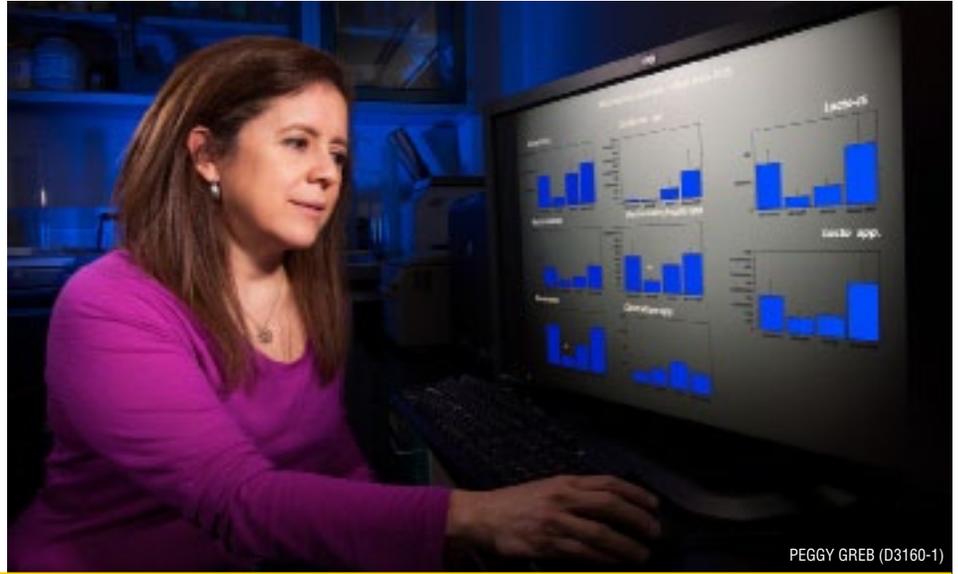
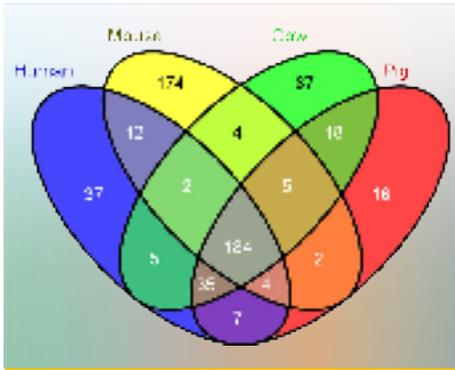


Pigs Useful in Immune and Obesity Research

HARRY DAWSON (D3162-1)



PEGGY GREB (D3160-1)

By comparing the number of shared immune response genes among humans, pigs, mice, and cows, ARS scientists discovered a high degree of similarity between the immune responses of pigs and humans.

Nutritionist Harry Dawson and microbiologist Gloria Solano-Aguilar, both scientists at the Agricultural Research Service’s Beltsville [Maryland] Human Nutrition Research Center (BHNRC), have teamed with scientists from ARS and other organizations to use the pig as an animal model to promote both human and animal health. This research focuses on assessing the effect of nutrition on immune and inflammatory responses.

Dawson helped develop and continues to curate the publicly available Porcine Translational Research Database of genes and proteins for comparison with those prominently studied in rodents and humans. “This database contains functional information on more than 5,800 genes commonly studied in humans, pigs, and mice, including about 2,240 that have been sequenced at BHNRC.” The database can be found at tinyurl.com/porcinedata.

The database contains “manually annotated” genes, meaning that all genes and protein sequences included in the database, as well as information about their functions, were manually entered. Annotated genes can also be entered by computer software programs that predict the structure and

Microbiologist Gloria Solano-Aguilar evaluates intestinal bacterial data from pigs consuming high-fat and low-fat diets. This data is helping researchers understand obesity in pigs, which can be a model for humans.

identity of genes and proteins based on algorithms.

“These computer programs, while fast, are prone to error that can be corrected only by manual annotation,” says Dawson.

