of misrepresenting their scientific credentials for financial gain. His principled stand won him acclaim and led to his appointment that year as chair of the Albanian Center for Human Rights.

Named president in July 1997, Meidani had a hard time adjusting to his new life. "I suffered in giving up a research career," he says. "It was the most fruitful time when I left." He now spends his days representing Albania abroad. Although Meidani's domestic authority is limited mostly to acting in a crisis—declaring a state of emergency, dissolving Parliament, and calling new elections—he exerts substantial influence as one of the few intellectuals who stayed to rebuild the country. While thousands of expatriates help prop up their homeland by sending hard currency to relatives in Albania, Meidani felt that the only way to fight for the university system was to remain in Tirana.

However, Meidani realizes that such beliefs make him an exception, and that the chances of luring back many senior scientists on a salary that tops out at about $250 per month are slim. (Meidani, the highest paid civil servant, receives $600 per month.) What's worse, opportunities for young scientists are practically nonexistent. At least during the Hoxha days, he says, there was a surfeit of idealism; "now it's money, money, money." On the other hand, notes geneticist Kostandin Hajkola, whose cash-starved Maize and Rice Institute is on the brink of collapse, "the last decade has convinced us that idealism alone can't hold institutes together."

Threatening to hasten the decline of Albania's crumbling scientific community is the perilous state of the country's primary and secondary schools. "I'm afraid there's little competence in secondary schools, which could lead to big problems," Meidani says. One proposed solution is to split the secondary schools into two branches, one oriented toward natural sciences and the other focused on social sciences, increasing the odds that the best science students get solid training early on. Putting Albania's science on a footing with the rest of Europe "will take many years," he notes, "and the desire to do so has to come from within." The question is whether scientist-statesmen like Rexhep Meidani can lead the way to such a transformation.

–RICHARD STONE

MEETING SOCIETY OF TOXICOLOGY

Toxicologists Hit the West Coast

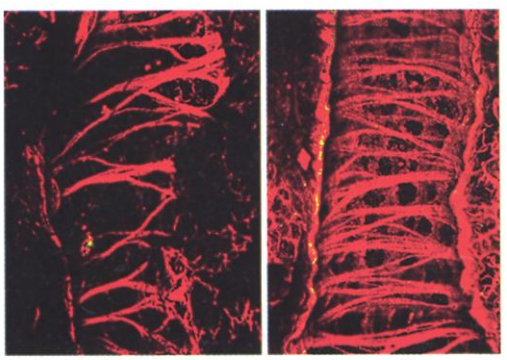
SAN FRANCISCO—A record-breaking 6000 toxicologists gathered downtown here 25 to 29 March for the 40th annual meeting of the Society of Toxicology. Among many topics discussed were how ozone pollution might spur childhood asthma and genetic diversity in enzymes that protect against DNA-damaging agents.

Smog a Culprit in Childhood Asthma?

For children and others with asthma, smog alerts are bad news. When ozone levels jump in cities, visits to hospital emergency rooms due to asthma attacks rise, too. But although ozone clearly worsens asthma, whether early ozone exposure makes children more likely to develop the disease has been controversial. New data suggest that it does. At the toxicology meeting, researchers reported that ozone exposure can restructure the lungs of young rhesus monkeys, apparently making them more vulnerable to asthma, which has risen sharply in the past decade in the United States and other industrialized nations.

Pulmonary toxicologist Charles Plopper of the University of California (UC), Davis, and his colleagues are working with monkeys to resolve questions that can't be answered with smaller lab animals. Rats can be made to develop asthma, but the newborn rodents' lungs develop in just 2 to 3 weeks—far more quickly than a child's (or a monkey's). The researchers showed that they could create asthmatic rhesus monkeys by giving both adults and infants injections and nasal sprays of house dust mites, a well-known allergenic trigger. When later exposed to dust mites, the monkeys showed signs of asthma: They breathed with difficulty, had more air flow–resistant airways, made antibodies to dust mites, and showed immune system changes such as having more cells called eosinophils.

