Unraveling the Genome of the Honey Bee, Pig, Cow, and Chicken

An Agency Effort To Sequence Genomes

Though mapping the human genome received a lot of media attention, scientists have been performing the same studies in other animals—with much less fanfare. Researchers from around the world are mapping, or have mapped, the genomes of several farm animals. In addition to helping with the study of agriculture, this work may help further the understanding of human health.

It's not a simple process to map and sequence the genome of an animal. It takes years to do the research. And it takes plenty of money. The National Institutes of Health's (NIH) National Human Genome Research Institute has contributed tens of millions of dollars to various sequencing centers working on other animal genomes. The U.S. Department of Agriculture's Agricultural Research Service (ARS) and Cooperative State Research, Education, and Extension Service have also contributed millions, as have universities and foreign governments.

"In the long run, it makes great business sense for all these organizations to fund genomic research," says Ronnie D. Green,

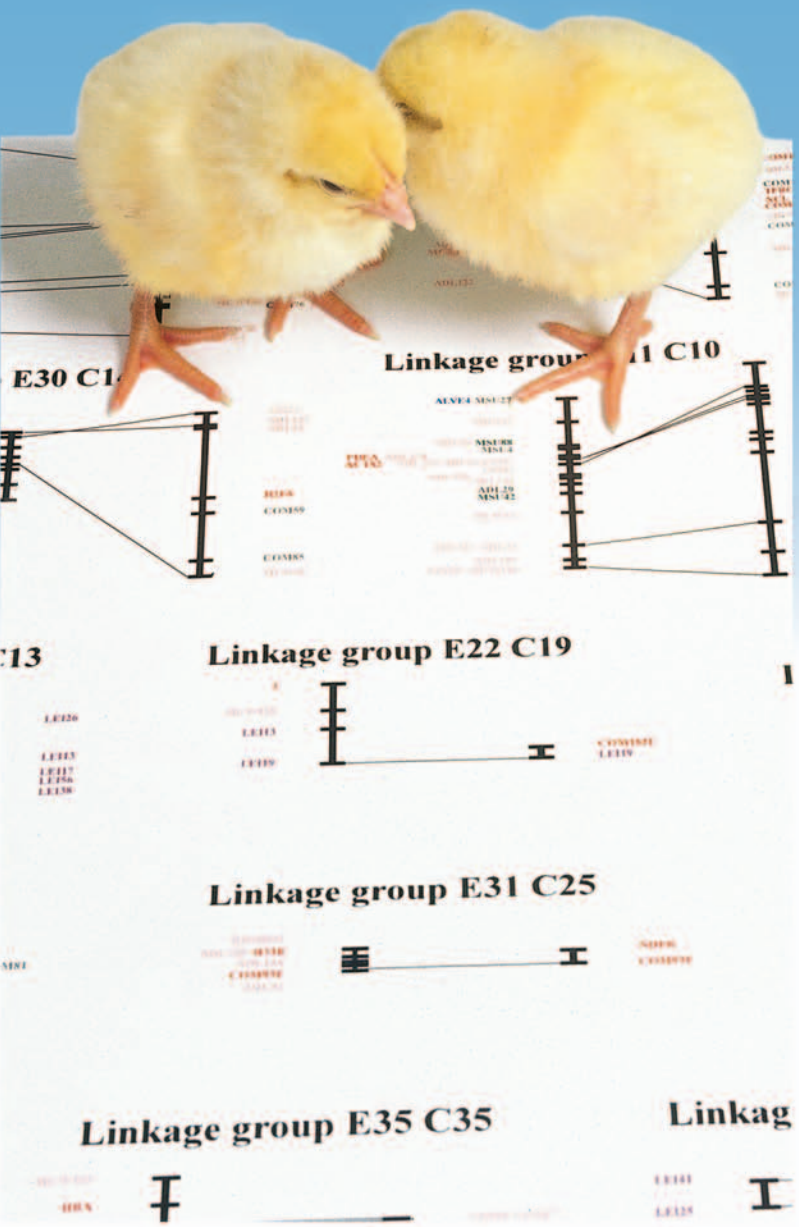
STEPHEN AUSMUS (D007-1)

Worker bees remove the mummified remains of larvae infected by the chalkbrood fungus *Ascosphaera apis*. ARS scientists are using the completed bee genome to help understand bee responses to this disease.

