

## Current Status of Genome Maps of Livestock

Menaibam Chawang, Asit Jain, Mohan Singh Thakur, Vaishali Khare, Akansha Singh, S. K. Joshi, S. S. Tomar and Farheen Ansari<sup>#</sup>

Department of Animal Genetics and Breeding, College of Veterinary Science & Animal Husbandry, Nanaji Deshmukh Veterinary Science University, Jabalpur (MP)  
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### *Abstract*

The technique of determining a gene's position on a chromosome is known as gene mapping. Linkage analysis was employed in early gene maps. Gene mapping of the genome entails dividing a number of genes into maps of distinct linkage groups and figuring out their linear order on each chromosome. Since the human genome was initially sequenced in 2001, our knowledge of how the genome is organized has greatly increased. The genomic maps have been summarized by sequencing of livestock and other model animals which help in identifying its genomic patterns and features.

### INTRODUCTION

Genetic maps were used by researchers to systematically map genes and markers in the genome before the majority of cattle and model animals had their genome sequences available. Basically, a genetic map is an illustration of how genes and other genetic elements are distributed throughout the genome of a single species. Specific techniques were developed to respond to questions such as in which particular order a small number of loci were mapped in a given chromosome.

#### Gene mapping

Gene mapping is a procedure used to recognize a gene's location and the length between genes. Gene mapping can also be used to explain the separations between different locations within a gene. The cornerstone of all genome mapping is the placement of many molecular markers at specified sites on the genome. Upon creating genome maps, genes can be ascertained as a distinct class of genetic markers mapped similarly to other markers. The two primary types of maps utilized in gene mapping are genetic linkage maps and physical maps. Genetic maps and physical maps are based on genetic



linkage data and physical distances respectively. The relative distances and position of each gene on a chromosome from one another are presented on genetic linkage maps. Genetic mapping is made possible by crossing over during meiosis. Alignment of chromosome occur in pairs in the centre of a cell and exchange of similar fragments among themselves during the first phase of meiosis. In order to determine which gene is present on each chromosome and where its location lies within that specific chromosome and to determine which gene is probably undergoing recombination distance between two genes is based, the genetic mapping makes its plausible.

### **Physical mapping**

The actual DNA base pair distances between landmarks are always provided by the physical maps. The accurate physical distance between genetic markers as well as the nucleotide quantities is provided via a physical map. With the use of DNA markers and fragments, physical mapping puts together larger DNA sections. The overlapping portions of the fragments allow researchers to pinpoint the positions of the DNA bases. It is possible to explore genomes of various sizes and gain varying degrees of precision using a variety of physical mapping techniques. In order to obtain a whole genome sequence and ascertain whether there is any association between the specific DNA sequence and phenotypic traits, physical mapping is a typical method employed in genome sequencing. To calculate the distance between genetic markers, genetic mapping approaches use recombination events. By analysing variations in homologous DNA sequences, random fragment length polymorphism (RFLP) determines the separation between two markers. Currently, short tandem repeat polymorphisms (STRP) are used in gene mapping analyses aimed at single gene disorders. Genome-wide association research and linkage analysis in genetics involve single nucleotide polymorphisms (SNPs). The inheritance of distinctive and genetic signatures, such as SNPs and microsatellites, is used to study linkage analysis. Through addressing the populace as a single, genome-wide association studies (GWAS) find the connections between traits and genetic markers like SNPs and microsatellites. The technique is used to map the roles of genes in common disorders. Lately, a notable achievement has been progressed in the area which leads in identifying of several quantitative trait nucleotides (QTNs) and diseases that contribute to economically important traits such as in milk or meat quality of cattle (Cohen-Zinder *et al.*, 2005). All single-nucleotide mutations in any breed can now be identified and genotyped due to the accessibility of whole-genome annotation in union with economical sequencing and genotyping techniques. Cooperatively with GWAS, this leads to the discernment of all common and some specific QTNs.



