

G_xE News Quarterly

A Newsletter of the

Center for Environmental Genomics and Integrative Biology

*“An NIH-NIEHS Center of Excellence
at the University Of Louisville”*

Kenneth S. Ramos, Ph.D., Director

J. Christopher States, Ph.D., Deputy Director

Jeannie Bowman, Administrator

The Center for Environmental Genomics and Integrative Biology focuses on the elucidation of gene, protein and metabolic networks involved in cardiovascular disease, cancer and developmental origins of health and disease, and the role of environmental factors in these disorders.

CONTENTS

[Director's Corner](#)

Welcome to CEGIB.

[CEGIB Sponsored Seminars and Enrichment Activities](#)

Details on Upcoming Events and Speakers

[Member Accolades](#)

Recognition and Accomplishments of our Members

[Member Highlight](#)

Get to Know our Members

[Career Development for New Environmental Health Investigators](#)

Mentoring Program for Young Investigators....

[Pilot Projects Program](#)

Funding Opportunities

[Bioinformatics, Biostatistics and Computational Biology Core](#)

CEGIB Services

[Integrated Health Sciences Facility Core](#)

CEGIB Services

[Community Outreach and Education Core](#)

Community Activities

DIRECTOR'S CORNER

On June 4, 2007 the Center for Environmental Genomics and Integrative Biology (CEGIB) activated its cores, programs and committees and formally launched the first NIH-funded Center of Excellence at the University of Louisville (UofL). This accomplishment is a culmination of the vision of institutional leaders and the outstanding efforts of our research community!

The overall goal of the Center is to elucidate gene, protein and metabolic networks involved in cardiovascular disease, cancer and developmental origins of health and disease, and the role of environmental factors in these diseases. Molecular investigations will be framed within the context of environmental genomics and integrative biology and aided by large-scale 'omics technologies, bioinformatics, biostatistics, computational biology and integrative health sciences. I look forward to working with all of you to advance the goals of the Center and to expand the intellectual strengths of UofL.

The *Bioinformatics, Biostatistics and Computational Biology Core (BBCB)* and *Integrative Health Sciences Facility Core (IHSFC)* have been organized to support the research efforts of Center members. The BBCB supports Center investigators with training and services in research design, data management, statistical analysis, and computational modeling relevant to environmental genomics and integrative biology. The IHSFC provides Center investigators with services and resources to facilitate the translation of basic research findings into clinical or public health applications. A third core, the *Community Outreach and Education Core (COEC)*, works to bring scientifically sound health and medical information to local communities. The Center also supports two major programs designed to promote career development of young investigators and a pilot project research program. Both of these programs are described in detail in this newsletter.

The date of April 11, 2008 has been set for the first meeting of the CEGIB External Advisory Board. Board members are Cheryl L. Walker Ph.D. (Chair), Daniel Acosta Ph.D., Thomas Gasiewicz Ph.D., Gary Marchant Ph.D. and Ilya Shmulevich Ph.D.. The program will include formal presentations by the core components of the Center as well as a mini-symposium on timely scientific topics in the area of systems biology. Please reserve this important day on your calendars.

The primary goal of the *GxE News Quarterly* is to exchange information related to the goals of the Center with the UofL community and beyond. Indeed, the major strength of the Center is its members. As we work together to meet the ambitious goals that we have set for ourselves, I encourage you to share your time and talents to make CEGIB a strong unit within the UofL community.

CEGIB is in its infancy and I hope that its future success is measured not by numbers, but by the scientific, clinical and public health impact of the science supported by the Center. – KSR



Kenneth S. Ramos, Ph.D.

CEGIB SPONSORED SEMINARS AND ENRICHMENT ACTIVITIES

In addition to symposia and courses coordinated by the facility cores, CEGIB will be co-sponsoring seminar speakers in conjunction with on going UofL seminar series. Chris States, Ph.D. is coordinating seminar sponsorships and welcomes your nominations for speakers.

