

# Evidence Inside Our Bodies

By Kelly Mills & Michael S. Broder

What do our bodies reveal about the toxicants to which we have been exposed? The chemicals that surround us can leave traces in our bodies and even alter our cells. Researchers at the School are using this information as a tool to identify which environmental exposures are affecting us, and to understand how they will influence our health throughout our lifetimes.

## BIOMARKERS REVEAL EARLY-LIFE VULNERABILITY

Biomarkers are measurable changes in an organism at the cellular or molecular level. One of the primary advantages offered by biomarker research is that by looking at cellular changes, risks can be identified without having to wait for a population to develop a disease. Biomarkers also allow scientists to mea-



sure exactly how certain exposures are metabolized in the body, and at what doses. They help uncover important evidence that some segments of the population may metabolize toxicants differently than others, and that it may depend on the exposure levels.

Associate adjunct professor **Nina Holland**, a director of the Children's Environmental Health Laboratory and the School of Public Health Biorepository, uses biomarkers in her research on children. Exposures can have a greater impact on children because they are still developing, both physiologically and cognitively, and their smaller size also makes them more vulnerable.

"Many things that can happen that affect the health for the rest of children's lives occur early, maybe even before the child is born," says Holland.

In collaboration with other researchers at the School, including the Center for Health Analysis of Mothers and Children of Salinas (CHAMACOS), Holland has examined the impact of a number of exposures on the short and long-term health of children. CHAMACOS, directed by professor of epidemiology **Brenda Eskenazi**, continues to develop findings from a longitudinal study of the impact of pesticides and other toxins on Latino children and mothers in the agricultural area. Holland and other CHAMACOS researchers look at biomarkers linked with pesticide exposure to determine the impact on growth, neurodevelopment, and respiratory health. Two studies published last year found that some newborns may be 26 to 50 times more susceptible to ex-

posure to certain organophosphate pesticides than other newborns, and 65 to 130 times more sensitive than some adults.

## OZONE EXPOSURE LEAVES SIGNS OF DAMAGE

Global warming and the consequent increase in ozone in the atmosphere have led Holland, with **Ira Tager**, professor of epidemiology, and **John Balmes**, professor of environmental health sciences, to examine the effects of chronic exposure to ozone on respiratory health, particularly as an antecedent to chronic lung disease. Balmes had previously conducted studies on the acute effects of

ozone in his lab at UCSF using controlled exposures. The researchers examined UC Berkeley students from Southern California and from the Bay Area to look at genetic markers of susceptibility to ozone, and they also took blood samples to examine markers of oxidative stress.

"We found some interesting differences in the kids who grew up in Los Angeles. versus the kids who grew up here in the Bay Area," says Balmes. "The students who grew up in L.A. had higher levels of oxidative stress, even though they were currently all here."

In a controlled experiment, they then took a subgroup of the students and exposed them to ozone comparable to red-day levels using the EPA's air quality index. The researchers found injury to chromosomes, as well as evidence of oxidative stress with the same biomarker used for the larger group. This validated the use of the biomarker for the population study.

The researchers hope to collaborate in future projects to explore this issue further. Tager and Balmes will both present findings at an upcoming National Academy of Sciences review panel on ozone and mortality. In collaboration with the Holland lab, they are also adding the samples to the biorepository, so that they will be available for continued research.

## METABOLISM MATTERS

Many chemicals that we think of as toxic aren't intrinsically so, but once they are metabolized, they can produce a host of very toxic byproducts. Adjunct professor **Stephen Rappaport** has examined biomarkers of exposure, or levels of chemicals or chemical products in the blood and urine of workers. After documenting exposures, his lab develops specific analytic tests for parent chemicals or metabolites in order to better understand the metabolism of the chemicals. Rappaport has looked at a variety of polycyclic aromatic hydrocarbons from asphalt work, jet fuel, and diesel exhaust.

He has also worked extensively with professor of toxicology **Martyn Smith** in evaluating occupational exposures to benzene. They recently found



that benzene is metabolized much more efficiently at lower exposure levels, to which most of us are routinely exposed from car exhaust and passive cigarette smoke. Since EPA's standards for benzene are based on risk estimates drawn from very highly exposed workers, this finding has important implications.

"Since in the case of benzene, the risk is related to metabolism, EPA's risk assessment assumes the rate of metabolism is the same at high and low exposure levels," says Rappaport. "In our studies, we found that people exposed to low levels of benzene produced about ten times more metabolites per unit of exposure than people who were exposed at high levels. So in fact the risk of leukemia from benzene exposure may be about ten times higher than the current EPA estimates based on the extrapolations." Significantly, the findings from the benzene study led the EPA to reduce the allowable levels of benzene in gasoline in 2006.

### BIOMONITORING IN POLICY DIALOGUES

In recent decades, scientists have used biomonitoring—a technique that looks at evidence of exposures in our bodies—to identify broad environmental health challenges in the population. **Amy Kyle**,

a research scientist and lecturer at the School, has been working with Smith and the UC Berkeley Superfund Center to develop methods for translating biomonitoring research findings for policy and stakeholder audiences. While biomonitoring itself is not new, its use as a method in public health surveillance and policy is new, says Kyle.

"What we've done in the research translation program at Berkeley, which I think is novel, is to start with the questions that people in our audiences want answered, rather than starting solely from whatever research results we're reporting," says Kyle. "We're trying to bring the intellectual and scientific knowledge that we have in the university setting into the grounds where people are actually working on public policy questions, and not necessarily limit it to our last published paper."

On September 29, 2006, Governor Arnold Schwarzenegger signed SB 1379 into law, establishing the California Environmental Contaminant Biomonitoring Program and making California the first state to enact such a program. Kyle and colleagues organized and led a series of workshops to help those involved in developing and implementing the legislation, which provided an opportunity for discussion among academic, government, and

non-government sectors.

Some of the discussion at the workshops touched on the importance of understanding the average experience of the population versus the importance of looking at people who are most affected—a classic public health question, says Kyle. Another important issue that came up concerned people's right to their own information. "This has been a big question in the national debate over biomonitoring," she says, "because the tradition of the medical community, and to a great degree the research community, is not to give people their information unless it has a very specific clinical interpretation. The environmental protection world, however, is more in the 'right-to-know' tradition." Ultimately, the decision for the legislation was that people have a right to know what chemicals are in their bodies. Kyle believes this will have repercussions over time for research. "It's more likely that research results will be provided to people who want to know."

Kyle notes the knowledge resources of the University, which were key to the bill's development, will continue to be important now that the bill has passed. For example, four of the nine members of the panel that will provide the scientific guidance for the bill's implementation come from the School of Public Health.

"What these discussions have done is make more of the parties who are going to be implementing the bill aware of the way that different people see it, and create more alignment in thinking and a deeper understanding of the issues," says Kyle. "For policy makers, having an opportunity to explore, engage, ask questions, think, and talk in an environment that's not political is invaluable." 

**1** Professor Nina Holland discusses the latest results from an experiment with her postdoctoral researcher, Connie Chen, Ph.D. '07, M.P.H. '03.

**2** Doctoral student Karen Huen, M.P.H. '05 (left), and undergraduate Seung Pak retrieve biological specimens from the liquid nitrogen tank.

