

Mapping the Way to Disease-Free Chickens

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—Hans Cheng

The newest version of a chicken genome map gives Hans H. Cheng hope for developing a chicken resistant to Marek’s disease, a viral disease that causes tumors in the birds.

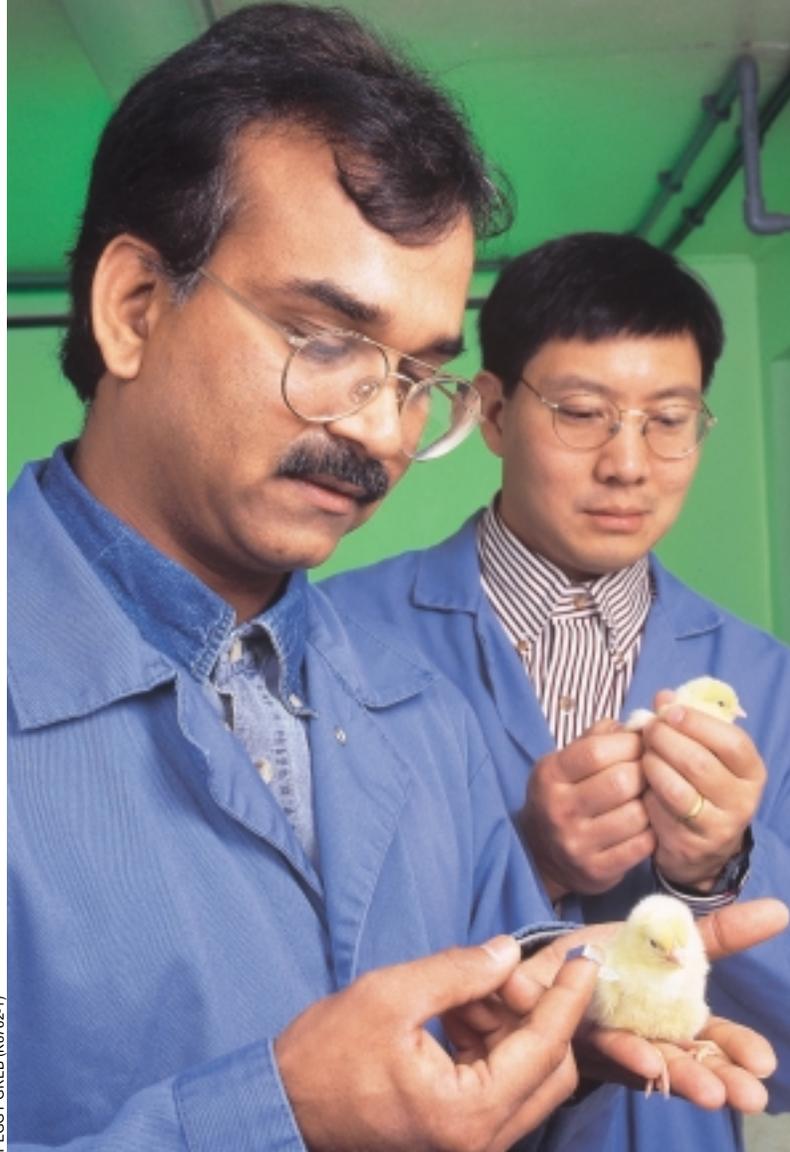
“The poultry industry is afraid it may start losing the vaccine race against Marek’s disease, as ever more virulent strains appear and cause unbearable losses,” says Cheng, a geneticist with USDA’s Agricultural Research Service. “That’s why using a genome map as a guide or road map to breeding chickens resistant to Marek’s disease is a priority.”

Before the first vaccine was developed in the late 1960s by scientists at the ARS Avian Disease and Oncology Laboratory in East Lansing, Michigan, the disease caused losses of \$300 million a year. Those losses came from a combination of deaths, fewer eggs, and condemnation of carcasses at poultry slaughter plants. Even with the vaccine, losses can still run as high as \$100 million a year.

The vaccine has to be updated periodically, in a race to keep ahead of ever more virulent strains. Cheng is counting on the genome map to help win the race.

“Chickens bred to resist Marek’s would be the first generation bred with modern molecular techniques,” Cheng says.

“The genome map will also help us build a superchicken, by helping us find the best combination of genes and proteins for resistance to many diseases as well as for productivity,” Cheng



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▲ Farm manager Raj Kulkarni (left) and geneticist Hans Cheng examine a day-old chick for disease resistance and susceptibility. Each chick is tagged with a wing band for identification.

▼ Research associate Hsiao-Ching Liu prepares a sample of chicken RNA. The samples are then run on DNA microarrays to screen thousands of genes simultaneously. This new technology is especially promising and should lead to the rapid identification of agriculturally important genes.

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says. Although their focus is on Marek's first and then other diseases, Cheng and his colleagues are also searching for genes that will promote better and more efficient growth.

The latest map can be viewed on the WWW at <http://poultry.mph.msu.edu/resources/conmap/conmap.htm>. It is actually a composite of three maps, including one jointly constructed by the Avian Disease and Oncology Laboratory and its neighbor, Michigan State University in East Lansing. The other two maps come from the Compton Institute for Animal Health in England and the Wageningen Agricultural University in the Netherlands. The new map is the product of the International Chicken Genome Mapping Project begun in 1994.

