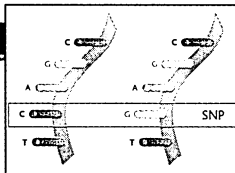


Turning back the Galápagos' ecological clock



The trouble with SNPs



Olympiad of the mind



GLOBAL WARMING

World Starts Taming The Greenhouse

To the surprise of many, representatives of 178 countries agreed early Monday morning on how to begin fighting global warming. Seventeen hundred diplomats established a complex method of accounting for greenhouse gas emissions and uptakes, which will allow countries to receive due credit for their efforts. The agreement allows countries considerable flexibility in meeting their goals for reducing greenhouse emissions, an aspect that derailed negotiations in The Hague last fall. Enough countries are expected to ratify the agreement to put the Kyoto Protocol into effect next year, without the United States.

The new agreement is seen by protocol supporters as the best start that could be expected under the circumstances. "Most people in the world do believe this was the only game in town," says Eileen Claussen, president of the Pew Center on Global Climate Change in Arlington, Virginia, an organization dedicated to reducing greenhouse emissions. After President George W. Bush rejected the Kyoto Protocol this spring as "fatally flawed," "countries had to rethink whether they wanted to do this," Claussen says. "They decided they did, and they made the needed compromises." The compromises are unlikely to entice the United States to ratify the protocol, but they do seem to promise broad enough support among other industrialized countries that the protocol will come into force.

The compromises encompass a range of policy issues. Flexibility will come from mechanisms such as emissions trading, the exchange of emission credits between countries able to cut emissions beyond their required amount and countries willing to purchase those credits; the Clean Development Mechanism, in which industrialized nations



Accord. Conference chair Jan Pronk and Japan's environment minister Yoriko Kawaguchi found common ground.

can receive credit for emission reductions achieved through projects such as hydroelectric dams in developing countries; and land use, the managing of soils and forests that can soak up carbon dioxide. The delegates failed to reach a compromise in one key area: compliance. Japan in particular was leery of harsh penalties for countries that don't meet their emission-reduction targets, so negotiators decided that enforcement will be determined once the protocol is in effect. That will be when the requisite 55 countries accounting for 55% of the industrialized countries' 1990 emissions have signed on.

Given the flexibility and the possibility of a light hand with enforcement, the environmental group Greenpeace has dubbed the current version of the protocol "Kyoto Lite," but a lightening up is not all bad, say some observers. "They've left the thing sufficiently loose that everyone's willing to join hands," says journalist-in-residence John Anderson of Resources for the Future, a Washington, D.C., economics think tank. "That's probably useful. Nobody knows how those mechanisms are going to work. Everyone needs to get real-world experience with what the costs are going to be before you can press hard. It's not a howling success, but it's not a disaster either." The protocol could be in effect, without the United States, by the 10th anniversary of the Rio Earth Summit next July.

—RICHARD A. KERR

GENOME RESEARCH

Map of the Human Genome 3.0

Like a traveler picking up a new language, geneticists are starting to recognize phrases and sentences as they read the babble of bases in the human genome. These grammatical constructs are discrete blocks of DNA that differ from one person to the

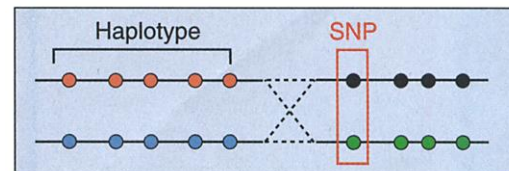
* Developing a Haplotype Map of the Human Genome for Finding Genes Related to Health and Disease, 18–19 July, sponsored by the National Institutes of Health.

next. And they may be common enough and account for enough of the genome, researchers concluded at a conference* held here last week, that it's time to create a new map of the genome, one that describes its blocky structure.

The new project is called a haplotype map—for desperate want of a better name. (In the hopes of finding a more palatable one, National Human Genome Research Institute director Francis Collins has informally launched a name-the-map contest.) Haplotypes are simply long stretches of DNA—including perhaps as many as 100,000 bases—at a given location on a chromosome. To their surprise, genome researchers have found that many such blocks come in just a few different versions, a discovery that should simplify the search for associations between DNA variations and complex diseases such as cancer, diabetes, and mental illness.

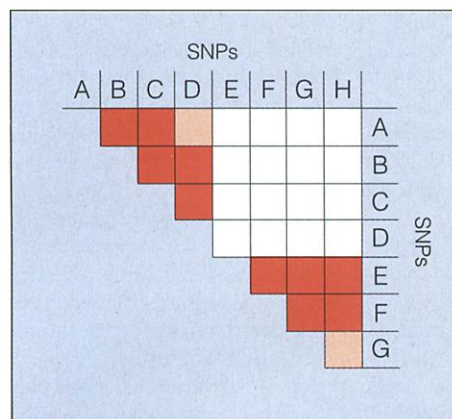
A haplotype map will thus, its creators hope, be a tool for pinning down the genes that contribute to the development of those conditions. "The reason for [the map's] existence," said Collins, "shall be to try to understand the reasons for disease and find therapeutics" to treat them.

The mapmakers emphasized this goal because a haplotype map could raise ethical concerns. More so than previous maps of the human genome, it might include markers that indicate someone's race and ethnicity. As a result, about half the meeting was devoted to figuring out the best scientific approach to building a haplotype map, whereas the rest was spent exploring social issues. Pilar Ossorio of the University of Wisconsin Law School in Madison pointed out one of the dangers. "As cognitive psychologists have shown," she said, "people take in information in a way that reaffirms their existing stereotypes," and creating a genome map that contains race-specific elements might imply a scientific seal of approval on race-based social perceptions.