Immune System Similarities

In addition, Dawson conducted a comparative analysis and assessment of specific portions of the swine, mouse, and human genomes. He found that humans share far more immune-system-related genes and proteins with pigs than they do with mice. He reported that when a functional part of a protein is missing among one of the three species, the chance that it is preserved only in pigs and humans is nearly two times greater than the chance it is preserved only in mice and humans. Dawson’s book chapter, “A Comparative Assessment of the Pig, Mouse, and Human Genomes,” was published by CRC Press in 2011 in *The Minipig in Biomedical Research*.

The first complete pig genome sequence, version Sscrofa 10.2, was released by the Swine Genome Sequencing Consortium in 2012 (see box). As part of that effort, a subgroup called the “Immune Response Annotation Group” annotated more than 1,400 swine genes involved in the animal’s immune response. This group included ARS’s Dawson, molecular biologist Celine

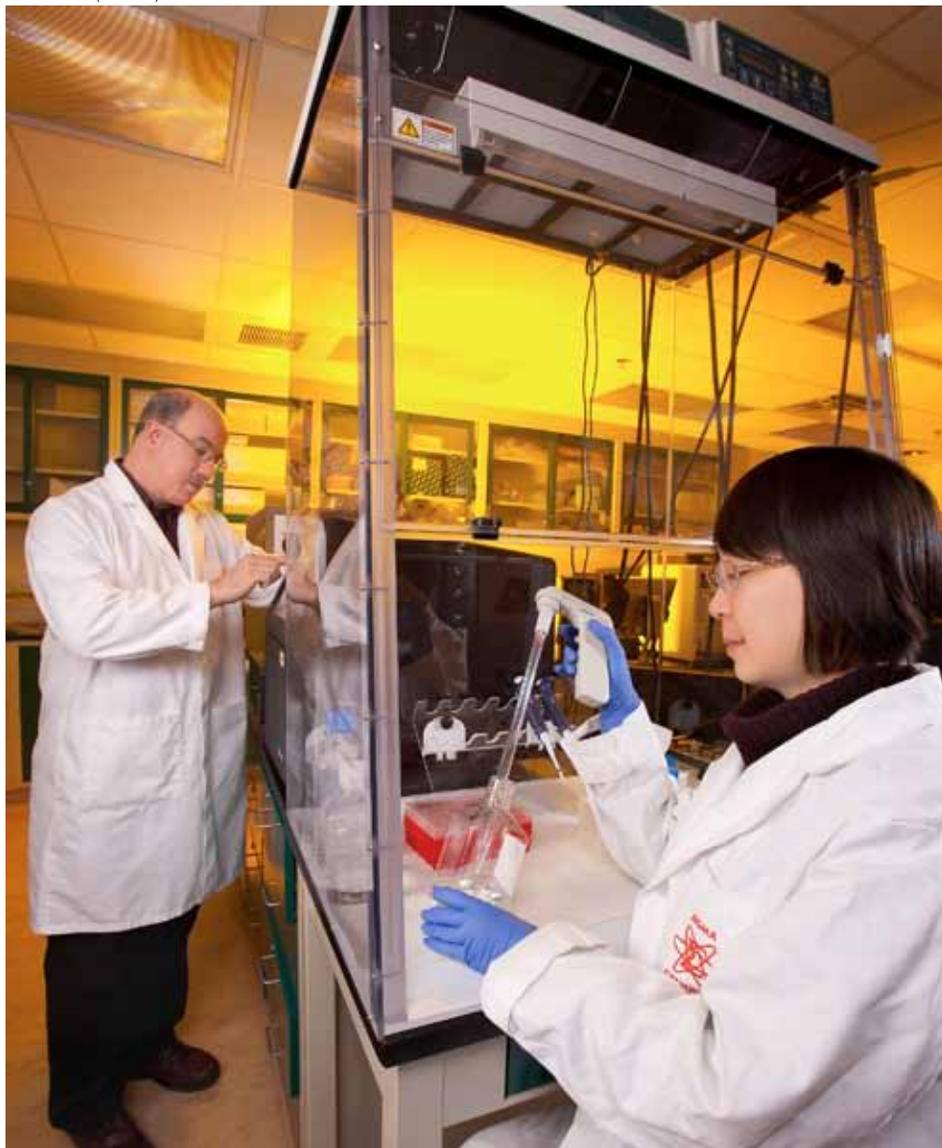
Chen, chemist Joan Lunney, and others.

