Your Health & the Environment

NEWS FROM THE UNIVERSITY OF ROCHESTER
ENVIRONMENTAL HEALTH SCIENCES CENTER • SPRING ISSUE 2002

Green Tea and Cancer Prevention

By Ph.D. student
Chrissy Palermo

Due to research efforts over the past 30 years, it is now known that many common foods have chemopreventive components that may provide protection against cancer. Recently, the possibility that green tea (GT) may offer protection against cancer and other diseases has become a focus of research. Epidemiological studies have found no clear-cut conclusions, yet, concerning the effect of GT consumption on human cancer risk. A number of studies in mammalian cell systems and laboratory animals have provided evidence indicating that chemical compounds present in GT are capable of giving protection against cancer initiation and its subsequent development. Unfortunately, the mechanisms responsible for these observations are not fully understood and are necessary to better understand the possible function of GT as a chemopreventive agent. GT contains polyphenolic compounds, including flavonols (also known as catachins), flavondiols,

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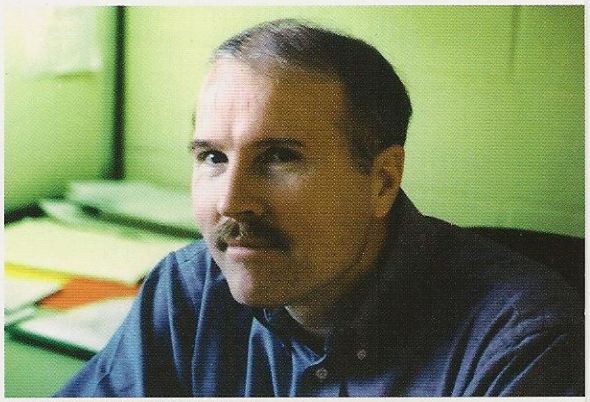
Thomas A. Gasiewicz, Ph.D., Named New Chair of Environmental Medicine,

Thomas A. Gasiewicz, Ph.D., has been named new Chair of Environmental Medicine. He succeeds Deborah A. Cory-Slechta, Ph.D., who stepped down from the position in October to devote more of her time to her duties as the medical school's Dean for Research and Director of the Aab Institute of Biomedical Sciences, as well as Director of the Environmental Health Sciences Center.

Dr. Gasiewicz has been a member in the Department of Environmental Medicine since 1979 and served as the Director of the Toxicology Training Program from 1991-1999.

Dr. Gasiewicz maintains an active research program focusing on the molecular mechanisms whereby the halogenated heterocyclic aromatics, such as dioxin, produce toxicity in mammals. Dioxin is an environmental contaminant and is an extremely potent toxic chemical.



Thomas A. Gasiewicz, Ph.D.

Much of his research is centered on understanding the properties of the cellular Ah receptor, its interactions with DNA, and the mechanisms whereby it modulates gene expression in a cell-specific manner. Part of this research is directed at determining the molecular mechanisms for the ability of chemicals to bind to the Ah receptor and act as an agonist or antagonist. Recent studies have focused on identifying the target cells and genes that are affected in developing animals.

The University of Rochester Environmental Health Sciences Center is housed in the Department of Environmental Medicine, and is one of 25 such centers sponsored by the National Institute of Environmental Health Sciences, a component of the National Institutes of Health. Its research programs are designed to expand our knowledge about those environmental factors that influence our health. Some of the work undertaken and reported on in this publication is supported by NIEHS Center Grant ES01247. For More information go to: www2.envmed.rochester.edu/envmed/

Environmental Manipulation of Gene Expression: Bringing the Genome into the Classroom

Drs. Dina Markowitz, and Andrew Brooks were recently awarded a one-year supplementary grant from NIEHS to develop a unique genomics education program for local high school teachers. This project is a collaboration between the University of Rochester's Life Sciences Learning Center and the Functional Genomics Center. The goals of this project are to increase current knowledge of genomics and proteomics and the ethical, legal and social implications of genetic research in environmental health sciences, as well as to facilitate the continued development of collaborative linkages among University of Rochester biomedical scientists and local science teachers and students.

The project involved the development of a workshop for high school science teachers. The first of these 2-day workshops was held January 29-30 for twelve local science teachers. It will be repeated in late June.

The workshop combined hands-on laboratory activities, in which teachers learned DNA genomics technology, with lectures and computer activities. Teachers also learned about the ethical, legal and social implication of genomics research. In-class presentations, including a video, are being developed to follow the workshops. Select activities from the workshop will be done with the teachers and students, in their classrooms. Data generated by the teachers, and analyzed by the students, will be used as part of a larger research project at the University of Rochester.

