GENOME MAPPING

Closing in on Human and Mouse Maps

The pace of mapping the terra incognita of mammalian genomes continues to accelerate. In a special June issue of *Nature Genetics*, two groups report that they are rapidly nearing their goal of completing rough maps of the human and mouse genomes that chart the relative positions of genetic landmarks along the chromosomes. Researchers use these markers, highly distinctive repeat DNA sequences, as first steps towards pinning down the location of genes, primarily those involved in inherited diseases.

Jean Weissenbach's group at Généthon in Paris report that they have isolated and mapped more than 2000 such markers along the human genome, up from only 814 at the end of 1992. (At a meeting early in May at Cold Spring Harbor in New York, the Généthon group upped the figure to 3300 markers.) And at the Whitehead Institute of the Massachusetts Institute of Technology (MIT), Eric Lander's group reports that it has now tallied over 4000 markers along the mouse genome, up from 1518 in October of last year. Since mice serve as experimental models for many human diseases, researchers expect the mouse map will prove vital in tracking down disease genes that are conserved in both species.

"It's going at a terrific speed, much faster than anybody anticipated a few years ago," says Bert Vogelstein, a specialist in tumor genetics at Johns Hopkins University in Baltimore. The main reason for the rapid progress, say Gabor Gyapay, director of the Généthon project, and Joyce Miller, a map-project director at MIT, is that both groups have found ways to automate many of the repetitive tasks involved in mapmaking. "Pipetting robots and automated computing and data-handling do a lot of the work for us. This allows technicians and lab aides to spend their time setting up experiments and analyzing results," Miller says. At this rate, the chromosome cartographers should reach their goals of 5000 markers for the human map and 6000 for the mouse map by the end of this year.

The mapmaking begins when geneticists chop up the DNA of a chromosome into tiny fragments and use genetic probes and other techniques to find the markers. They then determine the order and spacing of the markers along each chromosome. This is done by tracing marker inheritance patterns in DNA through successive generations of families. Two markers that are close together on a chromosome are likely to be passed on together to later generations; those further apart are more likely to be separated. By tracking the tendency of any two markers to be inherited together, scientists can derive the markers' relationships to each other.

Similarly, by seeing which marker tends to be inherited together with a disease in an affected family, researchers can close in on an undiscovered disease gene. The growing number of markers should make future gene searches easier. "Having genetic maps with a high density of markers is really a key to finding complex genetic diseases," says Leroy Hood, chair of the department of molecular biotechnology at the University of Washington School of Medicine. These are, he says, truly landmark studies.

–Robert F. Service

WILDLIFE CONSERVATION

Mystery Ailment Strikes Serengeti Lions

A mysterious neurological disorder is sweeping through the lions of Tanzania's Serengeti National Park and taking a deadly toll on the kingly beasts. Since 3 February, when a team of researchers recorded the first death, at least 40 of the park's 3000 lions have died, and at least 15 others now appear to be ill. Lab analyses of blood and tissue samples from the animals that have died offer some tantalizing hints, but so far scientists have been unable to identify the cause of the illness.

ROGER CARAS/PHOTO RESEARCHERS

Pride takes a fall. Lions like this one abound in Tanzania's Serengeti, but a group of them has been struck by a mystery ailment.

"It is a horrifying disease," says Craig Packer, a behavioral ecologist at the University of Minnesota who has been co-directing a study of the Serengeti's lions for more than 15 years. "The lions look as if they are suffering gran mal seizures. They are unable to stand and lose control of their limbs. They thrash about, have convulsions, and are completely unaware of their surroundings." Lions that are severely affected almost inevitably die, Packer notes, although others may experience milder cases. "Some of them just have the twitches and will involuntarily flail and jerk their limbs when they are resting," he says.

Yet when active, these less severely affected animals are still capable of hunting, suggesting to Packer that they may be recovering. "We're hoping that they are the survivors; that they have some immunity to whatever it is." A darker possibility, however, is that such lions are only in the first stages of the illness, and that the worst is still to come.

Packer is as yet unsure how devastating the current epidemic will prove to be for the overall population of the park's lions. His own study population of 250 lions has dropped by 20%. Yet because the Serengeti's lion population recently hit an all-time high, the epidemic so far has simply returned the population to its previous level. "The disease is not a disaster—as long as it stops," says Packer.

Whether it stops depends partly on the cause of the disease—which has thus far eluded discovery. "All that we can say for certain is that the disorder appears to be caused by an infectious agent," Packer says, since it affected lions across a 1000-kilometer area within 2 weeks. "But we don't know if it is passed from lion to lion, or if it is spread by ticks or some other vector." Packer believes that the disease is not new, since he and his team observed "twitching lions" as long ago as the late 1970s. At that time, however, the scientists didn't note any lethal consequences, and researchers would like to find out why the disease, if it is an old one, has suddenly become dangerous.

Melody Roelke, the head veterinarian of Tanzania's National Parks Service, recently led a team that collected blood and tissue samples from both healthy and dead lions. Preliminary analyses of the tissue have ruled out rabies and feline leukemia virus, but pathologists believe they have spotted telltale signs of another lethal pathogen: canine distemper virus. "That's our top suspicion right now," says Linda Munson, a veterinary pathologist at the University of Tennessee. Though named for dogs, the virus is "known to infect many carnivores, including lions, leopards, and tigers," says Munson. Careful examination of tissue samples during the next few weeks, she continues, should reveal whether distemper is indeed the culprit. And that, in turn, should indicate whether lions will remain the kings of the Serengeti. "What worries me the most," says Packer, is that the illness "will forever remain a mystery."

–Virginia Morell