Overlapping Maps

"This is the first such international effort," Cheng says, although individual countries such as the United States have worked on mapping chicken genes since 1936. "Chickens were the first farm animal to have their genes mapped. But, in the beginning, mapping was based on visible physical characteristics such as feather color, rather than today's biotechnology that allows DNA and RNA analysis."

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Cheng, one of the co-coordinators of the East Lansing map project, along with Jerry B. Dodgson, a microbiologist at Michigan State, says the DNA samples used in making these maps come from the East Lansing lab and the Compton Institute.

The East Lansing lab sends these DNA samples around the world; they were taken from the blood of 52 chicks that were specially bred in 1990. The Compton Institute likewise sends vials of DNA samples around the world that are taken from a similar "reference family" of chicks. The samples were collected years ago and only from those individual chicks.

"So," Cheng says, "the DNA samples are in limited supply. But modern molecular techniques have greatly reduced the amount of DNA needed for mapping, so there no longer seems to be a danger of running out of samples."

All three maps used for the latest composite are genetic maps. The Compton Institute published the first such map. Dodgson is a few years away from a more detailed genome map. It is

called a physical map because the breakpoints used to map genes are produced by a physical cutting of DNA fragments from chromosomes. This contrasts with the genetic map in which the breakpoints occur naturally, as a result of sexual reproduction. A physical map fine-tunes a genetic map, giving a higher resolution—like a more detailed street map.

Cheng says that mapping a genome is like mapping a city neighborhood. "First you need to use street signs as markers, then you go looking for individual houses or genes," he says.

"We have about 2,000 genetic markers to help us locate genes," says Cheng. "For chickens, somewhere between 2,000 and 4,000 genetic markers is a reasonable goal to begin to construct a genome map and locate genes. The problem is that about half of these markers have limited utility because they can only map an individual chicken's genome and that of its progeny. Unlike the rest of our markers, these markers don't always mark the same gene in the same spot for all other chickens," he says.

When Dodgson's physical map is ready, it or a composite version will be integrated with the composite genetic map. Overlapping the maps helps build a better genome map.

"Every time one researcher finds another marker, another street sign is found for the maps," Cheng says. Different maps are lined up to provide guides for where to go next to complete the map. A physical map may be deficient in markers so we can use a genetic map to find those markers and vice versa."

All Creatures, Great and Small, Share Some Identical Genes

The maps also benefit from being overlaid with those of the human genome and other animal species.

"It's surprising how well the human and avian genomes line up," Cheng says. The human genome and chicken genome projects complement each other. By lining up the two maps, human immunologists and avian health researchers can help locate genes for traits that improve disease resistance in both species.

"The amazing thing about evolution is that it leaves many species—from yeast to mammals—sharing some of the same large chunks of DNA," Cheng says. "The same mapping

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techniques work in all species—plants and animals—with nuances caused by differences in biology and reproduction, for example.”

Since tumors are so common in chickens, the first cancer-causing genes were isolated from chicken tumor tissue. A gene that causes cancer in chickens will have similarities to a gene that causes cancer in humans. The East Lansing avian lab contributed greatly to the work on human cancer in the 1970s.

The Ultimate Science

Collaboration among geneticists—sharing and comparing of genetic maps—is typical of how scientists often work together to discover something, Cheng says. And collaboration is particularly needed in genome mapping.

“In that sense, genome mapping is the ultimate science. We’re all forced to collaborate, and we benefit from others’ work,” he says.

“The final step, after the maps are made and all the genes are sequenced, is to identify genes that influence the trait you’re looking for—in this case resistance to Marek’s disease,” says Cheng.

As a practical matter, Cheng and his colleagues in effect work on all these steps somewhat simultaneously. They are drawing the map at the same time as they are driving city streets and looking for house addresses.

“We take the maps we have and use them to sequence and identify genes with resistance to Marek’s,” he says. He recently began a new DNA technique called microarray to find these genes. “It should pare years off the search,” he says.

The microarray technique allows a search for a great number of genes at one time, rather than for gene markers, Cheng says.

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Technician Laurie Molitor (left) and research associate Christiane Hansen analyze chicken genetic markers using DNA sequencers. These semiautomatic machines increase the number of samples that can be processed per day and minimize human errors.

“RNA is put on two microscope slides. The genetic material on one slide might be from a disease-resistant chicken, with the other slide containing RNA from a susceptible one,” he explains.

“A quick check of such samples, en masse shows differing responses in RNA levels between the two. The differences show which genes may be responsible for the trait. We hope this new technology, combined with gene mapping, will enable the rapid identification of genes for disease resistance,” he says.

As another aid to gene identification, Cheng and his colleagues have also recently developed 19 inbred lines of chickens that have disease-resistance traits linked to one or a few genes, rather than to a complex of numerous genes. This makes identifying genes for disease resistance easier, and facilitates creating chickens that either are or are not disease resistant—nothing in between that would hamper the search, he says.

“This unique genetic resource will work for other traits as well, giving us the opportunity to quickly isolate the responsible genes,” Cheng adds.—By **Don Comis**, ARS.

This research is part of Animal Genomes, Germplasm, Reproduction, and Development, an ARS National Program (#101) described on the World Wide Web at <http://www.nps.ars.usda.gov/programs/appvs.htm>.

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Chicks atop a picture of a genetic map of a chicken. The chicken genome has 39 pairs of chromosomes, whereas the human genome contains 23 pairs.