Issue Number 8

INTERFACE:

GENES AND THE ENVIRONMENT

CENTER FOR ENVIRONMENTAL GENETICS UNIVERSITY OF CINCINNATI Spring 1996

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# The Rural Coalition

The Community Outreach and Education Program (COEP), the newest Core facility in the Center for Environmental Genetics (**CEG**), was the subject of the last issue of ***Interface***, in which projects throughout the local community were detailed. In this issue we'd like to describe projects beyond the local community.

The COEP Core has developed a working partnership with the **Rural Coalition**, an advocacy organization located in Washington, D.C. CEG member **Eula Bingham** co-chairs the ***National Advisory Board on Community-Responsive Partners for Environmental Health*** and serves as a science advisor on a National Institute of Environmental Health Sciences (NIEHS) grant, entitled ***"Community-responsive partners for environmental health."*** More recently, CEG members **Eula Bingham**, **Katie Brown**, **Wilson Tabor** and **David Warshawsky** at the University of Cincinnati (UC) have collaborated with the Rural Coalition on a grant application submitted to the U.S. Environmental Protection Agency (EPA), entitled ***"UC-Rural Coalition collaborative partnership for environmental justice."***

The Rural Coalition is an umbrella organization for approximately 90 community-based groups that represent low-income rural communities and rural people of color throughout the U.S. and along the U.S.-Mexico border. This national alliance was founded in 1978. It is governed by a 15-member, elected Board of Directors. **Carlos Marentes** of the **Sin Fronteras Organizing Project** is the current Chairperson. The staff consists of **Lorette Picciano-Hanson** as the Executive Director and **Jill Gay** as the Health and Environment Officer.

The Rural Coalition is committed to promoting the long-term viability of rural communities. To promote this objective, the Rural Coalition advocates progressive national policies that are responsive to the unique issues and needs of rural communities. The Rural Coalition also supports the implementation of grass-roots programs, which develop the capacities of rural communities so that they might sustain economic viability and promote diversity. A guiding principle of the Rural Coalition is that ***"the long-term viability of rural communities rests on effective control and use of resources by the people living in rural areas."***

Since 1988, the Rural Coalition has been involved with environmental health issues and related public health concerns. In 1991, the Board of Directors identified public health and environmental quality issues as priority concerns. In 1994, **Pat Bellanger**, co-Chair of the Rural Coalition's Health and Environment Committee, served as co-facilitator of the NIEHS-sponsored ***Symposium on Health Research and Needs to Ensure Environmental Justice***. Subsequent meetings with **Ken Olden**, Director of NIEHS, and **Gerald Pojé**, NIEHS staff member, focused on ways to promote and sustain effective interactions between federally-funded researchers and communities.

The special environmental health problems, which have been identified or suspected by rural communities, are wide-ranging. It is clear that rural communities--particularly those with large minority populations--have become repositories for all kinds of industrial, energy-related and military wastes. Such waste materials represent a multitude of environmental and human health hazards. For example, the Latino and indigenous communities from Alaska to the Southwest and Great Lakes region are affected by nuclear hazards and toxic wastes. The African-American communities in the rural South are exposed to threats as diverse as toxic dumps, industrial

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pollution from petrochemicals and nuclear power--as well as bacterial and other hazards from the expanding poultry industry. Appalachian communities are affected by mining, dumping, and nuclear research and power plants. Rural women throughout the nation are affected by the working conditions in the textile industry. Migrant farmworkers are routinely exposed to high levels of pesticides and other hazards derived from industries operating along the U.S.-Mexico border.

Rural communities repeatedly have expressed their frustration about their inability to accurately identify and solve the environmental health problems which they have long perceived in their communities. These same rural communities are anxious to develop not only the resources, but also the skills, needed to decide upon and implement viable solutions.

The past experience of predominantly poor and minority rural communities being able to interact and collaborate on research with the scientific community, however, has been almost universally either negative or nonexistent. In some communities, studies sponsored by the offending industry were used to oppose the organizing efforts of the local residents. In other communities, researchers have collected and analyzed their data in isolation from the local residents, and then never returned to discuss their findings. Not surprisingly, these communities have had little confidence in the results of such studies. In general, poor rural communities feel that researchers have overlooked them.