The first CEGIB sponsored seminar speaker is **Thomas J. Begley**, Ph.D., assistant professor in the Department of Biomedical Sciences and Gen*NY*Sis Center for Excellence in Cancer Genomics of the University at Albany, State University of New York. Begley's laboratory uses a multidisciplinary approach to model and define cellular responses to damage. Specifically, he employs high throughput screens and computational analysis to build cell based models of exposure to toxicants and chemotherapeutic compounds. These systems-based approaches are also used to identify novel damage detection and signaling molecules that are then studied using targeted genetic and biochemical experiments. Dr. Begley is presenting "Systems Based Modeling Predicts Translational Responses to DNA Damage" on January 24, 2008, at noon, in the Pharmacology and Toxicology conference room (Building A, Room 1302).

- JCS



MEMBER ACCOLADES

Several of our members and their students have received recognition this fall for their research and professional contributions.

Students

Samuel C. McNeely (Ph.D. awardee, Chris States' lab):
Dissertation title: "*Sensitivity to Sodium Arsenite Depends upon Susceptibility to Mitotic Arrest-Associated Apoptosis*"

1st place, graduate student poster competition, Brown Cancer Center Retreat

Guy Stevenson Award, UofL Winter 2007
Commencement

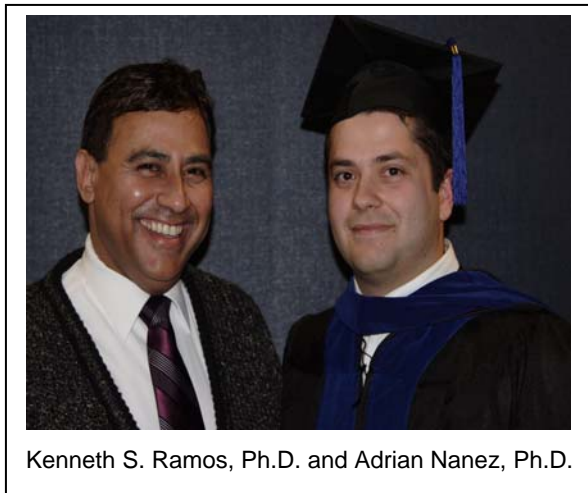
This award is for the most outstanding Ph.D. student in scholarship, leadership and service and is the highest honors for a Ph.D. student at UofL.



Sam McNeely receiving Guy Stevenson Award from President Ramsey at the doctoral hooding ceremony.

Nicholas Watson (Ph.D. Candidate, Glenn McGregor's lab): Watson, NB, Digman, M, McGregor, WG. *RAD18 function in human cells is essential for the recruitment of accessory DNA polymerases in translesion synthesis*. 6th Annual Brown Cancer Center Retreat, University of Louisville, Louisville, KY, November, 2007.

1st place, Masters student poster competition, OVSOT



Kenneth S. Ramos, Ph.D. and Adrian Nanez, Ph.D.

Adrian Nanez, Ph.D., - received his Ph. D in Biochemistry and Molecular Biology from the University of Louisville in November 2007. He then began a Post-Doctoral Fellowship in the laboratory of Dr. Cheryl Walker at the University of Texas M.D. Anderson. His primary research focuses center on determining the use of PET imaging as a molecular determinant for treatment efficacy in renal cell and endometrial carcinoma. He is also involved in studies examining the involvement of the mammalian Target of Rapamycin (mTOR) signaling cascade in carcinogenesis.

Thomas Schlierf (Masters student, David Hein's lab): Schlierf, TJ, Ynag, D, Doll, MA, Baumgartner, KB, Hein, DW. *N- Acetyltransferase 2 genetic polymorphism increases in breast cancer risk among women smokers in New Mexico*. Ohio Valley Society of Toxicology, Eli Lilly Corporate Center, Indianapolis, IN, November 2007. 1st place, Masters student poster competition, OVSOT

Krista A. Riggs (Ph.D. Candidate, Carolyn Klinge's lab): Riggs, K.A., McConda, D.B., Ivanova, M.M., Pierce, W.M., and Klinge, C.M. *Identification of COUP-TFII interacting proteins in tamoxifen-sensitive human breast cancer cells*. Research!Louisville University of Louisville, Louisville, KY, October, 2007.

