Meanwhile, computer scientists are working on the smart browsers and souped-up search engines that will make the fullest use of XML. Such "intelligent agents" would be able to answer queries current search engines can't touch: "Is there a university in a state bordering Virginia with an ROTC program, Japanese classes, and a Computational Biology major?" The answer (University of Maryland) happens to be where one of the first such search engines resides. The experimental browser, developed by computer scientist

James Hendler, can make the necessary connections because it works with an advanced markup language in which the XML tags indicate not only meanings but relationships between entities (universities are located in states, and majors are found at universities).

Even XML aficionados don't expect to see these kinds of tags popping up on every Web site. For displaying ordinary text documents, HTML is likely to remain the standard, and XML-capable browsers will still be able to read pages written in HTML. But they believe

that for specialized Web applications—in science, for example—XML will quickly make converts. "People predicted the Web would fail because no one would want to learn HTML," says Tim Finin, a computer scientist at the University of Maryland, Baltimore County. The pessimists were wrong, he notes, and "the same thing will happen with XML."

–Dana Mackenzie

Dana Mackenzie is a science and math writer in Santa Cruz, California.

GENOMICS RESEARCH

Year of the Cat—in More Ways Than One

Far from the limelight shining on the human and mouse genome projects, researchers have also been laboring on the genomes of a half-dozen other mammals. One of these efforts, the Feline Genome Project, is about to hit a major milestone. Researchers at the National Cancer Institute's (NCI's) Laboratory of Genomic Diversity in Frederick, Maryland, expect to complete a genetic map this year—appropriately, the Chinese Year of the Cat.

The immediate goal of the NCI effort, which will cost about $3 million, sounds modest: a map with about 950 markers spread across the roughly 3 billion bases in the cat genome. That's far less detailed than the human and mouse maps, each with more than 20,000 markers on genomes that also contain about 3 billion bases. And there are no plans to undertake the massive job of determining the complete cat genome sequence. But the cat map could nevertheless turn out to be a useful guide to human genetic diseases.

Cats and humans share almost 60 inherited diseases, including polycystic kidney disease, diabetes, heart muscle disorders, and certain common immune cell cancers. Once the cat map is in hand, the NCI group plans to use it to track down the cat disease genes and then mine the comparable regions of the human and mouse genomes for candidates for human disease genes.

If the same genes turn out to be at fault in both species, then cats would also provide good models for the human diseases. Animals like cats and dogs offer a "tremendous, rich resource of genetic diseases that can't be studied in mice," says Don Patterson, director of the Center for Comparative Medical Genetics at the University of Pennsylvania School of Veterinary Medicine.

Stephen O'Brien, chief of the NCI team, began mapping the cat genome 20 years ago because he thought that it might help him find cat genes that regulate the effects of a cancer-causing feline virus. When his first map attempt (*Science*, 16 April 1982, p. 257) revealed that gene arrangements on human and cat chromosomes are very similar—much

more so than those on human and mouse chromosomes—O'Brien quickly grasped the potential for "comparative mapping" between humans and cats. He has been working to complete the feline map ever since.

For the bulk of the mapping effort, the O'Brien group is using standard crossbreeding experiments—an effort aided by the availability of Asian leopard cats that the NCI team borrowed from the National Zoo in Washington, D.C., and bred with domestic cats to produce a handsome cross known as the Bengal. The leopard cats "were in the right place at the right time," notes NCI geneticist Leslie Lyons.

By following the inheritance pattern of cat genes in blood samples taken from crosses through three generations, the researchers can establish their relative positions on the map, because genes that are located near one another on chromosomes tend to be inherited together. Breeding domestic cats with Asian leopard cats helped, because the genes of the two species are sufficiently different that tracking cat genes to the third-generation crosses can be readily accomplished.

To fill some holes and add detail, the NCI team also applied a newer technique—radiation hybrid mapping—used for human genome mapping. NCI geneticist Bill Murphy irradiated cat cells, breaking apart their chromosomes, and then fused the cells with hamster cells. The cat chromosome fragments integrate into the hamster chromosomes in these hybrid cells, which are then tested for the presence of cat DNA markers. The nearer two markers are on a cat chromosome, the greater the likelihood that they will end up on the same fragment—and in the same cell.

Together, the crossbreeding and radiation

Cat tracks. Tracing genes in hybrids, such as this Asian leopard–domestic cat cross, is helping to produce a cat genome map.

mapping techniques will enable the NCI team to create a map showing the relative positions of about 350 genes. But although genes are needed to match to the corresponding genes in other species, they don't vary enough from one individual to another to be used as markers for tracking down unknown genes. So again using blood samples from the crossbred cats, geneticist Marilyn Menotti-Raymond is mapping cat microsatellite markers, short segments of repeating DNA that are variable enough for tracking down genes for diseases and other traits. When it's ready, the cat map will include about 600 microsatellite markers.

The next step will be to use the map to pin down genes that cause cat—and presumably also human—diseases. Lyons and Menotti-Raymond have already collected cat families with cancer, retinal atrophy, and polycystic kidney disease that they will use to track down human gene counterparts. Patterson expects the cat to be a better mirror of complex human diseases than lab mice, which he says are "essentially manmade organisms" that have lost many recessive traits and diseases through inbreeding. But the usefulness of cats as models of human disease remains to be shown.

O'Brien also expects benefits from comparing the genetics of the 37 cat species, which range from the tiny sand cat to the majestic lion. "Less than a tenth of 1% of all mammalian species that have existed survive," he notes. O'Brien believes the survivors' genes contain disease prevention secrets preserved by natural selection that could be identified by these studies. "We want to find out the things they have conjured up," he says, "because we might not be as clever ourselves."

–Ken Garber

Ken Garber is a science and health writer in Ann Arbor, Michigan.