In September 1994, with seed money from NIEHS, the first meeting of the ***National Advisory Board on Partnerships Between Communities and Federally-Funded Institutions in Community-Based Health and Environmental Assessment*** was held. CEG member **Eula Bingham** co-chairs this National Advisory Board with **Pat Bellanger** of the **American Indian Movement**. The role of the Board is to establish collaborations between environmentally-ravaged communities and federally-funded researchers, so that well-designed environmental assessments might be conducted and appropriate mitigation measures can be performed.

In 1994 the Rural Coalition received a $30,000 planning grant from the NIEHS to design an environmental health assessment project. This money was used for bringing together university-based scientists and Rural Coalition members to produce a grant application--which was submitted to NIEHS in January, 1995. The project, funded in mid-1995, is entitled ***"Community-responsive partners for environmental health***. The purpose of the project is to ***"develop problem-solving skills and strategies among isolated low-income rural communities and local health care providers... to identify and mitigate exposure to environmental hazards."***

One objective of the project is to develop collaborative partnerships among rural communities, local health care providers, and university-based environmental health researchers. In the end, rural communities will have**:** the research and analytical skills necessary to address locally-defined issues; contacts with which to broker relationships with university-based researchers and government agencies that are responsive to local concerns; and experience gained in developing strategies which foster local decision-making authorities.

Two model projects for this grant have been designed**:** ***"Environmental pollution and health problems in the Black community of Sumter County, Alabama"*** and the ***"Binational project to reduce pesticide exposure among Latino farmworkers"*** in El Paso, Texas. The unifying theme of these model projects is to promote the formation of partnerships between underserved rural populations affected by environmental pollution. Primary health care providers and NIEHS-sponsored scientists will assist communities in the assessment of locally-defined environmental and public health concerns, as well as in the appropriate strategies for reducing exposures.

The Sumter County project represents a partnership among **Cleo Askew** of the **Federation of Southern Cooperatives (FSC)** in Epes, Alabama, **Sandral Hullett**, Health Services Director of **West Alabama Health Services, Inc.**, and **Robert Snyder** and **Howard Kipen** of the **Environmental and Occupational Health Sciences Institute (EOHSI) at Rutgers University**, Piscataway, New Jersey. The objective of this collaborative partnership is **[a]** to assess whether the health problems of this low-income, African-American community are correlated with exposure to environmental contamination and **[b]** to identify ways to reduce any quantifiable exposures. This Alabama community is particularly concerned about the potential off-site contamination and health risks associated with the Chemical Waste Managment hazardous waste landfill, the largest in the country.

The El Paso project represents a partnership among **Carlos Marentes** of the **Sin Fronteras Farmworker Center**, **Mark Lyons**, a health educator at the **Maria de los Santos Clinic** in Philadelphia, Pennsylvania, and **Mark Robson** and **Michael Gallo** of **EOHSI at Rutgers University**. The purpose of this collaborative partnership is to use methods of participatory education for training farmworkers to reduce their exposure to pesticides (***Figure 1***). In a 1992 report, the U.S. General Accounting Office estimated that as many as 300,000 farmworkers are exposed to significant doses of pesticides each year. It is estimated that fewer than 10% of farmworkers know the symptoms of pesticide poisoning, understand the concept of "restricted entry interval," or have received training on how to protect themselves.

***Fig. 1.*** Jill Gay of the Rural Coalition being trained by José Morales, **Comite de Apoyo a los Tradajadores Agricolas** (CATA), in the methods of participatory education at the meeting of the ***National Advisory Board on Community-Responsive Partners for Environmental Health*** in March 1996 (Washington, DC).

Collaborative partnerships with the Rural Coalition are multiplying! In March 1996, a grant application, entitled the ***"UC-Rural Coalition collaborative partnership for environmental justice"*** was submitted to the U.S. EPA. This project represents a partnership among **Charlotte Keys**, Director of the **Jesus People Against Pollution (JPAP)**, **Jill Gay**, Environment and Health Officer of the **Rural Coalition**, **Cleo Askew** of the **Federation of Southern Cooperatives (FCS)**, and **CEG** members **Eula Bingham**, **Katie Brown**, **David Warshawsky** and **Wilson Tabor** at the University of Cincinnati. Residents of Columbia, Mississippi, are concerned about the potential off-site contamination and health risks associated with the Newsom Brothers/ Old Reichold Chemicals, Inc. chemical dump site. Over the years, this property was used as a sawmill and manufacturer of turpentines, resins and wood preservatives. The facility exploded in 1977 and became listed as a Superfund site in 1986.

