GENETICS

DNA Mutations Linked To Soviet Bomb Tests

CAMBRIDGE, U.K.—For survivors of the atomic bombs dropped on Japan at the end of World War II, the disfiguring burns and radiation-induced illnesses were all too real and agonizing. Now researchers have strong new evidence of a more insidious effect in other people blighted by nuclear weapons: unexplained DNA mutations from atomic tests in Kazakhstan in the early days of the Cold War.

Wasteland. Researchers from the International Atomic Energy Agency visited the Semipalatinsk nuclear facility last year.

On page 1037, researchers led by geneticist Yuri Dubrova of the University of Leicester, United Kingdom, describe a compelling connection between radioactive fallout and elevated mutation rates in families living downwind of the Semipalatinsk nuclear facility, the Soviet equivalent of the Nevada Test Site. The mutation rate of minisatellite DNA—short, repeating sequences that pepper the genome—challenges the conventional view that radiation inflicts its punishment on DNA solely by directly corrupting the nucleic acids. Some other mechanism must be at work amplifying the effect of the chronic low-dose radiation, because the number of mutations is "orders of magnitude too large for such an explanation," says Dudley Goodhead, director of the U.K. Medical Research Council's Radiation and Genome Stability Unit in Harwell. At the same time it's unclear whether such mutations are—or could ever be—linked to health effects.

The findings bolster a controversial 1996 report by Dubrova and a different group of colleagues that linked germ line mutations to fallout from the 1986 Chornobyl explosion. That study, published in *Nature*, described double the usual mutation rate in the children of men living in a region of Belarus heavily contaminated with cesium-137. The study was a revelation, as the Japanese bomb survivors and their families had showed no such mutations. But the study drew skepticism because Dubrova's team could not eliminate some other environmental factors and the researchers used British families as controls, as they were unable to obtain blood from nonirradiated Belarusans.

In the findings reported this week, Dubrova's team collected blood from three generations of 40 different families in the Beskaragai district of Kazakhstan, a desert region hit particularly hard by four atomic surface tests between 1949 and 1956. In each subject they examined eight minisatellite DNA regions that are prone to mutations. The naturally high mutation rate in this DNA allows researchers to detect statistically significant increases in mutation rates in small populations.

When the data came back, "I couldn't believe my eyes," says Dubrova. Compared to control families in a nonirradiated part of Kazakhstan, individuals exposed to fallout had a roughly 80% increase in mutation rate, and their children showed an average rise of 50%. Probing further, Dubrova's group found an apparent dose-related effect in the children: evidence that the radiation, not some other environmental factor, was inducing the mutations. The correlation "was the icing on the cake," says Dubrova. His group is now following up its Chornobyl findings with an improved study under way in Ukraine.

What these germ line mutations mean for health is a mystery, says Bryn Bridges of the Medical Research Council's Cell Mutation Unit in Brighton. "Is this just a biomarker or more?" he asks. Although minisatellites were once dismissed as "junk DNA," evidence is mounting that they affect gene transcription and are linked with disease predisposition. But looking for radiation-induced health effects in Kazakhstan would be fruitless, says Dubrova, because there are not enough people affected by the fallout who are still alive.

The germ line mutations are unlikely to become merely a Cold War footnote. "They present a potential challenge to the current paradigm used for assessment of genetic risk," says Goodhead, who notes that screening for such mutations might offer a new tool for monitoring radiation exposure. Indeed, says William F. Morgan, director of the Radiation Oncology Research Laboratory at the University of Maryland School of Medicine in Baltimore, the findings are relevant to the current debate over how to protect people from chronic low-dose radiation near some of the Department of Energy sites that represent the U.S.'s nuclear legacy.

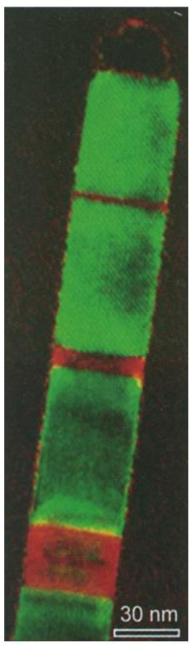
–RICHARD STONE

NANOTECHNOLOGY

Nanowire Fabricators Earn Their Stripes

Electronics makers love a good sandwich. By layering sheets of semiconductors, researchers have learned to control electrons and photons precisely enough to build everything from ultrafast transistors to ultrasmall lasers. Now three groups report that they have carried this sandwichmaking ability down to one dimension by creating tiny wires, each of which resembles a stack of pancakes composed of different semiconductors. The work could open the door to a host of new devices that would boost progress toward long-sought technological goals such as molecular-based computers, quantum computers, and chips that automatically cool themselves.

"These are very nice results," says Paul Alivisatos, a chemist and nanotech expert at the University of California, Berkeley. The ability to layer materials into two-dimensional sheets has been so important for research and applications, Alivisatos says, that "the ability to do it in one dimension has to be very important. There will undoubtedly be a lot of work in the next few years on this."



Nanowhisker. Gold-capped wire of indium arsenide and indium phosphide.

CREDITS: (TOP TO BOTTOM) WACLAW GUDOWSKI; M. T. BJÖRK *ET AL., NANO LETTERS* 2 (2002)

Nanowires have already generated considerable attention. Over the past few years, numerous groups have grown a variety of different semiconducting wires and have even managed to turn them into components of electronic devices, such as transistors. These early nanowires, however, lacked a key ingredient: variety. Although researchers made wires from various materials, each single wire was chemically uniform. If researchers could change that makeup, they would likely gain control over the movement of electrons and photons within individual wires, setting the stage for integrating devices right into the wires themselves—a development that could further shrink electronic circuits.