The UC Davis team also exposed groups of six infant monkeys to either ozone alone, ozone and dust mites, or just mites. Over 5 months, the researchers turned the ozone on for 5 days on and off for 9 days to simulate ozone-pollution episodes. They used levels of 0.5 parts per million—three to four times higher than in Los Angeles during smog alerts but about the same as a high-pollution week in Mexico City, Plopper says.



CREDIT: C. G. PLOPPER *ET AL*./UC DAVIS

Straining to inhale. The respirator bronchiole of a young monkey exposed to ozone and dust mites had more smooth muscle bundles than a normal bronchiole (left), making it less effective at allowing air to pass through.

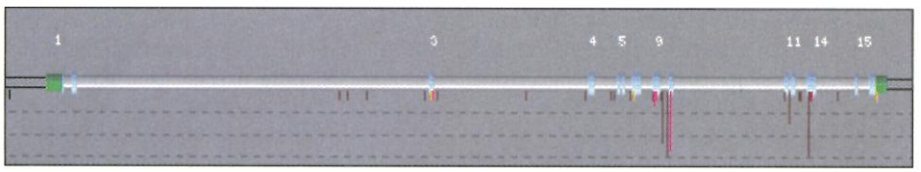
The ozone had dramatic effects, "remodeling" the infants' lungs in a way dust mites alone did not, Plopper reported. After 5 months, the monkeys exposed to ozone alone had developed just two-thirds as many airway branches as control monkeys had, and the dust mite–and-ozone-exposed infants had just half as many as controls. The ozone-treated monkeys also had more sensitive airway nerves, changes in bronchiolar smooth muscle, and depleted stores of glutathione, a chemical that protects cells against oxidative damage. When the researchers triggered asthma attacks in the monkeys, those that had grown up exposed to ozone and dust mites in combination had double the antigen response and airway resistance of controls. "We think the way airways are organized is critical for the way the asthma develops in children," Plopper says.

Because the air in industrialized cities is getting cleaner, experts have sought other explanations for soaring rates of asthma, such as lack of exercise or fewer infections to shape a child's immune system. But, says allergist David Peden of the University of North Carolina, Chapel Hill, the UC Davis monkey experiments "force us to reexamine the potential role that ozone exposure may have" in the induction of asthma.

Diversity in Mending DNA Damage

What are your odds of developing cancer from sunbathing, getting x-rays, smoking, or eating charred meat? One factor may be how well your DNA repair genes are working. These genes code for an army of enzymes that mend

damage to DNA from environmental agents that could otherwise put a cell on the path to cancer. At a symposium here, scientists described initial efforts to find out whether subtle changes in these DNA repair genes can increase a person's cancer risk. If they do, the goal is to identify individuals who are at greater risk so they can take precautions, such as avoiding the sun. So far, researchers have found intriguing hints, but the studies are still very preliminary.



Risk factor? Slight changes in DNA repair genes such as *XRCC1* might, in combination, raise or lower an individual's chance of developing cancer. (SNPs that change protein sequence in pink.)

At least 130 genes are known to code for enzymes that repair DNA, for instance, by fixing such damage as single DNA nucleotide mismatches inflicted by chemical carcinogens, or breaks in DNA strands caused by radiation (*Science*, 16 February, p. 1284). Serious defects in just one of these pathways can be quite dangerous: Xeroderma pigmentosum, caused by various mutations in genes that repair damage caused by ultraviolet rays, can raise a person's risk of skin cancer 1000-fold.

Although such major flaws are very rare, epidemiology studies have found slower overall rates of DNA repair in people with cancer. The explanation, researchers say, may be a constellation of minor mutations in DNA repair enzymes. "There are lots of ways that more subtle variations" could slightly raise a person's risk of cancer, suggests Harvey Mohrenweiser, a biochemist at Lawrence Livermore National Laboratory in California. To get a handle on what mutations exist in the population, Mohrenweiser's team is conducting a systematic survey of common variations in the genome—including tiny, one-base changes called single-nucleotide polymorphisms (SNPs)—in 32 DNA repair genes. Using DNA from an ethnically diverse U.S. population sample, his group is resequencing and comparing the coding regions of these genes in 92 people, enough to find mutations present in at least 1% of the population.