3rd place, Ph.D. student poster competition, Research!Louisville

Faculty

Awards and Recognition:

Gavin Arteel (Associate Professor, Pharmacology and Toxicology): Arteel, GA, Guo, L., Schlierf, T, Kaiser, JP, Chen, TS, Liu, M, Conklin, DP, Miller, H, States, JC. *Arsenic exposure synergistically enhances lipopolysaccharide-induced liver injury in mice*. Research!Louisville University of Louisville, Louisville, KY, October, 2007. Award for Scientific Importance, faculty poster competition, Research!Louisville

Susmita Datta has been elected as a member of International Statistical Institute for her distinguished contributions to the development or application of statistical methods Oct. 2007. She has become an associate editor of Statistics and Probability Letters and was invited to be on Scientific Committee of 'Critical assessment of Microarray Data Analysis (CAMDA) 2007, Valencia, Spain, December 2007 and to be on the program committee of Intelligent Systems in Molecular Biology (ISMB) 2007, Vienna, Austria, July 2007.

Craig McClain received several awards

VHA Advanced Clinic Access Champion Award, Louisville VAMC

AGA Foundation, 2007 Research Scholar Award (RSA) for Mentoring

University of Louisville, Department of Internal Medicine, Distinguished Investigator Award

AASLD Nominations Committee of the American Association for the Study of Liver Diseases

Greg Rempala received the highest university degree of 'doctor habilitatus' at the Warsaw Technical University in Warsaw, Poland in January, 2007. Doctor habilitatus is the highest academic qualification that a person, who already holds a Ph.D. degree, can achieve by his/her own pursuit in several European countries in which the habilitation qualifies the holder to become a university professor and supervise doctoral candidates. The habilitation qualification exists mainly in central and some western European countries, e.g., in Austria, France, Germany, Poland, and Switzerland. The process of habilitation, derived from the Latin *habilitare* which means "to enable", was introduced in the 18th century. Candidates for the degree doctor habilitatus must submit a dissertation in their field of expertise, present a colloquium summarizing their achievements, and give a lecture on a topic selected by the degree-granting committee. The reviewers of the dissertation are selected by a national scientific committee.

Promotions and appointments:

Gavin Arteel was appointed University Scholar

Craig McClain was appointed to two new positions:

Director, Clinical & Translational Sciences Institute, University of Louisville Medical School,

Associate Vice President for Translational Research, University of Louisville Medical School

Russ Prough ascended to President, International Society for the Study of Xenobiotics (2008-2009)

Greg Rempala was promoted to Full Professor of Statistics at UofL with dual appointment between departments of Mathematics in A&S and Biochemistry in School of Medicine).

Chris States was appointed Distinguished University Scholar, and is now on the Editorial Boards of *Toxicology and Applied Pharmacology* and *Reproductive Toxicology*

New grants received:

Carolyn Klinge received two new new grants:

NIH R21 CA124811 *Regulation of miRNA expression in breast cancer* (150k in year 1 and 125k in year 2; 6/1/07-5/31/09) and total costs of \$406k for the 2 yr. requested funding period. C.M. Klinge (PI at 10% effort); and Yong Li, Ph.D., also in Biochemistry & Molecular Biology, as Co-PI at 10%.

Kentucky Lung Cancer Research Program: Klinge, C.M. (PI); Co-Investigators W. Zacharias (UofL), K-B Kim and H. Swanson (UK) *Mechanisms for gender differences in lung adenocarcinoma* (9/1/07-8/31/09).

Principal Investigator: Klinge, Carolyn M. University of Louisville Research on Women Grant: Anticancer activity of anacardic acid in breast and lung cancer cells. (\$4,000, 1/1/08-12/31/08).

Ramesh Gupta received 3 new grants in 2007:

CA-118114 (Gupta) 04/07-02/11, NCI \$1,416,829, *Breast Cancer Chemoprevention Strategies*

CA-125152 (Gupta) 07/07-06/12, NCI \$1,850,000, *Breast Cancer Chemoprevention Potential of Common Spices*

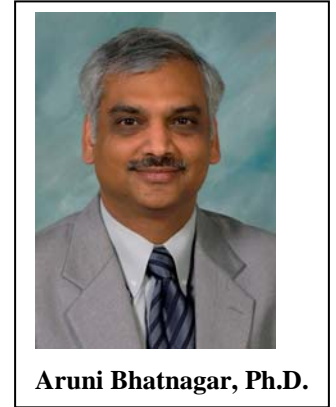
KY Lung Cancer Res. Board (Gupta) 09/07-08/09, \$149,939, *Effect of Estrogen on Polycyclic Aromatic Hydrocarbon (PAH)-Mediated Lung Cancer*



MEMBER HIGHLIGHT

Aruni Bhatnagar, Ph.D.