STEPHEN AUSMUS (D010-1)

ARS scientists and cooperators throughout the world are in the final stages of completing a bacterial artificial chromosome map of the cow. From this map, the cow genome is already being sequenced. The genome should be useful for selecting cows that resist disease or require less feed.

PEGGY GREB (K8764-2)



Chicks atop a picture of a genetic map of a chicken. The new chicken genome will make it much easier to locate genes, especially those for complex traits like disease resistance.

ARS national program leader for Food Animal Production and leader of ARS animal genomic research.

ARS scientists are working with collaborators to map the chicken, honey bee, cow, and pig genomes to learn more about these animals and what information they can provide for the study of humans.

The "Original Chicken" Donates Blueprint to Science

The campus of Michigan State University is home to Female #256, the Red Jungle Fowl *(Gallus gallus)* chicken whose blood samples gave researchers the 1 billion DNA units needed to create the first high-quality draft sequence of the chicken genome. She appears no worse for wear, despite her advanced age of 7 years. Wild Red Jungle Fowl are the ancestors of today's chickens. The breed has survived at large for about 8,000 years—rare for a wild ancestor of a domesticated animal.

STEPHEN AUSMUS (K11699-1)

Chemist Tim Smith and cattle wrangler Randy Scott record growth and health data of a heifer to look for correlation of DNA markers and performance at the U.S. Meat Animal Research Center in Clay Center, Nebraska.

Chickens were chosen for mapping because they are the premier nonmammalian vertebrate model organisms. They're one of the primary models for embryology and development since they grow inside an egg rather than a mother's uterus, making for easier study. Chickens are also a major model for research on viruses and cancer.

The framework for this genome sequence came from Jerry Dodgson, a molecular biologist at Michigan State University at East Lansing, and ARS geneticist Hans H. Cheng and colleagues at the nearby ARS Avian Disease and Oncology Laboratory.

STEPHEN AUSMUS (K11698-1)

Molecular biologists Steve Kappes (left) and John Keele use gene sequences and genomic sequence to assemble sequences and determine bovine gene structure and regulatory sites.

A genetic map is like an Interstate map. A physical map is like a local street map. Use of genetic markers allows integration of the two.

Dodgson created a physical map with Female #256's DNA. Cheng created a genetic map using DNA from progeny of Male #10394—a member of the same Red Jungle Fowl line—and a White Leghorn female from an experimental inbred line of chickens. The team used these two maps as the basis for sequencing chicken genes.

NIH funded the project, and the sequence is now online at www.ncbi.nlm.nih.gov/genome/guide/chicken.

A genetic map is a broad overview that shows the order of genes. A physical map shows the actual distance between genes. Using a driving analogy, the genetic map is like an Interstate map, and the physical map is like a local street map. Use of common genetic markers as landmarks allows for integration of the two types of maps. Aligning the genetic map with the genome sequence greatly facilitates scientific efforts to determine the function of each gene and how it influences traits.

At East Lansing, ARS maintains more than 50 inbred lines of chickens ideally suited for genetic studies. The collection—begun in the 1930s—is one of the best in the world.

Over the years, many universities have given up their living collections because maintenance costs were too high. Cheng says, "It's ironic that when the best tool for genetically analyzing these lines arrived, many universities no longer had the chickens around to analyze."

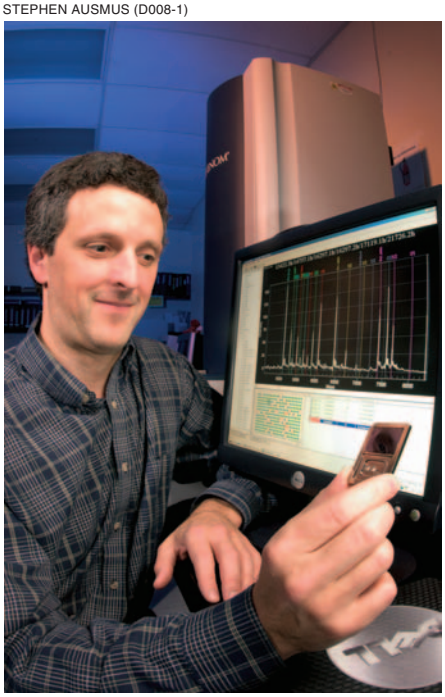
Cheng says that the new genome map to guide the search for genes makes a night-and-day difference. He went almost overnight from having 2,000 genetic markers to having potentially 3 million.

