Julie Long, Ph.D.
Poultry research physiologist, Animal Biosciences and Biotechnology Laboratory, Beltsville Agricultural Research Center
U.S. Department of Agriculture Agricultural Research Service
From Animal Genomes to Phenomes: What’s Next for Genomics

Dr. Julie A. Long
Poultry Research Physiologist
Animal Biosciences and Biotechnology Laboratory
Beltsville Agricultural Research Center
USDA Agricultural Research Service

Image from: Schwochow et al., 2017, PLoS One
In the decade that followed, many of the goals set forth in the blueprint were accomplished.

Genomes have been assembled and annotated for major agricultural species, including:

- **Chicken** – 2004, 10X coverage
- **Cattle** – 2009, 10X coverage
- **Turkey** – 2010, 6X coverage
- **Swine** – 2012, 10X coverage
- **Sheep** – 2014, 6X coverage
- **Catfish** – 2016, 6X coverage
- **Goat** – 2017, 2X coverage
Innovative Approach and Powerful Impact

- Combination of Roche 454 (long reads) and Illumina GAII (short reads) sequencing.
- Unique assembly allowed use of a BAC contig-based physical and comparative map, turkey genetic map and the chicken genome sequence.
- Result was the alignment of turkey sequence contigs/scaffolds to most turkey chromosomes.
- Chromosome locations are critical for genome-based selection approaches.
Affymetrix, Inc. has introduced Axiom® Turkey Genotyping Array, developed in collaboration with the USDA’s Agricultural Research Service, Aviagen and Hendrix Genetics.

- Includes 643,845 SNPs
- Enables turkey breeders to screen birds for economically important traits
- Markers associated with meat characteristics, health outcomes, and fertility

Over the past 10 years, genome-enabled technologies have become integral components of commercial animal breeding for many species as advances in DNA sequencing and genotyping dramatically increased the ability to obtain genome information.

International research consortia are using genomics to identify:

- Biomarkers for incidence of myopathies in live birds
  Occurrence of muscle myopathy is closely associated with up-regulation of protein metabolism and increased translation of proteins (Kuttappan et al., 2017).

- Chickens that are more resilient to the negative effects of heat stress
  Genes associated with cell movement and immune signaling could be promising candidates for selection to improve humoral-mediated immune responses in heat-stressed poultry (Monson et al., 2018).

- Genetic differences of laying hens producing either a high or low breaking strength egg shell
  Osteopontin, which inhibits the growth of calcite crystals, had higher gene expression in hens with low shell strength (Zhang et al., 2019).
The term “genome to phenome” describes the connection and causation between the genetic makeup of an animal (genome) and the totality of all phenotypes, or the observable physical or physiological traits or characteristics (phenome).
Science to Practice: Precision Selection and Management

State of the Art

Primary use is the identification of large numbers of SNP markers that represent genetic diversity and are associated with economically important traits.

High-throughput platforms for genotyping large numbers of these markers in a single assay have led to their widespread use in research that seeks to determine the genetic basis of traits and improve predictions of performance in offspring.

Identifying animals at an earlier age with higher genome estimated breeding values (sex- or age-limited traits).

Poultry industry example: Egg layer chickens for which young males can be genomically selected for traits that can be measured only in older females (egg production over extended periods).

Advancing the State of the Art

- Continue the development of species-specific genome tools and resources.
- Develop cost-effective methods to carry out genome analyses is critical if we are to make improvements over contemporary strategies.
- Collect new and more extensive phenotypes. Researchers must have access to large integrated data sets of easily searchable phenotypic, environmental, and genomic information. Comprehensive phenotypes should represent a wide range of production, reproductive, fitness, metabolic, welfare, disease susceptibility, and immune responsiveness traits.
- Identify causal alleles. Identifying and characterizing the alleles that directly affect the biochemical mechanisms underlying differences in phenotypes (and therefore economically important traits) will significantly enhance efforts to optimize breeding strategies.
Discovery Science: Genome and Functional Biology

Advancing the State of the Art

• Catalog gene expression
  Determining mechanisms that underlie phenotypic variation and regulation of gene expression across tissues and biological states is essential for incorporating molecular phenotypes into genetic improvement programs, especially between commercial animals and their unselected ancestors.

• Link genes to function
  Despite the ability to predict protein sequences from DNA sequences, the functions of many proteins remain unknown.

• Discover and exploit epigenetic factors
  Determining functional elements of gene expression, including epigenetic modifications of the DNA and chromatin structure, will improve the accuracy of phenotype prediction.

6–12 eggs within the first year of life
Photo credit: Peter Price, orientalbirdimages.org

200 eggs within the first year of life
Advancing the State of the Art

- Identify pathogens and diagnose diseases
  
  Reemerging/new diseases need to be addressed due to changes in management, climate and other abiotic factors. Host genomic and immunological knowledge will need to be integrated with outbreak tracking tools and complete annotated genomes and pathogen variance characterization to provide information associated with disease phenotypes.

- Develop tools for phenotyping
  
  Equipment and facilities that enhance and automate precision phenotyping of animals with disease must be developed. This includes assays to analyze cytokines and other immune biomarkers and cellular responses, identification of pathways, and networks associated with pathogen recognition and clearance.

**Discovery Science: Host-Pathogen Interactions**

- Avian H5N1 virus
- Eimeria maxima
- Mycoplasma gallisepticum

Photo: Dr. Takeshi Noda, University of Tokyo
Advancing the State of the Art

• Microbial genomes, transcriptomes, and metabolomes

The role of microbial populations (including bacteria, viruses, archaea, protists, and fungi) in animal health, production efficiency, and food safety has been confirmed in some cases. A proportion of observed phenotypic variation in animals may be due to differences in microbial populations.

