigmann
Center Director

Article by Anne Trafton, MIT News Office on June 6, 2013

Influenza viruses that emerge from birds or pigs can create pandemic flu if they gain the ability to spread from person to person. New research from MIT shows that two recently emerged bird flu strains, which do not spread easily now, could become much more infectious with just one or a few genetic mutations.

The studies, which focused on the H5N1 and H7N9 flu strains, should help public health officials monitor evolving flu viruses for potential human-to-human transmission. They could also guide the development of new vaccines, says Ram Sasisekharan, the Alfred H. Caspary Professor of Biological Engineering and senior author of two papers appearing in the June 6 online edition of the journal *Cell*.



MIT researchers focused two recent studies on the H5N1 and H7N9 (shown) flu strains.
Photo - Image: Cynthia S. Goldsmith and Thomas Rowe/Centers for Disease Control and Prevention

Flu viruses are classified according to the type of hemagglutinin (HA) protein they contain; the strains that most commonly infect humans contain H1 or H3 proteins. However, other HA types can evolve to attack human respiratory cells, potentially posing a significant threat because human immune systems are often not prepared to fight them off.

Sasisekharan and his colleagues set out to characterize the H5N1 and H7N9 viruses' ability to infect humans by analyzing the structure of their HA proteins. In previous studies, Sasisekharan has shown that whether a flu virus can infect humans depends on its HA protein, which binds to glycan or sugar receptors found on the surface of respiratory cells. These glycan receptors come in two shapes: one that resembles an umbrella, and another that resembles a cone. To infect humans, flu viruses must bind to the umbrella-shaped receptors.

In This Issue

Upcoming Events

Gerald N. Wogan Lecture to be held on October 13, 2013

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AWARDS AND HONORS

SOPHEA CHAN DIAZ RECEIVES THE MIT INFINITE MILE AWARD

Testimonials for **Sophea Chan Diaz** of this deserving award through the Vice President for Research Office:

"Sophea is a forward thinker and a wizard with numbers. She is the best at what she does: as a financial manager, god citizen to CEHS, teacher of hard things, and a wonderful friendly, warm person who provides exceptional service to faculty, staff, and students. Sophea is an innovator who has no fear of tackling new systems, software, or processes to improve efficiency and productivity. She is as much an educator as a manager, preparing training materials and teaching others all the helpful tricks she figures out. She moves fast, accurately, and leaves behind a legacy of having taught other how she achieves her low wind resistance so that we can stress less over the same job when we do it again next year."

Congratulations Sophea!!

PROFESSOR WALKER ELECTED TO THE NATONAL ACADEMY OF SCIENCES

Professor **Graham Walker** have been named to the prestigious National Academy of Sciences (NAS), an honor recognizing distinguished and continuing achievements in original research. NAS membership is one of the highest honors afforded to scientists and engineers.

For more information on this announcement, please visit *http://web.mit.edu/newsoffice/2013/four-mit-professors-elected-to-the-national-academy-of-sciences.html*

PROFESSOR FOX RECEIVES THE 2013 EXCELLENCE IN RESEARCH AWARD

Professor **James G. Fox** has been awarded the 2013 Excellence in Research Award from the Association of American Veterinary Medical College. This Award is in recognition of his exceptional accomplishments in not only advancing fundamental knowledge in this field but also fostering the research careers of next-generation veterinary scientists.

For more information on this announcement, please visit *http://web.mit.edu/newsoffice/2013/james-fox-aavmc-excellence-in-research-award.html*

Congratulations to Professor **Linda Griffith** named as one of the 2013 MacVicar Fellows, in recognition of her exceptional contributions to education at MIT.

For more information on this announcement, please visit:

http://web.mit.edu/newsoffice/2013/four-professors-named-macvicar-fellows.html

The 2013 MacVicar Faculty Fellows with Dean for Undergraduate Education Daniel Hastings (back row, center). Front row: Linda Griffith and Rob Miller. Back row: Laura Schulz, Hastings and Emma Teng.

PHOTO: DOMINICK REUTER

Awards and Honors continued

ELIZABETH M. NOLAN RECEIVES A 2013 SLOAN RESEARCH FELLOWSHIP

Professor **Elizabeth M. Nolan** has been awarded a 2013 Sloan Research Fellowship.

Sloan Research Fellowships are given to early-career scientists and scholars whose achievements and potential identify them as rising stars among the next generation of scientific leaders. This year's recipients are drawn from 61 colleges and universities across the United States and Canada.