The purpose of this collaborative partnership is to promote the local initiatives of **JPAP** and **FSC** by supporting the leadership with the information, skills and resources necessary for successful community-based approaches to characterizing environmental pollution and the health status of the community. This collaborative partnership also hopes to identify intervention and remediation strategies. As part of the project, the UC faculty will develop and conduct a risk assessment course for members of the Rural Coalition, JPAP, and FSC. This course would be presented at the FSC Rural Training Center in Epes, Alabama. The funding status of this project will not be known until approximately August 1, 1996.

The Rural Coalition and the CEG +Community Outreach and Education Program (COEP) share common objectives in their efforts to be responsive to the environmental and public health concerns of poor, environmentally-impacted communities. It is clear that--when community residents, health-care providers, and scientists work together to address locally-defined environmental and public health issues--community representatives can be trained in the tenets and strategies of environmental health assessments. These representatives can learn to critically evaluate published assessments and identify gaps in their knowledge. These representatives can also learn to assess the potential effectiveness of environmental intervention and remediation programs, and we can work together to promote appropriate monitoring and remediation strategies.

For more information about the **Rural Coalition** -- the address is 110 Maryland Ave., N.E., Suite 505, Washington, D.C. 20002; the phone number is 202-544-9611; and the e-mail address is RURALCO@AOL.COM.

# LETTERS TO THE EDITOR

## RESPONSES TO VARIOUS QUESTIONS

**Q** **I understand that a cloning company has filed patent applications on both the *BRCA1* and *BRCA2* genes and that they plan to market a *BRCA1* test in the second half of 1996. Isn't this contrary to the recommendations by the American Society of Human Genetics?**

**A** *Yes, the company* ***Genetics and I.V.F. Institute*** *(Fairfax, VA) has broken ranks with recommendations by the American Society of Human Genetics and most of the breast cancer research community by making available a $295 test for the* ***BRCA1*** *185delAG mutation. This mutation was reported 6-9 months ago to be the most common one among Ashkenazi Jewish women. But--if you find out you have this mutation, do you elect to have both breasts removed at age 25? And, if you do not have this mutation but have a mother, grandmother and great-*

*grandmother with breast cancers all before age 40, do you elect not to have your breasts removed? In addition,* ***Myriad Genetics Inc****. (Salt Lake City) has filed patent applications on both* ***BRCA1*** *and* ***BRCA2****, and the author-activist Jeremy Rifkin plans to file a petition with the U.S. Patent and Trademark Office challenging these patent claims.*

*As discussed in previous issues, both* ***BRCA1*** *and* ***BRCA2*** *together are responsible for probably the majority of early-onset hereditary breast and ovarian cancer. Given the last few months of published reports, however, it now seems clear that* ***BRCA1*** *and* ***BRCA2*** *are two of a minimum of four or more genes that provide an increased risk of breast cancer. Currently there are plenty of clinical reports of both incomplete penetrance (having the genotype without showing the trait of early-onset male breast cancer or female breast or ovarian cancer) and phenocopy (showing the trait but not having any of the established genotypes). These data simply suggest what is well known for many other inherited traits, i.e. that other modifier genes and/or environmental factors must be able to affect phenotypic expression. When we consider cancer susceptibility as primarily due to highly penetrant single-gene traits, it is too easy to lose sight of the importance of other genetic and environmental factors. This can hinder the search for environmental factors that actually might best be detected by studying people with similar genetic risks. The presence of modifier genes represents the "wild card" not placed on the table of statistical averages. For the particular individual, this wild card may determine what might be their correct choice of action--which can include surgical procedures and treatments. "As we enter this post-genomic era, we should expect more and more emphasis on something that could not be previously studied: the gene-gene and gene-environment interactions that we have always suspected would end up being important" [S.H. Friend, Nature Genet* ***13:*** *16-17 (1996)].*