"This map makes it much easier to find genes—especially those for complex traits like disease resistance," he says. "It eliminates a lot of guesswork. It's like suddenly having the complete 'parts list' for a chicken."

Before the map, Cheng had found what he thinks are three genes that confer resistance to Marek's disease, his chief interest. "This genome sequence will be an immense help in finding the rest of the resistance genes," Cheng says. "We found the genes using a unique, integrated functional genomics approach that combines DNA, RNA, and protein methods. The genome sequence will only enhance our power and accuracy."

He expects many other payoffs, including improved vaccines for Marek's and other serious diseases. "We'll also learn how to grow a more nutritious, tastier, and healthier chicken," Cheng says. "From the ARS viewpoint, mapping and sequencing the chicken genome makes sense because poultry and egg products are a $25 billion industry and poultry is the number-one meat consumed in the United States."

STEPHEN AUSMUS (D008-1)



The chip that geneticist Gary Rohrer is holding allows him to evaluate more than 380 pigs for genetic variations at 6 different regions of the genome. This information will help determine which genes affect reproduction in pigs.

Sweet Research

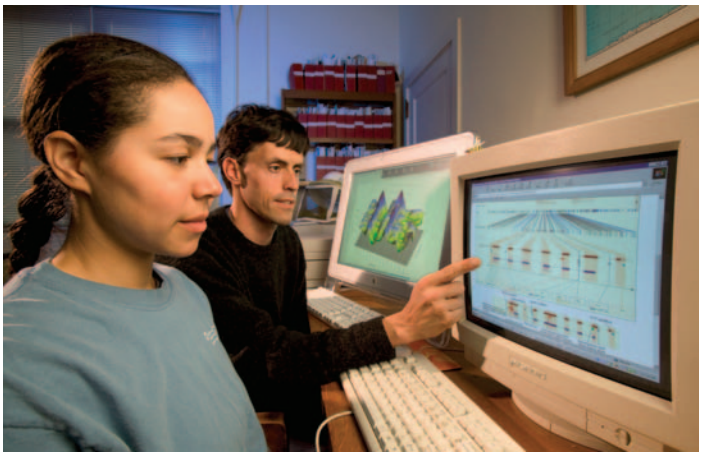
ARS scientists have been on the forefront of research both to breed a better honey bee and to manage the welfare and productivity of this important insect.

Humans have a vested interest in *Apis mellifera;* the honey bee's pollination of 90-plus flowering crops results in yield and quality improvements worth more than $14 billion annually. And don't forget the delectable byproduct of such pollination: honey.

Many dangers, from blood-sucking mites to disease organisms, constantly threaten to undermine the honey bee's efforts, keeping scientists on a fast-track search for new ways to safeguard the insect—and agriculture, no less. Now, a rough draft of *A. mellifera's* genome is at hand, and bee researchers are gobbling up the wealth of information.

"As an organism whose social order rivals our own in many ways, the honey bee will serve as a natural system for further agricultural studies, including social behavior, cognition, and immune system function," Joseph Jen,

STEPHEN AUSMUS (D005-1)



The bacterium *Paenibacillus larvae* causes American foulbrood disease. Entomologist Jay Evans and technician Tamieka Armstrong use genomic data to define honey bee genes involved in resistance to the bacterium.

Under Secretary for USDA's Research, Education, and Economics, noted shortly after the genome draft's January 2004 completion.

The honey bee's entire blueprint for life is only about one-tenth the length of the human genome. Still, writing that first draft was no easy task; the feat took a dedicated team of scientists—led by Baylor College of Medicine in Houston—about a year to complete using the latest in genome-sequencing technology and several million dollars in funding.

Kevin Hackett, ARS's national program leader for bees and pollination in Beltsville, Maryland, lists some of the exciting new research avenues that the honey bee genome has opened up: identifying genetic markers to expedite bee-breeding efforts, for example, to improve crop pollination, winter survival, and defensiveness against Africanized bees; host-pathogen modeling studies to better control organisms that cause honey bee diseases; and genome-driven studies to fine-tune honey bee nutrition and pollination.

"If you can locate the 'smelling' genes of bees," says Hackett, "you can use the information to improve their diet through supplementation as well as their ability to forage—with greater pollination resulting."