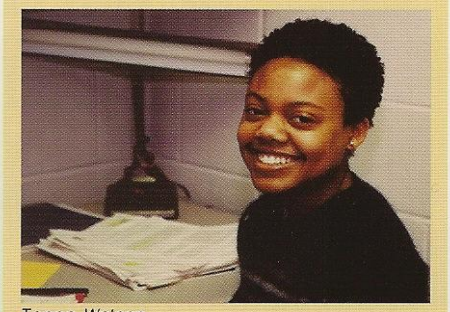
Hands-on laboratory activities included: isolation of RNA from cell cultures, synthesis of complementary DNA, production and processing of DNA microarrays, and data analysis of microarray studies performed by participants.

The teachers performed a DNA microarray experiment to investigate the interactions between inhaled ultrafine particles and specific cell populations. The experiment provided insight into the specific cellular mechanisms that are triggered following exposure to ultrafine particles. Drs. Jack Finkelstein and Gunter Oberdorster participated in the research portion of this project, and presented background information to the teachers on the use of DNA microarrays to study environmental health issues. Data collected by the teachers will be used by these two Center investigators in their research projects.

Participating teachers received curriculum materials and their classes will be able to host visits to their school by University of Rochester scientists for follow-up activities where they will see a video presentation of the teachers' lab experiences. There will also be an in-class demonstration of DNA microarray technologies and a discussion of bioethics and the human genome project.

For more information on this project, go to: www2.envmed.rochester.edu/LifeSciences / or contact Dr. Dina Markowitz at (585) 275-3171.

KODAK Toxicology Scholar Award Presented to Tenea Watson



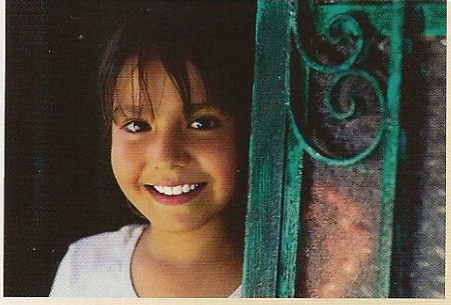
Tenea Watson

The University of Rochester's Toxicology Ph.D. Program is pleased to announce the selection of Tenea Watson, a fourth-year graduate student in the laboratory of Dr. Jack Finkelstein, as the recipient of the the Kodak Toxicology Scholar Award for the 2001/2002 academic year. The award recognizes the achievements of outstanding diversity students in the program, and encourages additional outstanding diversity students to join this Ph.D. program.

Watson is remarkable in many ways, however, what is particularly impressive is that she started her undergraduate studies when she was 14 at Mary Baldwin College in Staunton, VA. She entered the Toxicology Ph.D. Program at the University of Rochester at age 18.

This past June, Watson successfully completed her qualifying examination for her thesis project entitled "An immunoregulatory role for Clara Cell secretory protein". In addition, she has served as a hostess and ambassador in various recruitment activities.

The funding of this Award by the Eastman Kodak Company continues a long tradition of support for the University of Rochester's Toxicology Training Program.



Recruiting Children for Toxic Chemical Experiments

by Bernard Weiss, Ph.D.

President Bush recently signed the Convention on Persistent Organic Pollutants (POPs), a treaty supported by the Clinton administration. Those who will benefit most from banning these 12 hazardous chemicals are children. Although we recognize that children are vulnerable to such environmental perils, we have, thoughtlessly, allowed them to become subjects in a troubling experiment that exposes them to thousands of chemicals never tested appropriately for their toxic properties.

This lapse occurs because we fail to apply to chemical manufacturing the same ethical standards we demand in medicine and science, even though the consequences of commercial production are far more worrisome.

The University of Rochester adheres to policies similar to those of other research organizations. If I wish to conduct an experiment in which I expose human subjects to a toxic chemical, even in trace amounts, I have to submit my plans to our Institutional Review Board. My board members will closely scrutinize my proposal to make sure it abides by the ethical principles now universally accepted for the protection of human subjects. These principles grew out of deliberations by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which in 1979 translated them into three guidelines, intended mainly for clinical trials of new drugs or scientific studies.

One is "justice," which seeks some correspondence between who receives the benefits of the research and who bears its burdens. A second principle is "beneficence," which requires that researchers maximize the potential benefits to the subjects and minimize the risks of harm. A third is "respect for persons," the source of the directive for informed consent. It mandates that subjects enter into the research voluntarily and with adequate information. Children receive special consideration because they are held to lack adequate capacity for self-determination.

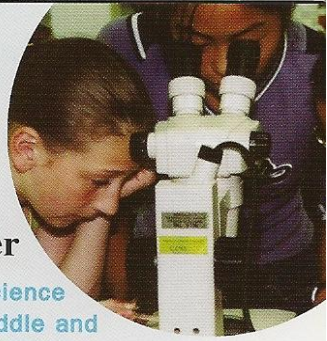
All three guidelines pose ethical dilemmas for industry, government, and the public when chemicals are created not for therapeutic interventions but, instead, are emitted into our environment by commercial activities.