He's finding lots of SNPs. Some are widespread, appearing in half the population, while others are rare. To explore whether these SNPs could affect cancer risk, Mohrenweiser's team has put seven variants of one altered enzyme, Ape1, through cell assays for DNA repair; three were more than 50% slower at mending DNA. At the meeting, Douglas Bell of the National Institute of Environmental Health Sciences (NIEHS) also presented preliminary evidence of an effect in humans: Smokers who had two copies of a certain SNP in the DNA repair gene *XRCC1* had twice as much of a molecular biomarker of DNA damage in their blood as did controls. That suggests that *XRCC1* was not doing its job as well. Bell is part of an NIEHS project studying hundreds of environmental susceptibility genes, from DNA repair genes to many others that metabolize toxicants (*Science*, 24 October 1997, p. 569; see www.genome.utah.edu/genesnps)

Although those studies are interesting, "the real test of whether the SNPs are significant or not," Mohrenweiser says, is whether they are linked to people with disease. In collaboration with Mohrenweiser, molecular epidemiologist Jennifer Hu of Wake Forest University School of Medicine in Winston-Salem, North Carolina, is testing whether people with breast, prostate, or colon cancer have more of certain SNPs than do controls. Some polymorphisms are more prevalent in people with cancer, Hu reported. Two particular SNPs, for example, were 12 times more common in women with breast cancer than in controls and five times more common in people with prostate or colon cancer. But in both her studies and Bell's, other SNPs didn't seem to matter.

Even when they seem to, geneticist Maynard Olson of the University of Washington, Seattle, cautions that associations between disease and SNPs can turn out to be "false positives." He thinks animal studies should be done on potentially important SNPs before researchers expend too much effort on case control studies. Tying SNPs to risks for exposure-related disease "will be a long, slow, and difficult problem," agrees Bell.

–JOCELYN KAISER

CELL BIOLOGY

New Clue to How the Cell Controls Its Proteins

A possible new role for the COP9 signalosome may help explain its function plus that of a recently discovered regulatory process called "neddylation"

Even Leonard Bernstein might have been daunted by the prospect. Somehow, the cell conducts an orchestra with tens of thousands of players—its proteins—ensuring that they come in at the right time and at the right level, harmonize with other players, and stop when their part is finished. Just as it wouldn't do for the French horns to blare their way through an entire concerto, the proteins that drive cell division, say, shouldn't stay active all the time. If they did, the result could be the discordant growth of cancer. Now, two papers published online today by *Science* (www.sciencexpress.org) describe what may be an important new role in this virtuoso performance for a hitherto mysterious eight-protein complex known as the COP9 signalosome (CSN).

Xing-Wang Deng's group at Yale University identified CSN about 7 years ago as a regulator of photomorphogenesis, a developmental response that plants make to light. CSN suppresses the response in the absence of light. Researchers soon learned that the protein complex is widely distributed in animals as well as in plants, but they had few clues to how CSN exerts its effects. The two new papers—one from Deng and his colleagues and the other from Raymond Deshaies's group at the California Institute of Technology (Caltech) in Pasadena—indicate that CSN plays a key regulatory role in a recently discovered process known as "neddylation," at least in some cases turning down a protein by fostering its degradation. CSN may have other biochemical activities as well, however.

One of the major discoveries of the past 15 years was that proteins are regulated not just by addition or removal of small groups such as phosphates, but also by addition of other proteins. The best known of these, ubiquitin, tags proteins for destruction by a large protein complex called the proteasome. In the past few years, cell biologists have found more of these protein tags, including one called Rub1 or NEDD8—hence the term neddylation. Researchers are just beginning to understand what role the addition and removal of NEDD8 plays in protein regulation, but one emerging idea is that NEDD8 indirectly influences protein destruction, possibly through the ubiquitin system. Deng's and Deshaies's teams' work indicates that CSN is a partner in this activity.

The researchers found that CSN removes NEDD8 from an enzyme called SCF,

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