Jay Evans and Katherine Aronstein, ARS entomologists who participated in the honey bee genome project, are using information from the advance to identify immune system genes that keep bees healthy. Of particular emphasis is characterizing genes involved in potential resistance to the bacterium *Paenibacillus larvae,* which causes foulbrood disease in honey bee larvae. Along with insect pests, parasites, and other pathogens, foulbrood outbreaks in U.S. hives cause $5 million annually in crop-pollination losses.

At their respective labs in Beltsville and in Weslaco, Texas, Evans and Aronstein are studying a handful of genes and gene products, or proteins, that may stymie honey bee diseases. One tantalizing lead is abaecin, a peptide that honey bees produce to varying degrees when attacked by pathogens.

STEPHEN AUSMUS (D006-1)

Research associate Laura Decanini and technician Andrew Ulsamer rate honey bee colonies for signs of disease.

"We know these bees are responding to foulbrood by producing abaecin," Evans says. "But we're not sure whether a bee that produces more of this peptide is indeed foulbrood resistant."

With the honey bee genome, it's possible to cast a wider net for other such genes and characterize them in hopes of eventually using the information to improve honey bee breeding and management, he adds.

Aronstein has focused her work on a large family of receptors that play roles in the bee's first line of defense against invading microorganisms–what's known as innate, or inborn, immunity.

"The outcome of this genome sequencing research won't give immediate results to the beekeeping industry," says Aronstein. "But it's long-term research with huge potential for a better understanding of bee biology and improvement of management practices."

Studying the Cow Genome

Steven M. Kappes, now ARS Deputy Administrator for Animal Production and Protection, was one of the leaders of ARS's work on the bovine genome at Clay Center, Nebraska. As director of the Roman L. Hruska U.S. Meat Animal Research Center, Kappes worked with a dozen ARS scientists plus many from around the world in developing the physical, bacterial artificial chromosome—BAC—map of the cow.

The scientists first started this project in spring 2000 and are in the final stages of putting the map together.

Though the scientists have not completed the BAC map, researchers are using part of it to sequence the cow genome. "We are already using the BAC map to find DNA markers," Kappes says.

The physical map was developed by researchers in the United States and Australia, Canada, Brazil, France, New Zealand, and the United Kingdom.

PEGGY GREB (K10974-1)

The high-capacity DNA sequencer being loaded by geneticists Curt Van Tassell (left) and Tad Sonstegard will increase the number of genetic markers available for screening in livestock populations.

Being able to sequence the genome may lead to new knowledge about human health, particularly reproduction traits and immune functions. The knowledge will also obviously help agricultural researchers. Based on evidence from other species, Kappes believes we will be able to find genes that influence feed efficiency in cattle. Cattle producers would use the information to select cows that require less feed. Not only would this reduce the cost of beef production, but it could also mean fewer nutrient and odor problems.

Kappes also notes the possibility of being able to identify cows that are resistant to bovine spongiform encephalopathy—or mad cow disease—by knowing what DNA changes are responsible for the resistance. Then scientists would be able to breed cows naturally immune to the disease.

Many ARS scientists from around the country worked on the cattle genome. Those that had an active role include geneticist Timothy P.L. Smith of the Nebraska lab and Beltsville geneticists Curt Van Tassell and Tad Sonstegard. Van Tassell found 25 regions in cattle genomes, called quantitative trait loci, that may prove economically important to dairy producers.

Don't Forget the Pigs

Compared to the other animal genomes under study, the pig's has the farthest to go. Animal geneticist Gary A. Rohrer at Clay Center is leading ARS's efforts in sequencing the swine genome. "The sequencing effort is still in its infancy and is evolving as we go," Rohrer explains.

An international consortium has completed the physical map and has started to analyze it. Researchers can view this information at www.sanger.ac.uk/Projects/S_scrofa/. Rohrer believes that it may take 3 to 5 years to complete the actual genome sequencing work.

Rohrer is part of the Swine Genome Sequencing Consortium, which features representatives from governmental agencies and universities from around the world. The group is still developing strategy on coordinating the eventual sequencing work. They are also working to secure funding for the project.—By **David Elstein, Don Comis, Jan Suszkiw,** and **Alfredo Flores.**

This research is part of Food Animal Production, an ARS National Program (#101) described on the World Wide Web at www.nps.ars.usda.gov.

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