I Was There and Saw the Olympic Flame

It's impossible to describe the pride I felt the day I received notification that I had been selected to be an Olympic Torch Support Runner. I am an average person and was honored to have been chosen. When I arrived at the meeting place for all of the participants, adrenaline was rushing through my veins. Getting to know the torch bearers for my segment of the run was great. I had the pleasure of meeting some of the inspirational people who would be participating with me. Each of these individuals had a story to tell and after hearing them I began to realize how lucky I have been in my life to never have had to face the obstacles that they have been faced with.

I felt pride in my country, and most importantly, I was a part of local history, I accompanied the torch bearers who proudly carried the flame and I was proud to play a part in this Olympic tradition.

Joyce Morgan is the Coordinator of the Toxicology Ph.D. Program



Life Sciences Learning Center

A unique hands-on science inquiry center for middle and high school students and teachers

The Life Sciences Learning Center (LSLC) located at the University of Rochester Medical Center, is devoted entirely to pre-college science education. The programs target middle and high school students and teachers throughout western New York.

The objectives of the LSLC are:

- To provide an interactive, hands-on learning environment for students with programs that align with New York State science education standards.
- To develop instructional programs and materials to make cutting-edge science accessible to teachers and young people.
- To train educators for laboratory-based teaching in the life sciences.
- To provide a "lending library" of state-of-the-art lab equipment and materials for teachers.
- To be a resource for teachers in developing new curricula.

The LSLC offers a variety of science education programming, including:

- Laboratory Investigations Programs for middle and high school students and Advanced Placement Biology classes
- Professional development workshops for science teachers.
- Saturday Science Program
- Summer science camps.

The LSLC is supported, in part, by a Science Education Partnership Award from the National Center of Research Resources (RR12411).

For more information please visit the web site at:
www2.envmed.rochester.edu/LifeSciences/ or contact LSLC Director, Dr. Dina Markowitz at (585) 275-3171.

Green Tea Continued From Cover


Chrissy Palermo

flavonoids and phenolic acids. One class of these agents is the bioflavonoids. These compounds are known to alter many biochemical processes but the relationship between these actions and their anti-carcinogenic effects are not well understood.

One cellular process that has been implicated is the effect of bioflavanoids on the aryl hydrocarbon receptor (AhR). The AhR is a ligand inducible transcription factor responsible for mediating the transcription of the CYP1A subfamily of genes. These CYP1A enzymes are responsible for the conversion of many carcinogens into their highly reactive intermediates. We believe that certain bioflavonoids, particularly those found in green tea, are potent known AhR antagonists. It is thought that this interaction may modulate several biochemical pathways, thus preventing the effect of carcinogenic agents. Through organic extraction techniques, I hope to identify the individual active compounds in green tea responsible for antagonizing the AhR. Using these antagonists as ligands for the AhR, I hope to understand the mechanism of action through which these compounds alter AhR activation. These studies may define the most sensitive pathways for the actions of these bioflavonoids, providing a mechanistic basis for their chemopreventive actions.

One of green tea's chemopreventive mechanisms may be through inhibition of AhR transcription, and thus, inhibition of transcription of carcinogen activating enzymes. We hypothesize that GT functions through multiple mechanisms, including one which does not involve direct competition for binding to the AhR.

Through extraction techniques, we have identified only two compounds in green tea, epigallocatechin gallate (EGCG) and epigallocatechin (EGC), capable of inhibiting AhR transcription. Interestingly, these compounds are reaching this endpoint through very different mechanisms. The most potent antagonist, EGCG, does not compete for binding to the AhR but, rather, inhibits binding of another molecule, called DRE. This data suggests that individual chemicals in green tea are capable of altering AhR transcriptional activity and that these compounds function through multiple mechanisms.

Though exact mechanisms of action of these compounds is not yet known, our data suggests that multiple compounds within green tea are functioning through multiple mechanisms to inhibit AhR function. In the future we hope to elucidate these exact mechanisms as well as determine the role, if any, of the AhR in other signal transduction pathways, which these green tea compounds are known to affect.

Faculty and Student News

New EHSC Faculty: Drs. Andrew Brooks, Patricia Chess, Eric Richfield, Patricia Sime, Berislav Zlokovic, William Tank, and Hermes Yeh.

Congratulations: The following students recently had their qualifying exam: Chris Helt, "The role of the cyclin dependent kinase inhibitor P21(CIP1/WAF1) in the response to hyperoxic damage"; Gary Minsavage, "Identification and characterization of phosphorylated sites that are required for aryl hydrocarbon receptor (AhR) DNA binding and transactivation"; and Joe Zhou, "The influence of gene-and ligand-dependent interactions of the Ah receptor on regulating differential gene induction."

Awards: Donna Lee, Gary Minsauage and Carissa Filbrant are the recipients of Travel Awards to attend the annual Society of Toxicology meeting to be held in Nashville, Tenn., March 17-21, 2002.

Please visit www2.envmed.rochester.edu/envmed to meet our students and see what activities they are involved in.

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