For more information on this news, please visit
http://web.mit.edu/newsoffice/2013/six-mit-researchers-win-sloan-research-fellowships.html

Photo courtesy of the Chemistry Department

MARTIN POLZ RECEIVES THE AMERICAN SOCIETY FOR MICROBIOLOGY'S ELANCO AWARD

Department of Civil and Environmental Engineering Professor, who studies wild microbial communities, is the first ecologist to be selected.

The American Society for Microbiology (ASM) announced in March that **Professor Martin Polz** of the Department of Civil and Environmental Engineering is recipient of the Eli Lilly and Company-Elanco Research Award, ASM's oldest and most prestigious prize.

Professor Polz, a microbiologist whose research explores the relationships between structure and function in microbial communities in the wild, is the first ecologist to be selected in the 77-year history of the award, which rewards fundamental research in microbiology or immunology by a scientist not yet 45 years old. Professor Polz will receive the award and give the Eli Lilly Award Lecture during the ASM's 113th General Meeting was held in Denver in May.

For more information this news, please visit
http://web.mit.edu/newsoffice/2013/cees-martin-polz-elanco-award.html

Department of Civil and Environmental Engineering Professor Martin Polz
PHOTO: L. BARRY HETHERINGTON

Congratulations to Professor **Steve R. Tannenbaum** for receiving the 2013 Division of Toxicology Founders Award from the American Chemical Society. This Award recognizes Professor Tannenbaum's extraordinary career contribution to the field of toxicology broadly as well as to this ACS Division.

CEHS Event Highlights

2013 Poster Session Event

The Center for Environmental Health Sciences (CEHS) at MIT held its annual poster session on May 10th 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. More than 70 posters 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.

CEHS has as its overall mission 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 are split into two categories, graduate students and postdoctoral scholars. For each category, the prize for first-place was $500, second-place prize was $100, and the third-place prize is CEHS memorabilia. 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.

Marcus Parrish, *first place winner in the Graduate Student Category*

Marcus Parrish of Professor Bevin P. Engelward's lab won first place in the graduate student category. Marcus presented his work on "Investigation into the Role of DNA Damage and Repair during Influenza Infection." We had a tie for second place. Anthony Soltis of Professor Ernest Fraenkel's lab, who presented his work on "Integrated Systems Analysis of High-fat Diet Induced Hepatic Dysregulation." Fabio Caiazzo of Professor Steven Barrett's lab presented his work on "Air Pollution and Early Deaths in the U.S. Quantifying the Impacts of Major Sectors in 2005. We also had another tie for third place. Bridget Wall of Professor Jacquin Niles' lab presented her work on "Leveraging Defective DNA Repair in *Plasmodium falciparum* to Develop a Mutator Strain." Jun Jie Ian Tay of Professor Bevin P. Engelward's lab who presented his work on "Application of a High-throughput DNA Damage and Repair Platform in a Screen for Genes that Modulates Repair."

Bogdan Fedeles, *first place winner in the Postdoctoral Scholar Category*

In the postdoctoral scholar category, first place went to Bogdan Fedeles of Professor John M. Essigmann's lab who presented his work on "Mapping the Road from Chronic Inflammation to Cancer: the Mutagenic Properties of the Inflammation Biomarker 5-chlorodeoxycytosine Revealed by a Multidisciplinary Study." Second 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. And lastly, we have another tie for third place. Stephanie E. Woods from the James G. Fox lab presented her work on "Laser-assisted Zona Drilling Improves *in Vitro* Fertilization using Fresh and Frozen Spermatozoa and Enables Efficient Recovery of Genetically Modified C57BL/6 Mouse Lines with Low Fertility." Nicole M. Iverson of Professor Gerald N. Wogan's lab presented her work on "*In Vivo* Utilization of Near Infrared Fluorescent Single Walled Carbon Nanotubes as Tissue Localizable Biosensors.

