

FUNCTIONAL GENOMICS

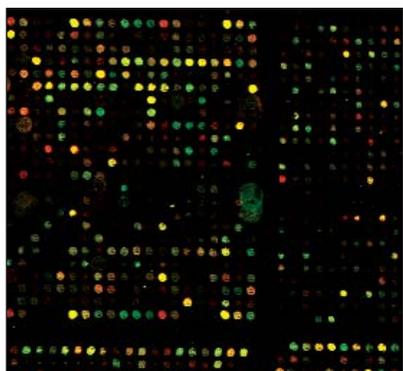
How to Make Sense of Sequence

As the final bases are mapped onto the human genome in the next month, a familiar refrain is growing louder: What comes next? At an unusual workshop last week, representatives of the National Human Genome Research Institute (NHGRI) sought to answer that question for potential grantees gathered at the institute's home base in Bethesda, Maryland.

In late February, NHGRI invited applications for its newest genome project: the Encyclopedia of DNA Elements, or ENCODE.

Now that the sequence's 3 billion letters have been spelled out, ENCODE's goal is to locate and identify all of the genome's components. These include DNA that codes for proteins and DNA that doesn't, as well as elements that mediate gene expression.

Because ENCODE is a novel venture for NHGRI, and because its details are still malleable, the institute took the unusual step of inviting interested applicants to ask questions and offer feedback to help shape the project.



In focus. A new initiative aims to identify genes (as depicted in this array) and other features of the human genome.

As the meeting opened, the sense that NHGRI was undertaking a daunting mission pervaded the room. "Everyone's looking really glazed at the moment, like 'Are we really going to do this?'" said institute director Francis Collins, surveying an audience of about 70.

NHGRI plans to commit \$36 million to ENCODE over the next 3 years. The project will initially focus on just 1% of the genome. Most of the money will be parceled out among five to 15 groups, each of which

may use computer-based analyses and lab experiments to identify all the functional elements in that same 1%. When finished, the teams will compare notes to determine which technologies proved the most efficient and accurate. NHGRI envisions then scaling up the project to annotate the other 99% of the genome.

Despite uncertainty over how grants will be awarded and how

ENCODE will proceed, participants say the venture is the first opportunity to dig deep

into the human genome. "In an understated way, I think this is an extraordinarily significant event," said John Stamatoyannopoulos of the Dana-Farber Cancer Institute in Boston. "They could spend \$1 billion on this; [it's] much bigger than the genome in terms of scope."

ENCODE's organizers hope that industry will participate in the venture. A minority of the funding—\$6 million—is intended to spur academics and private companies to develop technologies that can identify and verify the genome's components. ENCODE may also include international members; Tim Hubbard, head of genome analysis at the Wellcome Trust Sanger Institute in Hinxton, U.K., said that Sanger will "definitely participate."

Coordinating ENCODE will be a challenge for NHGRI. For one, the institute will have to settle on quality standards soon. They're still up in the air for this type of data, and the project requires that findings be quickly released into the public domain. But the most difficult job for NHGRI and the eventual grantees, who will be announced in September, lies in making sense of the mass of interpretations of the DNA sequence. "We're looking for things we've never found before," says Eric Green, chief of the genome technology branch at NHGRI.

—JENNIFER COUZIN

ARCTIC ECOLOGY

For Precarious Populations, Pollutants Present New Perils

The biggest ever study of Arctic pollutants paints a picture of an ecosystem under siege—with potentially grave consequences for denizens of Earth's northernmost reaches. For the first time, long-standing villains such as pesticides, polychlorinated biphenyls (PCBs), and mercury have been linked to weakened immune systems and developmental deficits in Inuit children. "We believe we're beginning to see early human effects," says oceanographer David Stone, northern research director for the Canadian government. And efforts to clamp down on the release of these pollutants may not be enough: The study has identified a slew of other compounds that could pose a long-term threat to humans and wildlife.

The findings, presented at a symposium on the second *Canadian Arctic Contaminants Assessment Report (CACAR II)* last week in Ottawa, are the latest fruits of Canada's 10-year, \$38 million Northern Contaminants Program (NCP). In 1997, *CACAR I* found that a bevy of pollutants—including the pesticides DDT and chlordane, as well as

PCBs and other industrial chemicals—are building up in the Arctic. Because these compounds degrade less readily in frigid conditions, levels in the Arctic are among the highest in the world. Thus, for example, the Canadian government estimates that three-fourths of Inuit women have blood PCB levels that are up to five times higher than those deemed safe. Experts fear they are seeing only the tip of the iceberg. "We do not know what the effects of long-term exposure will be on the human population and on the ecosystem," says Peter Johnson, chair of the Canadian Polar Commission.

CACAR II, perhaps the last installment of the acclaimed NCP, ratchets up the level of concern. Particularly disturbing are early findings from a study in Nunavik, Quebec, funded by NCP and the U.S. National Institutes of Health. Toxicologist Éric Dewailly of the University of Quebec Medical Center (CHUQ) tracked infections in 199 infants from birth to 12 months. His team found that the risks of two infections—upper respiratory and gastrointestinal—were signifi-

cantly elevated in babies whose mothers had the highest blood levels of DDE, a pesticide.

Another study led by CHUQ developmental psychologist Gina Muckle found subtle deficits in memory—the ability to recognize objects—in infants whose mothers had higher levels of PCBs, and heavy metals such as lead and mercury appeared to lengthen the amount of time the babies needed to remember information and to reduce their ability to remember while distracted. "Older studies looked at one contaminant at a time," says toxicologist Deborah Rice of the U.S. Environmental Protection Agency. By examining several contaminants as well as dietary factors, she says, Muckle's approach "represents a real step forward." But although the findings are intriguing, Stone cautions that "much more research is required."