Mix and match. Long stretches of DNA with a distinctive pattern of SNPs are called haplotypes. Successive haplotypes can combine in many different patterns.

ScienceScope



Identifying blocks. Hypothetical SNPs A through D are correlated (red) and probably constitute a haplotype. SNPs E through G are also fellow travelers.

Only in the past year or so have genome researchers realized that a haplotype map might be feasible. Until now, they have focused mainly on identifying DNA variations called single-nucleotide polymorphisms (SNPs)—sites along the genome at which individuals differ by just one base—to use in tracking disease genes. And although they've had some success recently in identifying genes associated with diabetes and the gastrointestinal ailment Crohn's disease, it's been an arduous, expensive process (see p. 593).

Because there's roughly one SNP for every 1000 bases of DNA, there might be a huge number of SNP patterns over a given stretch of sequence. If, for example, a 50,000-base sequence contains 50 SNPs, those SNPs could, in theory, come in 2^{50} different variations. Computer simulations suggested that haplotype blocks—DNA stretches containing the same SNP pattern—would stretch only 3000 to 8000 bases—too short to make a haplotype map worth the trouble for tracking disease genes. But the reality turned out to be much more promising.

As several teams reported at the meeting, haplotype blocks are at least 10 times longer than predicted, and there are a relatively small number at each chromosomal position. For some sequences of 50,000 bases, for example, just four or five patterns of SNPs—that is, four or five different haplotypes—might account for 80% or 90% of the population. "It didn't have to be this way," said Eric Lander of the Whitehead Institute for Biomedical Research/MIT Center for Genome Research in Cambridge, Massachusetts. But because it is, instead of trying to correlate each of the 50 SNPs with disease, researchers can restrict their studies to SNPs that differentiate the few common patterns. This should ease their work by cutting down on the amount of DNA they have to scan to identify disease genes.

No one is sure yet why the genome is so blocky, but geneticists mention two candi-

date explanations. During the meiotic divisions that give rise to sperm and eggs, the two copies of each chromosome sometimes swap stretches of DNA, or recombine. If, for some unknown molecular reason, some parts of the chromosome are less likely to recombine than others, some stretches of DNA will be conserved as blocks while others change rapidly across generations.

Population bottlenecks apparently contribute as well. As Kenneth Kidd of Yale University and others have found, there is a greater diversity of haplotypes in people in Africa, where humans first arose, than in other populations. In addition, descendants of people who settled in Asia carry a somewhat different set of haplotypes from those who settled Europe.

And that's what raises the ethical issues discussed at the meeting. Researchers are still figuring out how to construct the haplotype map—what pilot studies to run, for instance, and how to standardize the definition of a haplotype. ("This notion of a block is a little hazy," said Leonid Kruglyak of the Fred Hutchinson Cancer Research Center in Seattle to much laughter.) But their most pressing problem may be whether to include ethnic or geographic identifiers on DNA samples. Such identifiers were stripped from the samples used to create the human genome sequence and SNP maps. But as Collins points out, if certain haplotypes are more common in some ethnic groups than others, haplotype mappers run the risk of missing distinctive patterns of DNA that might predict disease susceptibility in some populations but not others.

Summing up the meeting, Collins said that there was a "consensus" that the project "would have considerable medical value" and is worth pursuing. He solicited volunteers for two working groups that in the upcoming weeks will do the heavy lifting—a scientific steering committee to nail down working definitions of haplotypes and set priorities for pilot studies, and a second group to keep an eye on social and ethical issues.

—LAURA HELMUTH

GENOME RESEARCH

DNA Sequencers To Go Bananas?

Among scientists, the banana gets little respect. It's one of the most popular fruits on Earth and the developing world's fourth most important food crop, yet only a handful of labs are working on it. Now, a group of researchers is hoping to put the banana (*Musa*) on the scientific map. On 19 July, an international consortium announced that it hopes to sequence the entire banana genome, perhaps as early as 2006. The announcement of the multimillion-dollar effort

Reaching Out The recent India-Pakistan summit may have ended in a diplomatic stalemate, but it did produce new joint research and training opportunities that the Indian government hopes will provide a back channel for improving relations between the two nuclear neighbors. Prime Minister Atal Bihari Vajpayee earlier this month unveiled a plan to award 20 scholarships to Pakistani students to attend Indian technical institutions and invited Pakistani academics to visit "as guests of the government." The focus would be on education, health, environment, and gender equity.

"There is an enormous amount of misinformation about India in Pakistan," says Pavagada Venkata Indresan, former president of the Indian National Academy of Engineering. "But once young minds can be trained at India's top technical institutions, a more positive message would certainly go out." Pakistan reacted cautiously, with a government spokesperson calling the idea "peripheral" to diplomatic efforts.

Bioprospecting Under the Microscope The National Park Service is starting a court-ordered environmental study of revenue-sharing agreements with firms that make profitable discoveries in national parks. Officials plan to kick off the bioprospecting assessment next month after getting public comment on the issues the study should address.

After Yellowstone National Park signed a 1997 profit-sharing deal with a San Diego biotech, bioprospecting opponents sued, charging that commercial activities in the parks violated federal law (*Science*, 13 March 1998, p. 1624). A federal judge suspended the deal earlier this year, ruling that Yellowstone could make such agreements, but that it first had to study their environmental impacts. In a 25 June *Federal Register* notice, the service said it would study bioprospecting impacts at all 384 of its parks in order to formulate consistent policy.

Critics want the study to take a careful look. By allowing exploitation, "these types of agreements fundamentally change the spirit of what the parks are about," says Joseph Mendelson III of the International Center for Technology Assessment, a Washington-based group that participated in the earlier legal challenge. Comments on the study's scope are due 10 August, with a draft expected in the fall.

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