The news articles of this event can be found at http://web.mit.edu/newsoffice/2013/cehs-2013-poster-winners.html

***Anthony Soltis** and **Fabio Caiazzo,** second place winners in the Graduate Student Category.*

***Zachary Nagel**, second place winner in the Postdoctoral Scholar Category.*

(Left): ***Bridget Wall** and **Jun Jie Ian Tay**, third place winners in the Graduate Student Category. (Right): **Nicole Iverson** and **Stephanie Woods**, third place winners in he Postdoctoral Scholar Category.*

CEHS News

2013-2014 Pilot Project 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:

- **Steven Barrett**, Assistant Professor of Aeronautics and Astronautics; **Noelle Selin**, Assistant Professor of Engineering System and Atmospheric Chemistry; and **Steve Hung Lam Yim**, Research Scientist of Aeronautics and Astronautics, "*The Health Impact of Use of Leaded Aviation Gasoline"*.
- **Bevin Engelward**, Associate Professor of Biological Engineering, and **Gerald Wogan**, Emeritus of Biological Engineering, "*Development of Application of the RADR/GptΔ Mouse Model: Convergent Technologies for Revealing the Mutagenic Potential of Inflammation".*
- **Jonathan Runstadler**, Assistant Professor of Biological Engineering and Division of Comparative Medicine, and **Wendy Puryear**, Research Scientist of Division of Comparative Medicine, *"Investigating the Differential Environmental Stability of Influenza Virus Particles: Does Variation in Lipid Content Explain Host Shift Events?".*

And a Translational Pilot Project award recipient and its project title:

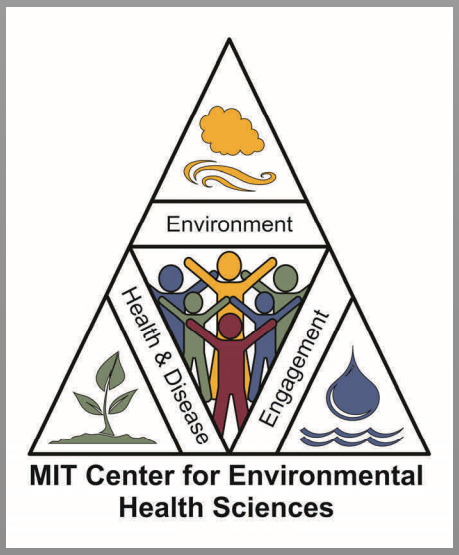
- **Jacquin Niles**, Assistant Professor of Biological Engineering, and **Bogdan Fedeles**, Senior Postdoctoral Associate of Biological Engineering, *"Characterizing Oxidative DNA Damage and Repair in Plasmodium falciparum"*.

Welcome new HQ Staff

We are delighted to introduce a new staff of the Center Headquarters, **Jennifer A. Henry**, Office Assistant.

Jennifer manages all of the CEHS events and seminars. Jennifer is located in office 56-669 and can be reached via email jahenry@mit.edu or by phone 617-452-2072. Please join us in welcoming Jennifer to the Center!

Check out our new design below! Let us know what you think at cehs@mit.edu



CEHS COE^{2}C HIGHLIGHTS

CEHS COE^{2}C Pilots "Understanding Air" Lesson Materials

By Kathleen Vandiver, CEHS COE^{2}C Director

"What's all the fuss about CO_2?"

Often the general public finds it hard to take a stand on environmental health issues such as climate change and air pollution because people feel uncertain about the basic facts. Thus the CEHS Community Outreach Education and Engagement Core (COE^{2}C) in partnership with the Kroll Lab and the MIT Edgerton Center created a hands-on way to deliver the essential facts about air and combustion for general audiences as well as for science classrooms.

Employing the LEGO® Atoms & Molecules Set where each color LEGO brick represents a different elemental atom, participants happily start by constructing molecules. The bricks are familiar materials and it is fun to model the tiny lumps of matter that make up air. First in the lesson, the constituents of air and their relative concentrations are modeled. Next the products of the chemical reaction combustion can be discovered when the initial atoms come apart and then recombine into different molecules inside the engine's combustion chamber. Therefore the products from burning fossil fuels become self-evident when working with the models. These are: carbon dioxide, carbon monoxide and carbon (soot) as well as NO_x and SO_x and ground-level ozone (O_3).

To study the impact of the "Understanding Air" curriculum with the LEGO models, COE^{2}C utilized an evaluation instrument called a SAMI card (System for Assessing Mission Impact) developed by the St. Louis Science Center. We looked at two different audiences: 1) a middle school science classroom at the Susan B. Anthony Middle School in Revere, MA with 8th graders and 2) a booth at the Science Family Days Event at the American Association for the Advancement of Science (AAAS) Conference on February 16, 2013 in Boston, MA where the audience was mainly family groups.

COE^{2}C volunteers at the American Association for the Advancement of Science (AAAS) Boston Family Days Event.

Biological Engineering graduate student Bridget Wall ready at the first station of the COE^{2}C booth at AAAS Family Days Event.