That could be hard, as scientists are aiming at a moving target. Although *CACAR II* notes that the levels of certain pollutants, including DDT and chlordane, are waning in parts of the Arctic, previously unidentified compounds are on the rise. The study has re-

CREDIT: NIH

NIH Sets Data Sharing Rules

Starting 1 October, researchers who get big grants from the National Institutes of Health (NIH) will have to submit a plan outlining how they will share their data. The new policy, finalized last month, is "a first incremental step" toward coverage of all grantees, says Belinda Seto, NIH's acting deputy director of extramural research.

After receiving several hundred comments on a draft policy released last year (*Science*, 8 March 2002, p. 1811), NIH decided to initially limit the new requirement to grants with at least \$500,000 a year in direct costs. Data are to be shared once they are accepted for publication. Grantees can get advice on protecting patient privacy and intellectual property at grants.nih.gov/grants/policy/data_sharing/index.htm.

Although generally satisfied with the revised policy, the Association of American Medical Colleges (AAMC) would have preferred to have disciplines develop their own standards first. Proteomics researchers haven't ironed out how to share array data, for example, notes AAMC Senior Vice President David Korn. "They've pulled the trigger on this," Korn says. "I just wish they had gone through a deliberative process." —JOCELYN KAISER

EPA Unveils Risk Guidelines

In a bid to align regulations with current science, the U.S. Environmental Protection Agency (EPA) has unveiled new guidelines for assessing pollutant cancer risks, including its first draft directive aimed at children.

The new guidelines, released 3 March, attempt to make risk assessments more straightforward. They emphasize a "weight of evidence" approach, encouraging regulators to consider risk factors such as the molecular mode of action and the likelihood of exposure. When crucial data are missing, the guidelines spell out alternatives, such as extrapolating from animal studies. And they urge regulators to pay attention to populations that might be more susceptible to carcinogens, such as people with a genetic predisposition to cancer.

The draft guidelines for children note that youngsters can face greater cancer risks than adults due to an array of factors, including diet and behavior. The draft is a good start, says the Natural Resources Defense Council, an advocacy group. But it would like to see the guidelines expanded to cover all carcinogens, such as hormone-mimicking chemicals, and not just ones that damage DNA. EPA will be taking comments on both sets of guidelines until 1 May. —ERIK STOKSTAD

vealed "a huge sweep of new contaminants" washing into Arctic ecosystems, says Lars Otto Reiersen, Oslo-based director of the Arctic Monitoring and Assessment Program. Of greatest concern, perhaps, is a rapid rise in polybrominated diphenyl ethers (PBDEs), a group of chemicals used as fire retardants in electronics that have been linked to thyroid defects in lab rats. Between 1997 and 2002, PBDE levels doubled in Arctic char, says chemist Derek Muir of Environment Canada, and PBDEs are starting to accumulate in mammals, from whales to humans. Although PBDEs were banned this year in Europe, Muir notes, their use in North America remains unchecked.

Another type of flame retardant showing up in the Arctic is perfluorinated acids. These chemicals, used in firefighting foams, herbicides, and paints, are classified as cancer promoters and don't appear to degrade at all in the environment. *CACAR II* flags the rapid buildup of one in particular, perfluorooctane sulfonate, in polar bears. "It has stealthily achieved high levels," says Muir, who adds that concentrations are approaching levels known to cause weight loss in monkeys; that could prove to be a mortal blow for some individuals in a species whose bulk allows it to survive on the ice.

Despite the emergence of new threats, it appears unlikely that Canada will extend NCP, which is set to expire at the end of this month. Stone says that officials have assured him that they are "committed to finding the funds" to continue human health studies in the Arctic, but most other studies seem destined for the chopping block. An "NCP lite" was not palat-



Hardscrabble life. Canada's Inuit are vulnerable to pollutants building up in the Arctic.

able to some high-level delegates at the Ottawa conference. "The government is walking away from its key environmental and health research program in northern Canada," asserts Terry Fenge, research director for the Inuit Circumpolar Conference, which promotes indigenous interests. Loss of the NCP, adds Reiersen, "will be a real pity." The pollutants, on the other hand, are not going away any time soon.

—PAUL WEBSTER

Paul Webster is a writer in Moscow.

ENVIRONMENTAL PROTECTION

Pentagon Wants Out From 'Green' Rules

Even as they prepare for a war in Iraq, Pentagon strategists are also drawing up political battle plans on the home front. The Department of Defense this week asked Congress to exempt the nation's armed services from a host of environmental requirements said to be a growing hindrance to combat readiness. But the push is meeting resistance not just from scientists but also from some Bush Administration officials.

"There are problems, but the evidence doesn't justify the kinds of changes they are proposing," says Brock Evans of the Washington, D.C.-based Endangered Species Coalition, an advocacy group. Even Environmental Protection Agency chief Christine Todd Whitman has raised doubts about the move, telling a Senate panel last month that she wasn't aware of any environmental laws that target military training.

All sides agree that the Pentagon—the third largest landowner in the United States—

controls some of the nation's most ecologically sensitive real estate. Its 10 million hectares of military bases are home to an estimated 300 endangered species, ranging from fragile flowers and fairy shrimp to showy woodpeckers and heavily armored desert tortoises. The bases also include some of the last large tracts of undeveloped land in heavily populated areas, such as southern California.

But as urban sprawl has hemmed in some bases, neighbors have begun to complain about everything from noise to pollution. And species displaced by development have taken up residence on Pentagon lands, requiring the military to take evasive maneuvers. Navy forces, for instance, schedule some beach exercises around the time birds nest.

Military planners say the regulations have become too burdensome. So last week they unveiled a 15-page package of changes to five major environmental laws. An amendment to the Endangered Species Act would bar fed- ▶