**COMMENT** **Back in issue #1 we proposed a possible link between the "Gulf War Syndrome" (variable illnesses in the military population due to unknown environmental agents, possibly including exposure to nitrogen mustard or sarin nerve gas) and the human paraoxonase (*PON*) polymorphism (individuals having high, intermediate, or low enzyme activity for breaking down organophosphates). In issue #6 we mentioned the work of M. Abou-Donia (Duke University) in which he suggested that the combination of dermal exposures to permethrin and *N,N*-diethyl-*m*-toluamide (DEET), plus high doses of oral pyridostigmine, might have led to a delayed toxic impact known as "organophosphate-induced delayed neurotoxicity" (OPIDN). Now, from the University of Washington (Seattle), Clem Furlong has direct evidence for the metabolism of sarin by human paraoxonase.**

**Paraoxonase is a high-density lipoprotein (HDL)-associated serum enzyme that hydrolyzes several organophosphorus insecticides. Previous studies have shown that a mutation at amino acid residue 192 is responsible for the paraoxonase polymorphism. One isoform, with arginine at position 192 (R192), reflects high enzyme activity, and the other isoform with glutamine at position 192 (Q192) shows low activity for paraoxon, chlorpyrifos-oxon, and phenylacetate. Interestingly, Furlong and coworkers find that the activity polymorphism of this enzyme is just reversed for diazoxon, soman and sarin hydrolysis, i.e. R192 homozygotes have low activity while Q192 homozygotes have higher rates of hydrolysis. In both cases, heterozygotes have intermediate levels of activities. Now that it is firmly established that "paraoxonase" and "sarinase" are one and the same enzyme, will anyone be able to demonstrate an effect on Gulf War Syndrome patients by this polymorphism?**

**COMMENT** **Back in issue #5 we quoted S. Safe as saying that the contribution of estrogenic industrial compounds is 0.0000025% of the daily intake of estrogenic flavonoids in the diet. Very recently, however, a report [*Science* 272, 1489-92 (1996)] suggests that environmental chemicals in *complex mixtures* are synergistic in their activation of estrogen receptor-dependent gene transcription. This synergism makes some chemicals 160- to 1600-fold more potent, when compared with analysis of each chemical alone. The bottom line is that we don't have all the answers in yet!**

## CEG-SPONSORED SPEAKERS

**Professor Peter Herrlich, Ph.D.**
Institute of Genetics, Forschungszentrum, Karlsruhe, Germany
MARCH 6, 1996 (Departmental Seminar) ***"Metastatic tumors recruit embryonic gene expression patterns,"***
MARCH 7, 1996 (Distinguished Lecturer) ***"Environmental influences on signal transduction"***

**Peter J. O'Brien, Ph.D.**
Dean of the Faculty of Pharmacy, University of Toronto, Ontario, Canada
MARCH 27, 1996 (Departmental Seminar) ***"Peroxide-mediated oxidative stress and hepatocyte cytotoxicity,"***
MARCH 28, 1996 (Distinguished Lecturer) ***"Reductive stress and cell death--a new concept"***

**Professor K. Walter Bock, Ph.D.**
Institute of Toxicology, Eberhard Karls University, Tübingen, Germany
MAY 23, 1996 (Special Seminar) ***"Mechanistic studies on liver tumor promotion by the environmental toxin 2,3,7,8-tetrachlorodibenzo-p-dioxin"***

# CEG Members in the News

**Dan Nebert** was invited to organize and chair a session on "Modulation of Drug-Metabolizing Enzymes by Oxidant Stress," at the 11th International Symposium on Microsomes and Drug Oxidations (Los Angeles, CA) in July 1996. The title of his talk will be ***"Role of the [Ah] gene battery and Ah receptor in oxidative stress."*** He has also been asked to organize and chair a workshop on "Pharmacogenetics at the Molecular Level," at the 9th International Congress of Human Genetics (Rio de Janeiro, Brazil) in August 1996. The title of his talk there will be ***"Evolutionary reasons as to why drug-metabolizing enzyme polymorphisms might exist."***

**Zalfa Abdel-Malek** was a co-chairperson for the Melanocyte Biology Session at the 57th annual meeting for the Society of Investigative Dermatology, in May 1996 (Washington, DC). She gave a presentation entitled ***"Paracrine regulation of human melanocytes by the interaction of a-melanotropin with endothelin and agouti signaling protein."***