In both settings, the engagement level was high. Notably, 100% of the 8th graders (n=137) responded positively to "Did you learn something?" The SAMI Card had three questions, each with a four point Likert scale, with "4" as the maximum score. The averaged scores were: "Liked this activity" = 3.4± 0.6; "Learned from this activity" = 3.3± 0.6; and "Would like to learn more" = 3.2± 0.6 (n=137). Additionally the SAMI Card had an open-ended question, "Please tell us two things you learned from this activity", 30% of the answers related to the composition of air, 26% to combustion, and quite importantly, 11% of the responses related to health. Similar but even higher averages were obtained from families at the AAAS event: "Liked this activity" = 3.8± 0.4; "learned from this activity" = 3.3± 0.6; and "would like to learn more" = 3.5± 0.8 (n=88).

These very positive results have encouraged MIT CEHS COE^{2}C to design an "Understanding Air" package to share with other peer P30 COEC sites and other university outreach programs. The building instructions, posters, and volunteer briefing papers will be posted online. The LEGO Atoms & Molecules Set curricular materials are currently available at http://mindandhand.mit.edu/educators/curriculum-packages/air.shtml.

CEHS Featured Article Continued

Continued from page 1

So far, neither H5N1 nor H7N9 has been able to efficiently bind human glycan receptors.

H5N1

H5N1 leapt from birds to humans about 10 years ago; it has since infected nearly 600 people around the world, and about 60 percent of those infections have been fatal.

In the new *Cell* paper, the MIT team studied the structure of HA proteins from hundreds of H5N1 strains and identified three HA regions where one or two mutations would enable the HA to bind efficiently to human receptors. Most of these regions affect the base of the receptor-binding site.

The researchers also found that H5N1 has been evolving rapidly since 2005, but none of the current strains have all of the mutations needed to spread from human to human. However, the researchers found one strain that needs only a single amino-acid switch to become highly infectious, and several others that need only two. "There are multiple different ways that this can happen," says Sasisekharan, who is also a member of MIT's Koch Institute for Integrative Cancer Research.

Furthermore, because of all of the viral evolution that has occurred since 2005, the H5N1 vaccines that governments have stockpiled would probably no longer be effective, Sasisekharan says. "There is cause for concern," he says. "Yet these findings open opportunities to make sure that some of these newer strains do become part of the stockpiling, because they are closer to human adaptation."

H7N9

H7N9 has infected at least 132 people this year, mostly in China, and there have been 37 deaths, according to the World Health Organization — a lower fatality rate than that of the H5N1 virus.

The MIT researchers found that although the current circulating forms of H7N9 bind weakly to human receptors, a change in just one amino acid would dramatically increase the HA protein's binding strength. "It was not a marginal increase; we saw a pretty significant increase in receptor binding," Sasisekharan says. "Our research provides insights to help keep track of potentially important mutations so that proactive steps can be taken to be better prepared against dangerous viruses."

H7 typically circulates only in nonhuman animals, so most people would not be able to mount much of an immune response against H7N9. There are some H7 vaccines now in development, but the strains being used to create those vaccines are so different from H7N9 that they would likely not offer any protection, Sasisekharan says.

The information provided by the two studies should have a direct impact on both influenza risk assessment and vaccine development, says Linfa Wang, director of the program in emerging infectious disease at the Duke-NUS Graduate Medical School in Singapore.

"Their unique approach, incorporating structural topology of the host receptor glycan bound to key viral surface protein (HA) and the inter-residue interaction network in the receptor binding site of HA, is extremely powerful in providing crucial information within a short time period," says Wang, who was not part of the research team.

Lead author of the H5N1 paper is MIT research scientist Kannan Tharakaraman. Other authors are research scientist Rahul Raman, research affiliate Karthik Viswanathan, graduate student Nathan Stebbins, postdoc Akila Jayaraman, technical associate Arvind Krishnan and visiting scientist Viswanathan Sasisekharan.

Tharakaraman and Jayaraman are lead authors of the H7N9 paper. Raman, Viswanathan, Stebbins and Sasisekharan are also authors of that paper, along with technical associate David Johnson and research affiliate Zachary Shriver.

The research was funded by the National Institutes of Health and the Singapore-MIT Alliance for Research and Technology.

To view this article online, please visit http://web.mit.edu/newsoffice/2013/keeping-an-eye-on-bird-flu-0606.html

Another related article that might be of interest: http://web.mit.edu/newsoffice/2013/potential-flu-pandemic-lurks-0510.html