The major emphasis of Bhatnagar's research program is to understand the cardiovascular effects of aldehydes that are generated from lipid peroxidation and those that are produced in the environment. One of his group's most provocative findings is that in addition to causing toxicity, aldehydes generated from lipid peroxidation play an important role in cell signaling. They have found that inhibition of aldehyde metabolism abrogates cytokine and growth factor signaling, which prevents mitogenesis in smooth muscle cells and apoptosis in endothelial cells. Because these aldehydes are generated during oxidation of lipoproteins, our findings have wide reaching implications in understanding how oxidized low-density lipoproteins induce and sustain atherogenesis. Although they are still unraveling the signaling processes that are interrupted by preventing aldehyde metabolism, our results suggest that agents that inhibit such signaling may represent a new class of anti-inflammatory drugs that could be used for treating chronic inflammation during atherosclerosis, ischemic heart disease, sepsis, and long-term diabetes.



Aruni Bhatnagar, Ph.D.

The Bhatnagar group has also found that analogous to endogenous aldehydes, aldehydes present as pollutants in the air, water, and food also affect cardiovascular health and induce chronic inflammation. They have preliminary evidence suggesting that exposure to environmental aldehydes accelerates and exacerbates atherosclerosis in mice. These data support and strengthen the epidemiological link between pollution and heart disease. They are currently devising new experimental paradigms to help us test more rigorously the epidemiological link between particulate air pollution and the fundamental mechanisms that contribute to the increase in clinical events in people with existing heart disease. They hope that these studies will lead to the identification of environmental pollutants as heretofore unrecognized cardiovascular disease risk factors and spur the development of the new discipline of "Environmental Cardiology".



CAREER DEVELOPMENT

Career Development for New Environmental Health Investigators. CEGIB provides strong mentoring to young members of the NIEHS Center. The Career Development uses senior faculty to assist award recipients in launching their careers. Monthly meetings with Russell A. Prough, Ph.D. or assigned mentors monitor progress toward grant submission, meeting attendance, and attendance at special training programs at NIH or universities. Funds are provided by the Center to support travel to meetings and training conferences, laboratory setup costs, and course fees and books. Two promising young UofL faculty members have been selected for support. Yong Li, Ph.D. and Qunwei Zhang, Ph.D. and their research projects will be described in future newsletter articles. CEGIB's Career Development Core is soliciting nominations for additional faculty for the second year of the CEGIB Career Development Program.

Nominations for junior members for this Career Development Program will be received through March 15, 2008. Announcements of the candidates selected will occur on or before April 1, 2008. Department Chairs, Division Chiefs, Center Directors, and Senior Faculty members may nominate candidates by providing:

1. A letter of nomination, including current plans for mentoring and career development within the department, division, or research unit
2. A *Curriculum Vitae* of the candidate
3. A written plan of career development prepared by the candidate and his/her chair/chief/supervisor/colleague currently implemented, including statement of how the individual's career development will involve research in the area of environmental health sciences. (Limit to 5 pages or less)
4. Copies of recent grant applications of the candidate

-RAP



PILOT PROJECTS PROGRAM

Doug Darling, Ph.D.

Building, Constructing, Strengthening the foundation. These are the central goals of CEGIB, which aims to build environmental genomics and integrative biology research at UofL. This includes ambitious goals of facilitating new research directions, and bringing new people into the field. Towards this goal, Dr. Ramos has dedicated significant funds to the CEGIB Pilot Project Program. The specific aims of this program are to encourage new and innovative research approaches with emphasis given to creative new lines of research in environmental genomics and integrative biology. The Pilot Program supports short-term research projects to enable researchers to collect the data necessary to obtain funding through governmental and private sector agencies. As with any building project, the interactions between the structural elements are key aspects of the strength of the building. One of the aims of the Pilot Program is to build new interactions between investigators at UofL. For example, emphasis has been given to providing funds for collaboration between new faculty members with expertise in a novel technology and senior investigators with experience in environmental studies.