The group discovered that the immunity genes of pigs and humans are very similar and evolve at a similar rate in both species. These findings were reported in the journal *Nature* in 2012.

Later, the group published a study that further characterized the structure and function of the porcine immunome. An immunome is a collection, or reference set, of immune-system-related genes and proteins of a given species. The group provided new immune-response annotations for more than 500 porcine genes and 3,472 protein-coding transcripts.

“The porcine genome is not yet complete, and additional genes may be discovered,” says Dawson. “But these comprehensive and integrated analyses provide important tools for measuring the porcine immune response.” The findings were published in *BMC Genomics* in 2013.

These comparative studies provide compelling evidence for using swine in research on both human and animal health, says Dawson. “These studies indicate that pigs are a good species to further test concepts and principles that have been discovered by first using mice as a model, particularly for immune-response research.”



Nutritionist Harry Dawson (left) checks the performance of the DNA sequencer, while molecular biologist Celine Chen prepares samples of pig macrophages (immune cells) for sequencing.

Obesity Research Goes to the Hogs

Also at the BHNRC, Solano-Aguilar has worked on a series of studies showing that the pig is instrumental as a model for human obesity-related research. She worked with Kati Hanhineva, of the University of Eastern Finland in Kuopio, to study metabolic changes that occur in pig tissues and biofluids after the pigs consumed a high-fat diet.

The researchers studied the Ossabaw pig because it has a greater tendency to deposit excess fat and develop obesity-related diseases when fed a high-calorie diet, compared to other pig breeds. The emphasis was on using juvenile pigs as a model for obesity in children. “This is an important area because it is generally difficult to evaluate obesity-related

metabolic disturbances in children,” says Solano-Aguilar.

The authors wanted to study diet-induced metabolic changes taking place in the tissues they collected from the pigs—liver, pancreas, brain, and intestine. And they wanted to compare whether the changes they found in the tissues were also present in the pig’s urine and plasma—biofluids that are typically collected during human clinical studies.

The study pigs were fed either a maintenance diet or a high-fat diet. The researchers found changes in lipid metabolites in all analyzed host tissue samples from the pigs fed the high-fat diet. Some tissue-dependent changes were not reflected in the biofluids.

The First Swine Genome Assembly

If you overheard scientists talking about the genome sequence of an organism, you might think they were talking about software programs. The first “genome assembly” released for a given species gets a release date. Subsequent assemblies for the same species get a new name and a higher number.

The human genome version h37 was released in 2009. The mouse genome version m38 was released in 2011. And the first pig genome version, Sscrofa 10.2, was released in 2012 by an international coalition of researchers called the “Swine Genome Sequencing Consortium.” The project was supported in part by a USDA grant and by Agricultural Research Service scientists headed by animal geneticist Gary Rohrer at the U.S. Meat Animal Research Center in Clay Center, Nebraska.

Using swine as a biomedical research model was useful for studying metabolic effects induced by a high-fat diet, says Joseph Urban, a coauthor at the BHNRC laboratory who initiated a multi-institute cooperative agreement with the Finnish scientists.

“Biofluids give us part of the picture,” Urban says, “but being able to look at organ tissue helped us target changes that are indicative of both disease and poor response to diet.” The study was published in the *Journal of Proteome Research* in 2013.—By **Rosalie Marion Bliss, ARS.**

This research is part of Human Nutrition (#107) and Animal Health (#103), two ARS national programs described at www.nps.ars.usda.gov.

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