**Nira Ben-Jonathan** presented two talks in a symposium titled: "From Gene to Protein and Therapy" (Brussels, Belgium) in May 1996. These talks were entitled ***" Regulation of prolactin gene expression and release by endocrine and paracrine factors,"*** and ***"Extrapituitary prolactin: distribution, regulation and function."*** She also presented a talk for the "Hot Topics" section of the International Meeting of the Pituitary Society (San Diego, CA) in June 1996 entitled ***"Induction of hyperprolactinemia by the environmental estrogen bisphenol A."***

**Bob Bornschein** and Scott Clark, of the Department of Environmental Health, participated in an international conference, giving a seminar entitled ***"Environmental pollution and child health: critical needs and issues for central and eastern Europe***" in May 1996 (Sosnowiec, Poland). **Bornschein** also presented a paper entitled ***"Lead and arsenic exposures in mining and smelting communities."***

**Tom Doetschman** has been invited to present talks at three conferences: the Engineered Animal Models Conference in May 1996 (Baltimore, MD); the Weinstein Cardiovascular Development Conference in June (Philadelphia, PA); and the Molecular Biology of the Normal, Hypertrophied and Failing Heart Conference in August 1996 (Snowbird, UT). He also presented the Keynote Address at the Sigma Xi Banquet in April 1996 (Kansas City, KA) and in September 1996 will present seminars at the New York University Medical Center (New York, NY) and at the Eppley Cancer Research Center (Omaha, NE).

**Greg Grabowski** was invited to present a paper entitled ***"Enzyme therapy for Gaucher disease: variations on a theme"*** at the American College of Medical Genetics meeting in March 1996 (Bethesda, MD). He also was invited to present a talk entitled ***"Developmental expression and function of prosaposin: a multifunctional protein"*** at Children's Hospital Research Foundation and the Graduate Program in Developmental Biology in April 1996 (Cincinnati, OH).

**Joanna Groden** gave an invited seminar entitled ***"Form and function: alternative splicing of the APC gene"*** in March 1996 (Reston, VA) at the annual meeting of the American Gastroenterological Association, and ***"A new twist for Bloom's syndrome"*** in April 1996 at the University of Utah Huntsman Cancer Institute (Salt Lake City). She also was invited to give a talk entitled ***"The genetics and biochemistry of Bloom's syndrome"*** in April 1996 at the University of Alberta (Edmonton, Canada).

**Grace Lemasters** received notice that the Defense Women's Health Research Program funds will be awarded by the U.S. Army for her proposal entitled ***"Female reproductive effects of exposure to jet fuel at U.S. Air Force Bases."*** This 4-year study will be a collaborative effort between the U.S. Air Force, NIOSH and University of Cincinnati investigators. Potential differences between women exposed to jet fuel and an unexposed group will be examined. Racial differences in both uptake and elimination of jet fuel and in reproductive health responses will also be investigated.

**Frank McCormack** was invited to give a lecture entitled ***"Structure and function of surfactant protein A"*** at the Thomas L. Petty Aspen Lung Conference on Genes and Gene Therapy as featured state-of-the-art speaker. The conference was held in June 1996 (Aspen, CO). He also received a Career Investigator Award of $105,000 for his proposal entitled ***"Surfactant protein A in macrophage/P. carinii interactions."***

**Steve Potter** gave an invited lecture at the Medical University of South Carolina (Charleston) entitled ***"Hox genes and pattern formation"*** in March 1996. He also will attend the Gordon Conference on Mammalian Gametogenesis and Embryogenesis taking place in August 1996 (Colby-Sawyer College, NH).

**Alvaro Puga** is editing a book with Dr. Kendall Wallace of the University of Minnesota entitled ***"Molecular Biology Approaches to Toxicology"*** and hopes that each of you will buy a copy.

**Nancy Steinberg-Warren** received a grant from the Great Lakes Regional Genetics Group for $2,500 to provide preconceptional and folic acid information to high-risk teens in urban schools of six midwestern states. She also spoke to Milford High School students on "Career Day" in May 1996, about ***"Careers in genetics,"*** and to the Ohio Genetic Counselors and Educators Group (Columbus, OH) on the subject of ***"Clinical supervision."***

**Glenn Talaska** will present a paper entitled ***"Occupational exposures to carcinogens and DNA adducts in exfoliated urothelial cells"*** at a meeting in June 1996 (Stockholm, Sweden). The meeting theme is "DNA Adducts and Mutations in Human Biomonitoring."