The three groups hit on the same solution. One team, led by Charles Lieber of Harvard University, reports its results this week in *Nature*. The other two—one led by Peidong Yang of the University of California, Berkeley, and a second led by Lars Samuelson of Lund University in Sweden—report their results in the February issue of *Nano Letters*.

To pull off the feat, all three groups tweaked the method for making single-composition nanowires. In each case they started with tiny gold particles—each just tens of nanometers across—which they placed on a surface inside a vacuum chamber. They then used either lasers or chemical methods to vaporize the semiconductors that were to make up the first segment of the wire. The semiconductor vapor condensed around the gold particle and began to crystallize out between the gold particle and the surface in a tiny cylinder that eventually raised the particle off the surface. To change the composition of the next bit of wire, the researchers simply fed the chamber a different precursor semiconductor, which was deposited between the gold particle and the previous semiconductor. Together the three teams showed that the process works for several of the most important types of semiconductors, including silicon, silicon-germanium, gallium arsenide, gallium phosphide, indium arsenide, and indium phosphide.

The striped wires could prove handy in molecular electronics, the effort to fabricate computer chips by assembling individual molecules into complex circuits. Striped nanowires are likely to make that assembly easier because they can create transistors and other devices within current-carrying wires, says Mark Gukiksen, a Harvard graduate student and first author on the *Nature* paper. Yang adds that striped nanowires should do wonders as well for thermoelectrics, materials that can use electricity to pump heat. Thermoelectrics are layered materials whose efficiency is expected to rise as their size gets smaller, a property Yang's team is now testing. Finally, Samuelson believes that the technique can be used to grow wires composed of numerous electron-trapping quantum dots. Because these dots are the basis for many quantum-computing schemes, striped nanowires could propel research in this area as well. With so many possible applications, Samuelson says, "it might quickly become a very crowded field."

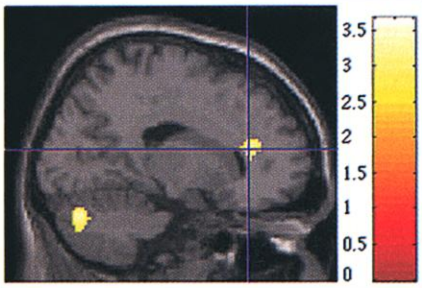
–**ROBERT F. SERVICE**

NEUROSCIENCE

Drugs and Placebos Look Alike in the Brain

Researchers in Sweden and Finland say they have finally shown what scientists have long suspected: that a placebo activates the same brain circuits as painkilling drugs. This first brain imaging study of placebo analgesia, reported online this week by *Science* (www.sciencexpress.org), graphically illustrates the principle that higher brain functions help control how humans perceive pain, say the researchers, headed by neuroscientist Predrag Petrovic of Stockholm's Karolinska Institute.

Psychoneurologist Pierre Rainville of the University of Montreal describes the



Painless. This is your brain on placebos.

finding as "really great news." There is already considerable evidence that placebos harness the same endogenous painkilling circuits as do opioid drugs. But the evidence is all indirect, drawn primarily from studies showing that compounds that block opioid action also block a placebo's analgesic effect. "For at least 5 years we've been waiting for a good functional imaging study of placebo effects," says Rainville.

To provide such images, Petrovic and his colleagues used positron emission tomography to scan the brains of nine men while a 48°C metal surface was pressed to the backs of their hands. The team compared brain responses after subjects were given intravenous injections—by a doctor in a white coat—of either an opioid painkiller or a placebo.

Both the genuine analgesic and the placebo led to increased blood flow in areas of the brain known to be rich in opioid receptors: the brainstem and the rostral anterior cingulate cortex (ACC), which exchanges information with a network of brain regions, including the orbitofrontal cortex, a relatively sophisticated part of the brain known to process emotions. Furthermore, those people who responded most to the placebo—according to their ratings on a scale of 0 to 100 of how much it reduced their pain—also showed more rostral ACC activation from the drug. This,

ScienceScope

Exodus, Chapter 7 Marvin Cassman, director of the National Institute of General Medical Sciences (NIGMS) in Bethesda, Maryland, announced this week that he is heading to California in May to head up a new state-funded quantitative biology institute. Cassman is the seventh top administrator to leave the National Institutes of Health (NIH) in the past 2 years, including former NIH director Harold Varmus. One vacancy has been filled: Andrew C. von Eschenbach, formerly of the M. D. Anderson Cancer Center in Houston, took the oath as director of the National Cancer Institute on 4 February.

At NIGMS, Cassman says, he favored a "complex systems" approach that applied engineering, computational science, physics, and other quantitative disciplines to basic biology. Now he intends to implement this strategy as head of "QB3," a quantitative biology consortium that includes University of California (UC) schools in San Francisco, Berkeley, and Santa Cruz. Lab construction will begin soon at UCSF's Mission Bay campus; the budget has not been set.

Delayed Again The long-awaited operation of a nuclear research reactor in Garching, outside Munich, has again been delayed, this time because of safety concerns in the wake of the 11 September attacks. The federal environment ministry says that FRM-II, which is also a neutron source, needs to develop rules for dealing with accidents and a better plan for the disposal of its spent fuel, highly enriched uranium, to prevent its use in a bomb. The delay comes amid the finalization of plans by Germany's red-green government to phase out nuclear energy production.

FRM-II was completed in August 2000, and Germany's radiation protection agency gave it a thumbs-up in December for experimental operation. The Bavarian government, which has to gain the approval of federal authorities, said it would submit a revised application by May, and federal officials have promised a speedy review.

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