

GEMS series highlights mechanisms in the prevention and cure of cancer

By Richard Spane

The Genetics and Environmental Mutagenesis Society (GEMS) is marking its 31st anniversary in 2013, with an integrated pair of workshops on cancer.

GEMS, (<http://www.gems-nc.org/>) led this year by President Tom Hughes and President-elect William Kaufmann, Ph.D., held its spring symposium May 21 at the Environmental Protection Agency (EPA) in Research Triangle Park (RTP), with a program of talks on “Mechanisms of Environmental Carcinogenesis.” Six scientists from North Carolina’s major biomedical research centers explored the latest developments in basic research on ways environmental exposures trigger DNA mutagenesis and damage responses that can cause cancers and promote their spread throughout the body.

The group will take the bold next step with its fall meeting Oct. 23 at the Sheraton Imperial Hotel in RTP. The ambitious program on “Exploiting the DNA Damage Response to Prevent and Cure Cancer” will feature presentations by leaders in the field of cancer prevention and treatment. Speakers scheduled to present include Aziz Sancar, M.D., Ph.D., from the University of North Carolina at Chapel Hill (UNC) School of Medicine; William Gmeiner, Ph.D., of the Wake Forest University (WFU) School of Medicine; and pediatric cancer specialist Michael Kastan, M.D., Ph.D., of the Duke University Cancer Institute.

As it has in past years, the GEMS fall meeting will also highlight talks by enthusiastic students and postdocs, with a travel award to a national meeting for the best talk and a cash award for the best poster presentation.

Looking at mechanisms

“Most of us are concerned about cancer,” said Kaufmann, as he opened the spring symposium. “Why are certain agents making us, our children, and our parents sick, and giving us cancer?” Kaufmann said, it is our mission to resolve this question through our research, and we need to accurately translate and apply the latest basic mechanistic research, if we really want to prevent and cure cancer.

Possible environmental mutagens abound, from ultraviolet radiation to computer tomography (CT) scan radiation, to arsenic and pesticides, and the symposium’s speakers addressed many of them. Robert Smart, Ph.D., of North Carolina State University, stated that nonmelanoma skin cancers occur more frequently in humans than do breast, prostate, lung, and colon cancers combined. The NIEHS grantee explained that UVB exposure adversely affects the S phase of the cell cycle, the point at which genes replicate. A person’s genetic makeup and age act as compounding factors.

Arsenic, a well-known toxicant, is now recognized as a mutagen, by its ability to induce chromosome instability during mitosis, explained EPA’s Andrew Kligerman, Ph.D., in his exploration of its mode of action. WFU’s Mark Miller, Ph.D., threw suspicion on the safety of X-ray computed tomography, or CT scans, which he said may act as a promoter of carcinogenesis, an adverse effect that for some patients may actually outweigh the value of CT scans in early detection.

In Miller’s studies, tumor incidence in mice increased after CT exposures comparable to what humans receive. Further study will be needed to determine the specific human risks.

NC biomedical researchers and GEMS — marking 31 years together

GEMS is a regionally active group of interested environmental scientists, toxicologists, and geneticists sharing a common interest in the interplay of genetics and the environment.

The group holds two meetings each year, one in the spring and a larger event in the fall that features talks and poster session competitions for students and postdoctoral fellows. The programs usually draw upon the considerable talent from North Carolina’s major biomedical research centers, but each year’s president-elect, who designs the workshops, may also reach farther from home to schedule leading authorities on specific topics from across the U.S. to participate.

To find out more about upcoming programs sponsored by GEMS, or to join the group, visit the group’s [Web page](http://www.gems-nc.org/). (<http://www.gems-nc.org/>) GEMS actively promotes the involvement of students and postdocs, by offering annual memberships for just \$15.00. Regular membership costs \$25.00, annually, and a lifetime membership is available for just \$125.00. GEMS encourages participation by minority groups, women in science, people with disabilities, and other historically underrepresented groups.

Other speakers included Cyrus Vaziri, Ph.D., of UNC, who presented his recent findings on the integration of translesion synthesis with checkpoint signaling and cell cycle progression, and Michael Goldstein, Ph.D., of Duke, who addressed nucleolin mediation of nucleosome disruption and promotion of DNA double-strand break repair.

A new concept in cancer development — mutational clusters

Dmitry Gordenin, Ph.D., a yeast genetics expert in the NIEHS Laboratory of Molecular Genetics, explained that mutations are typically perceived as random, independent events. However, he observed nonrandom clustered mutations, also called mutational showers, made at transient single-strand DNA, near DNA double-strand breaks, and at replication forks, in yeast.

According to Gordenin, mutation rate in cluster can exceed the average rate across the genome by a hundred-fold or more, and generate genetic variants at a rapid rate. Importantly, clusters also occur in sequenced human cancers. Gordenin presented analysis indicating that APOBEC cytidine deaminases, enzymes that normally act in anti-viral innate immunity, are a source of mutations in clusters, as well as across cancer genomes. A better understanding of clusters may provide important clues regarding pathways leading to rapid genetic variation and instability, which in turn leads to cancer.

(Richard Sloane is an employee services specialist with the NIEHS Office of Management.)



As he welcomed attendees to the spring meeting, Hughes thanked GEMS members George Woodall and Carol Schwartz for making it possible to stream the symposium for remote viewing by people at local universities. (Photo courtesy of Steve McCaw)



In his opening remarks at what was GEMS first entirely free symposium, Kaufmann cautioned the audience that childhood UVB exposure, resulting in sunburn, is a precursor of malignant melanoma. "One of the best things you can do is protect the little ones," he said. (Photo courtesy of Steve McCaw)



Smart's lab has studied a family of CCAAT/Enhancer Binding Proteins (C/EBP), which serves as a master regulator of cell cycle exit and terminal differential. He said C/EBP is inactivated in numerous cancers. (Photo courtesy of Steve McCaw)



Gordenin, who was born in Soviet-era Russia, quipped that DNA mutations leading to cancer are all equal in their ability to lead to cancer, but, as in socialism, some are just more equal than others. (Photo courtesy of Steve McCaw)



Many of the GEMS faithful, including NTP geneticist Jack Bishop, Ph.D., were on hand for the talks. (Photo courtesy of Steve McCaw)



Likewise, NTP biologist and veteran GEMS member Diane Spencer was sure to make this spring's symposium. (Photo courtesy of Steve McCaw)

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