# SCIENCE LITE

## MONK GLOATS OVER YOGA OLYPMICS CHAMPIONSHIP

***"I am the serenest!" he says***

LHASA, TIBET---Employing the brash style that first brought him to prominence, ***Sri Dhananjai Bikram*** won the 1996 Olympics International Yoga Competition yesterday with a world-record point total of **873.6**. "I am the serenest," Bikram shouted to the estimated crowd of 20,000 yoga fans, vigorously pumping his fists. "No one is serener than Sri Dhananjai Bikram. I am the greatest monk of all time!"

Bikram averaged 1.89 breaths a minute during the 2-hour competition, nearly 0.3 fewer than his nearest competitor, second-place finisher and two-time champion ***Sri Salil "The Hammer" Gupta***. The heavily favored Gupta was upset after the loss. "I should be able to beat that guy with one lung tied behind my back," Gupta said. "I'm beside myself right now, and I don't mean that in a trans-bodily sense."

***Bikram*** got off to a fast start at the Lhasa meet, which--like most major yoga competitions--is a six-event affair. In the first event, he attained Total Consciousness (TC) in just 2 minutes, 34 seconds, and set the tone for the rest of the meet by repeatedly shouting, "I be blissful! You be blissful?! I be blissful!" to the other yogis.

Bikram, 33, burst onto the international yoga scene with a gold-mandala performance at the 1994 Bhutan Invitational. At that competition he premiered his aggressive style, at one point in the Flexibility Event, sticking his middle toes out at the other yogis. Whereas no prohibition exists against such behavior, according to the Yoga League Commissioner ***Swami Prabhupada***, such behavior is generally considered "unBuddhalike."

"I don't care what the critics say," Bikram said. "Sri Bikram is just gonna go out there and do Sri Bikram's own yoga thing." Before the Bhutan meet, Bikram had never placed better than fourth. Many said he had forsaken rigorous training for the celebrity status accorded by his Bhutan win, endorsing Nike's new line of prayer mats and supposedly dating the Hindu goddess Shakti. His performance this week, however, will regain for him the number one computer ranking and earn him new respect--as well as new respect for his coach ***Mahatananda Vasti***, the controversial guru some have called "Bikram's guru."

"My special training diet for Bikram--of one super-charged, carbo-loaded grain of rice per day--was essential to his win," Vasti said.

The defeated Gupta denied that Bikram's taunting was a factor in his inability to attain TC. "I just wasn't myself today," Gupta commented. "I wasn't any self today. I was just an egoless particle of the universal no-soul."

In the second event, Flexibility, Bikram maintained the lead by supporting himself on his index fingers for the entire 15 minutes, while touching the back of his skull to his lower spine. The feat was matched by Gupta, who had first used this position at the 1990 Tokyo Zen-Off. "That's my meditative position of spiritual ecstasy, not his," complained Gupta. "He stole my thunder."

Bikram denied the charge, saying, "Gupta's been talking like that ever since he was a 3rd century Egyptian slave-owner." Nevertheless, a strong showing by Gupta in the third event, the Shotput, placed him within a lotus petal of the lead at the competition's halfway point.

But event number four, the Contemplation of Unanswerable Riddles (known as koans) proved the key to victory for Bikram. The koan had long been thought the weak point of Bikram's spiritual arsenal, but his response to today's riddle---***"Show me the face you had before you were born"***---was reportedly "extremely illuminative," according to Commissioner Prabhupada. While koan answers are kept secret from the public, for fear of exposing the uninitiated multitudes to the terror of universal truth, insiders claim his answer had Prabhupada and the two other judges "highly enlightened."

With the koan event victory, Bikram built himself a nearly insurmountable lead, one he then sustained through the Yak-Milk Churn and Breathing events, in order to come away with the upset victory.