• Building the microbiome into animal production strategies

The inclusion of microbial data into animal phenotypic models will improve the accuracy of prediction in agricultural species. Development of rapid and inexpensive methods to characterize the components of an animal's microbiome will allow analysis of entire populations.

Figure from Maki et al., 2019, Microorganisms
Advancing the State of the Art

• Develop pan-genomes for agricultural animals

   Existing reference genomes often represent a single, inbred individual. All animal species of agricultural importance should be characterized by pan-genome assemblies that, as with the human genome, provide full annotations of genomic features.

• Catalog genetic variation

   In addition to multiple annotated genomes that encompass the diversity of each species, databases of sequence variants need to be maintained and shared.
Advancing the State of the Art

- Improve cryopreservation protocols

*Species-specific protocols must be developed to the degree they can be routinely used to preserve sufficient germplasm for all agriculturally important animals.*

Characterizing genetic diversity:

<table>
<thead>
<tr>
<th>Chicken line</th>
<th>Week</th>
<th>Eggs Set</th>
<th>Unfertile</th>
<th>Early Dead</th>
<th>Viable</th>
<th>Hatch</th>
<th>Total Fertility</th>
<th>Viable Embryos</th>
<th>Hatched</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADOL</td>
<td>1</td>
<td>94</td>
<td>91</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>3.2</td>
<td>3.2</td>
<td>100</td>
</tr>
<tr>
<td>Line 0</td>
<td>2</td>
<td>83</td>
<td>84</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>96</td>
<td>82</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
</tr>
<tr>
<td>VA Tech</td>
<td>1</td>
<td>89</td>
<td>86</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>3.4</td>
<td>3.4</td>
<td>100</td>
</tr>
<tr>
<td>Hi BW</td>
<td>2</td>
<td>93</td>
<td>89</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>4.3</td>
<td>4.3</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>93</td>
<td>93</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
</tr>
<tr>
<td>AR</td>
<td>1</td>
<td>89</td>
<td>49</td>
<td>4</td>
<td>36</td>
<td>36</td>
<td>44.9</td>
<td>40.4</td>
<td>100</td>
</tr>
<tr>
<td>Regressor</td>
<td>2</td>
<td>88</td>
<td>66</td>
<td>0</td>
<td>22</td>
<td>22</td>
<td>25</td>
<td>25</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>93</td>
<td>88</td>
<td>0</td>
<td>5</td>
<td>4</td>
<td>5.4</td>
<td>5.4</td>
<td>80</td>
</tr>
</tbody>
</table>

Sue Lamont with an inbred chicken from a line used for disease resistance/tolerance studies at Iowa State University.
ABSTRACT

The world’s population is expected to reach more than 9 billion by 2050, creating a grand societal challenge: supplying agricultural productivity to feed the globe. Livestock and poultry products are key to the world supply of protein, but genetic diversity of livestock is fading. The number of breeds has declined as farming practices have focused on a small number of high-producing breeds to meet low-cost meat demands. In fact, up to 25% of global livestock breeds are either extinct, endangered, or have already been lost. In the face of the mounting depletion in genetic diversity among livestock species, there is an urgent need to develop and maintain an intensive program of sampling and evaluation of the existing gene pools. Genetic diversity can be preserved through living populations or cryopreserved for future use. Living populations can adapt to changes in the natural or production environment, provide value in research, and contribute to specialty breeding programs.

This CAST Issue Paper is available at www.cast-science.org/publications.
Livestock and poultry products from 7 domesticated species are key components of the world’s supply of dietary protein.

The world’s population is expected to reach more than 9 billion by 2050.

There are 7,745 agricultural breeds left in the world (FAO 2019).

The urgent process needed today to address the most challenging problems requires leveraging capabilities across the scientific and technological enterprise in a convergent research approach.”

Will need a two-fold increase in animal protein through:
1) 10-fold increase in the rate of genetic improvement;
2) development of precision livestock production systems.

Breeds with unknown risk status = 67%
Breeds at risk of extinction = 26%
Breeds not at risk = 7%

doi.org/10.17226/25059
Impacts of the Genome to Phenome Blueprint for the Poultry Industry: the “Omics” Revolution

1. Enable **better disease detection and management** using a data-driven approach through the development and use of sensing technologies and predictive algorithms.

2. Accelerate **genetic improvement in sustainability traits** (fertility, improved feed efficiency, welfare, disease resistance) using big genotypic and sequence data sets linked to field phenotypes and combined with genomics, advanced reproductive technologies, and precision breeding techniques.

3. Determine **objective measures of sustainability and animal welfare**, how those can be incorporated into precision systems, and how the social sciences can inform and translate these scientific findings to promote consumer understanding of trade-offs and enable them to make informed purchasing decisions.

4. Further work will be needed to **continue to reduce the costs and increase performance of genotyping platforms**, particularly for industries in which the economic value of an individual animal is low relative to genotyping costs.
Acknowledgements

New Blueprint taskforce
Jim Reecy (Iowa State University)
Caird Rexroad (USDA-ARS)
Jeff Vallet (USDA-ARS)
Lakshmi Matukumalli (USDA-NIFA)

The development of this Blueprint was supported by AFRI grant 2017-67015-26907 project accession 1013525 from the USDA National Institute of Food and Agriculture and support from the ARS Office of National Programs, and the National Agricultural Library.


doi: 10.3389/fgene.2019.00327