In the past, the Pilot Program has set the bar high for the scientific quality of the funded proposals. This has paid off in helping to obtain at least 2 R01 grants, and greater than a 10-fold return on the funds invested in pilot projects.

Recipients of awards and their project titles in the current year:



Lu Cai
"Genomic and Epigenetic Mechanisms for Environmentally Cd-induced Carcinogenesis"



Yong Li:
"Benzo[a]pyrene-Dysregulated MicroRNAs in Lung Cancer"



David A. Scott
"Tobacco Smoke-induced Alterations to Porphyromonas Gingivalis"



David W. Powell
"Defining the Functional Interaction Partners for Hepatic P450s"

The CEGIB P30 grant will support at least three more yearly rounds of funding for pilot projects. The Request for Applications for the next round of the funding is available from Jeannie Bowman (jeannie.bowman@louisville.edu), and has a submission deadline of February 15, 2008 for projects to start April 15th. We anticipate funding five projects this year.

CEGIB may not be the most visible of all the construction projects on the Health Sciences Campus, but it is already having a significant impact. In future newsletters, we will highlight some of the projects that are currently funded through the CEGIB Pilot Project Program.



BIOINFORMATICS, BIOSTATISTICS AND COMPUTATIONAL BIOLOGY CORE (BBCB)

Nigel Cooper, Ph.D.

The goal of the CEGIB, Bioinformatics, Biostatistics and Computational Biology Core (BBCB) is to partner with environmental health investigators to aid them in their analyses of the large data-sets produced by the 'omics cores. To accomplish this goal, the BBCB has recruited a multi-disciplinary team of experts representing the fields of life sciences, bioinformatics, computer science, mathematics and statistics. This is a unique development at the UofL. The team is assembling the computational infrastructure required to store and query large data-sets, as well as to build the new informatics tools required for analyses. The team is also developing workshops, conferences and classes for training researchers and their students in the computational methods required.

The BBCB Team Members include:

Informatics Group (IFG)

- Ted Kalbfleish, Ph.D. (group leader)
- Eric Rouchka, Ph.D.
- Nigel Cooper, Ph.D. (Director, BBCB)
- Sabine Waigel (operations manager)

Biostatistics Group (BSG)

- Susmita Datta, Ph.D. (group leader)
- Guy Brock, Ph.D.
- Alex Cambon
- Qiang He

Systems Modeling Group (SMG)

- Grzegorz Rempala, Ph.D. (group leader)
- Eric Rouchka, Ph.D.

The BBCB team members are building computational methods and new algorithms for: quantitative analyses; pathway analyses; discovery of gene-regulatory networks; data-integration techniques.

The development of conferences and workshops include:

NIEHS SNP Workshop

January 10-11, 2008 Brown Hotel, Louisville, KY

Regional Bioinformatics Summit

March 28-30, 2008 Lake Barkley State Park Cadiz, KY

Classes include:

CECS 660 Introduction to Bioinformatics
CECS 694 Bioinformatics Journal Club
MATH BIOC 591 Mathematical Models in Computational Biology
PHBI 750 Statistics for Bioinformatics
PHBI 751 High Throughput Data Analysis

The outcome of these partnered activities will be enhanced insight of cellular regulatory systems with the ultimate goal of advancing knowledge in the area of environmental health.

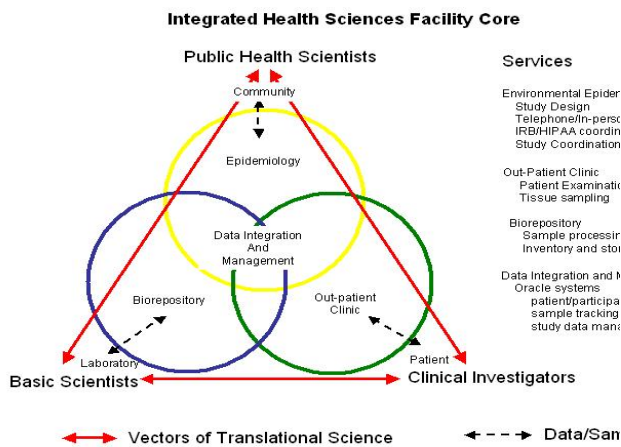


INTEGRATED HEALTH SCIENCES FACILITY CORE (IHSFC)

David Tollerud, M.D. & Roland Valdes, Ph.D.