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***"I think it would be a good idea" --***
***Mahatma Ghandi when asked what he thought of Western civilization.***
Extracted from the WWW, with modifications

## WHAT IS THE PUBLIC SUPPOSED TO BELIEVE?

The public is bombarded almost daily with news flashes suggestive of major breakthroughs in the field of epidemiology. One report will indicate that "too much mayonnaise will cause heart attacks," and the next report might state that "mayonnaise helps prevent heart disease." One week "vitamin A prevents cancer," and the next week "vitamin A causes cancer." "Coffee increases your risk for pancreatic cancer," but then "coffee prevents psychiatric depression." How long can the public put up with such nonsense?

**Epidemiologists are interested in any environmental factor** (chemical, physical, dietary, lifestyle, etc.)--not directly linked to a genetic origin--**that will cause disease and premature death**. During the past 50 years, they have succeeded in identifying the more conspicuous determinants of noninfectious human diseases. For example, cigarette smoking was found to increase the risk of developing lung cancer by as much as 3,000% (30-fold). Exposure to diethylstilbestrol during pregnancy causes a very rare type of vaginal cancer 10-20 years later in the child. Vinyl chloride in the workplace causes a very rare type of blood vessel tumor in the liver. Now, however, colleagues are "pushing the edge of what can be done in epidemiology." What does it mean when researchers report a "20% enhanced risk of breast cancer from drinking alcohol," or a "50% increased risk of oral cancer from the regular use of mouthwash?" Answer: it depends a lot on how the study was set up, and how the experimental and control groups were chosen.

The "blame" has to be shared among**:** the scientific journals that report such work as a "major breakthrough"; the researchers who run to the news media with such miniscule findings; and journalists who overemphasize the worth of such individual studies. This subject is excellently reviewed in ***Science* 269,** 164-169 (1995).

## NICE BUNS, BUT NOT IN A BAKERY!

About 15 years ago, an Oklahoman sheep farmer noticed that some of his livestock had bulging hindquarters and well-sculpted muscles and saw dollar signs. He tried to cross this trait to create an entire flock of bulging hindquartered sheep, but it was not as easy as he thought. At first it seemed to be another case of ***incomplete penetrance*** (having the genotype but not showing the trait). But then it got more complicated.

At a recent Cold Spring Harbor genome meeting, Noelle Cockett and her colleagues (Utah State University, Logan) reported that they have been able to map the mutated gene to sheep chromosome 18. They named the gene ***callipyge***, Greek for "beautiful buttocks." Lambs normally seem to add muscle to their bodies when young and they accumulate fat as they get older. The mutant ***callipyge*** allele, however, apparently lengthens the period of muscle addition and delays fat accumulation.

Lambs born to ***callipyge*** females mated with normal males grow up with their fathers' trait (normal buttocks). Such "one-sided inheritance patterns" are usually a sign of ***imprinting***, a genetic phenomenon in which the gene contributed by one parent is somehow shut down, leaving the other parent's gene as the only functional copy. But researchers then found that lambs receiving two alleles of the ***callipyge*** gene (one from each parent) still came out looking perfectly normal! And if the homozygous ***callipyge*** animal (showing normal buttocks) is mated to a homozygous normal gene female (also showing normal buttocks), the resulting heterozygotes once again exhibit the beautiful buttocks trait! This is a case of a so-called "***overdominant gene.***" The gene is expressed most strongly in heterozygotes and, for some reason, cancelled out in homozygotes. This is why the original Olkahoma farmer got frustrated with what he thought was "simple" genetics.

Such rare gene expression offers insight into a whole new class of non-Mendelian inheritance patterns that might have relevance for human diseases. For example, in Hirschsprung's disease (disorder of the colon) not everyone with a mutant gene gets the disorder, and girls appear to be much less likely than boys to exhibit the trait (***i.e.*** show the symptoms). Finally, do you think humans might have genes that determine the shapes of their buttocks? Of course they do!

## Pilot Project Program Award Recipients for year 05

Seven awardees from six departments once again underscore the success of this Pilot Project Program in attracting new investigators from widely diverse departments.

**Francis X. McCormack,** Internal Medicine
*"Structure/function analysis of surfactant protein A: role in protection from ozone-induced lung injury"*

**Howard G. Shertzer,** Environmental Health
*"The polymorphic aromatic hydrocarbon receptor as a genetic determinant of TCDD-inducible chronic oxidative stress"*

**Mary Beth Genter,** Mol. and Cell. Physiology
*"Conditional knockout of protein kinase C and calmodulin pathways in catecholamine cells in transgenic mice"*

**George D. Leikauf,** Environmental Health
*"Genetic determinants of susceptibility to particulate matter"*

**Daniel J. Hassett,** Mol. Genetics, Biochem.& Microbiol.
*"Role of ozone and cigarette smoke in alginate production by Pseudomonas aeruginosa"*

**Donald L. Allen,** Cell Biol., Neurobiol. & Anatomy
*"Genetic susceptibility to reproductive dysfunction caused by environmental estrogens"*

**N. A. Granholm,** Path. & Lab. Medicine
*"The impact of apolipoprotein E polymorphisms on CS* $_2$ *toxicity"*

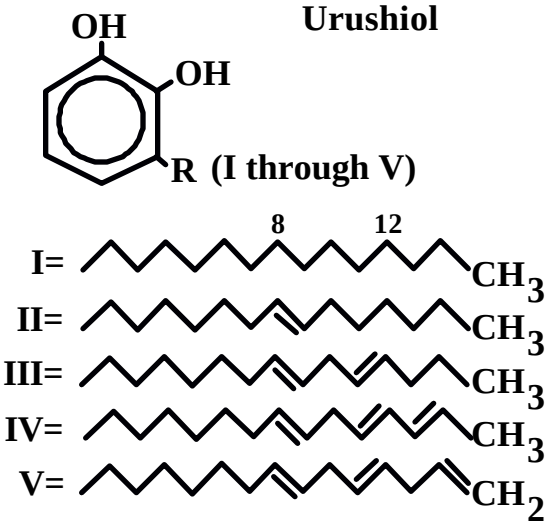
# Observations by a Biologist

## Why does urushiol make some of us itch?

As I sit here at my desk this spring covered with caladryl lotion, I got to thinking about urushiol (see the Figure)--which is the main constituent of the irritant oil from several plants of the genus *Toxicodendron, Anacardiaceae*. These plants, which make some of us but not others itch, include: poison ivy [*Toxicodendron radicans* (L.) Kuntze], poison oak (*T. diversilobum*), and the Asiatic lacquer tree (*T. verniciferum D.C.*). Urushiol is a mixture of several compounds which are derivatives of catechol, having saturated or partially unsaturated $C_{15}$ side chains. Urushiol from *T. verniciferum* is a mixture of sidechains I through IV, and from *T. radicans* is a mixture of I, II, III and V. These plants (leaves, buds) put out very high levels of these chemical irritants in the spring (when they are determined to go through their growing and reproductive stages), as compared with very low amounts in autumn (when they are essentially content with having completed their annual cycle). The roots always contain high amounts; burning of these plants in the autumn, as is well known, may cause formation of a great deal of antigen in the smoke.

In addition, the chemical urushiol can be used as a "desensitizer." For example, American Indians learned that they could become resistant to the skin reactions by chewing on the leaves of these plants. The antitoxin (antibody to the toxic urushiol) is also sometimes used to treat severe cases of poison ivy.

Given the same level of exposure, some humans appear to be relatively resistant while other humans react quite violently to these extremely active allergens. There might also be an age-dependent effect: a person who appears resistant at age 15 suddenly becomes markedly sensitive at age 35. The skin reactions may get out of hand (as it always does in my case), requiring large doses of steroids by mouth to reverse the allergic reaction. Why these particular chemical structures cause this dermatologic response is unclear. Ortho catechols, and their corresponding quinones, are among the most potent of electrophiles (electron-loving molecules that seek out extra electrons, especially on nitrogen atoms, which can lead to covalent bonding). Haptenes are that portion of an antigenic molecule that determines its immunologic specificity. After haptene formation of urushiol with body proteins (exact types unknown), these compounds are processed by Langerhans and/or dendritic cells, which present them to T-cell receptors ($CD4^+$ cells) within the context of MH2II-class molecules. When $CD4^+$ cells are activated with these agents, a subtype produces interleukin-2 (IL-2) and interferon-gamma (IF$\gamma$ ), which then direct the immune response to "delayed-hypersensitivity" T cells that migrate and sensitize the entire skin (especially the flexor surfaces). The effects of urushiol in the human population, then, are another example of differences in toxic or allergic responses due to underlying genetic predisposition.

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