The philosophy underlying the IHSFC is that a major limitation to translational research is not physical facilities, but dedicated human capital. The IHSFC brings together basic clinical and public health researchers in regular discussions focused on translation of basic discoveries to human applications. IHSFC members represent a broad range of disciplines that meet monthly in a roundtable forum to discuss new technologies and research discoveries and to identify areas that merit consideration for early translational applications. Support services target the most promising leads and advice is provided to promote development of clinically/public health relevant approaches. The IHSFC serves as an incubator of new collaborations between basic researchers and clinical and public health researchers, fostering new applications of promising biomarkers, therapies and preventive treatments.

The figure below depicts the IHSFC as a Venn diagram consisting of three overlapping nodes that represent public health, clinical, and biorepository components, with a central data integration and management component. Examples of the services provided by each component are shown on the right. The dotted lines represent the flow of data/samples from the components to external agencies in the community, clinic/hospital, or laboratory. Supported studies utilize the services of two or more of the components and the data integration/management component. Thus, the IHSFC is explicitly designed to facilitate and promote translational research among bench, bedside, and community.



IHSFC services include:

- Clinical and public health study design and statistical support
- Human subjects, HIPAA, blood borne pathogens, other regulatory compliance
- Ethical, Legal and Social Implications (ELSI) research support services
- Access to outpatient clinical facilities and a mobile health unit
- Biorepository services
- Access to key technologies
- 'omics technical advice services
- Interface of researchers with community-based organizations and agencies that impact clinical and public health research in the region.

COMMUNITY OUTREACH AND EDUCATION CORE (COEC)

-Irma Ramos, M.D.

The Community Outreach and Education Core (COEC) provides education to disadvantaged populations in the Metro Louisville Area on the importance of interactions between genes, environment, culture, and disease. The COEC has developed a culturally-sensitive lay health worker network and initial efforts are being directed at the growing Hispanic populations in the area. The educational program has been developed to target diseases with a significant environmental component such as diabetes, cancer and hypertension.

Within the framework of the CEGIB initiative, a community is defined as a complex network that in many ways resembles the complexity of biological systems. As such, working with communities requires the use of systems approaches similar to those applied in biomedicine to understand and facilitate knowledge exchange within the community and to improve individual and community health. Current efforts are focusing on strengthening partnerships and building credibility with community organizations and individuals providing services to Hispanic residents in Shelbyville, including El Centro Latino, the Hispanic/Latino Coalition, Al Dia en Americas – one of the Hispanics Newspapers, the Americana Community Center and the Health Department.

Highlights of recent COEC activities include:

3rd Hispanic Health Fair, the largest Hispanic health fair in the Metro Louisville Area at the Americana Community Center - October 9, 2007.

Kentucky Bi-National Health Fair at Centro Latino in Shelbyville- October 20, 2007.

3rd Kentucky Hispanic and Immigrant Networking Summit in Shelbyville - October 4, 2007

In addition, Irma Ramos was invited to present her work at the National Institutes of Health on October 10, 2007 on environmental justice and community-based participatory research. Her presentation focused on ways to encourage socially or physically isolated communities to take ownership of environmental health projects. She also chaired a session entitled *Children, Nature and Land Use at the 1st Annual Conference, on Law, Ethics and the Life Sciences* at the University of Louisville Louis D. Brandeis School of Law on October 26, 2007.



Community residents chatting with Irma Ramos, M.D. at the 2007 KY Bi-National Health Fair, Shelbyville, Kentucky



Questions, Comments or Suggestions?
Contact

Jeannie Bowman (Administrator)
gjbowm01@gwise.louisville.edu

J. Christopher States (Editor)
jcstat01@gwise.louisville.edu