### **Somatic cell hybrid maps**

The genes G6PD, PGK, GALA and HPRT, which are situated on cattle chromosome X, were linked for the first time using interspecies hybrids of somatic cells (Heuertz and Hors-Cayla, 1978). Later, after a hamster-cattle somatic cell hybrid panel was constructed, a sizable number of cattle markers were mapped containing 31 distinct clones (Womack and Moll, 1986). Nearly 2,700 genes are now present in the cattle somatic cell hybrid map, out of which a Japanese research team genotyped over 1,400 on the cattle-hamster somatic cell hybrid panel (Itoh *et al.*, 2003). By genotyping more than 200 microsatellite markers from the linkage map on the somatic cell hybrid panel, the somatic cell hybrid map and the USDA-MARC linkage map were combined (Kappes *et al.*, 1997). Another intriguing effort to enhance the cow somatic cell hybrid map was undertaken by Laurent *et al.* (2000), where 233 human expressed sequence tags (ESTs) PCR primers that amplified cattle sequences to map additional type I markers on cattle chromosomes were used. In due course, 60 human ESTs to cattle chromosomes out of which 46 ESTs had the assignments consistent with the human-cattle chromosome. Details regarding the chromosomal locations of gene markers or microsatellites were provided by somatic cell hybrid maps, but the particulars about the order of markers in chromosomes was very finite. Yet, these maps were highly obliging for assigning radiation hybrid or ordered genetic linkage groups to cattle chromosomes.

### **Linkage maps**

In 1994, the first whole-genome linkage maps of cattle were released which contains over 200 and 300 polymorphic markers respectively, with an average interval between markers >10 cM (Bishop *et al.*, 1994). A significant advancement in cattle linkage mapping have been achieved by setting up of the USDA-MARC linkage map, comprising of around 1,200 polymorphic markers with an average spacing of 2.5 cM and a total genome length of 2,990 cM (Kappes *et al.*, 1997). This map enhanced the effectiveness of quantitative trait loci (QTL) discovery and served as the foundation for the integration of four linkage maps (Bishop *et al.*, 1994; Georges *et al.*, 1995; Ma *et al.*, 1996). An addition of 2,277 microsatellite markers was one of the next notable improvements of the MARC map which resulted in the generation of a 3,802-microsatellite map with an average interval between markers of 1.4 cM (Ihara *et al.*, 2004). Later the sequence cattle genome became accessible, hence, the cattle linkage maps were enriched for dual allele SNP markers. For instance, Arias *et al.* (2009) published 6,924 SNP markers of a cattle linkage map from Affymetrix 10K bovine SNP array. On this high-resolution linkage map, the average marker spacing is 1 cM, while the genome's total length is 3,249 cM. This map was incorporated with the latest construct of the cattle genome assembly (Btau 1534



4.0) and impart a direct link between mapped QTL intervals and actual genome regions.

### **Current status of the livestock genomes**

In 2001, while the initial version of the human genome sequence was delivered, the initial sequences of the genomes of the livestock such as cow, chicken, pigs, etc, were not available for several years. Despite the fact that complete genomes can be sequenced using a variety of techniques, all of them eventually generate a pool of millions of short (75-150 bp) or long (>500 bp) sequence reads. Identification and assembly of overlapping sequences into larger fragments called contigs is the initial step in characterizing a genome and will eventually be used to reconstruct the sequence of whole chromosomes. For this, new bioinformatic software capable of handling these huge data sets had to be created and installed. The initial genome drafts in all species had a number of gaps that resulted in incomplete chromosomes. However, as newer versions were made available, these gaps were gradually filled in. The exception is the chicken genome, which is structured in 38 autosomes, many of which are relatively small and uniform in size, often termed microchromosomes. Even in the latest version of the genome, There are some that haven't been assembled or partially assembled due to several properties such as %GC, gene density and repeat density (Warren *et al.*, 2017). In this species, linkage groups estimated from linkage maps are still of use to study genes located in these missing regions.

### **Sheep gene mapping**

The sheep genome has a medium-density linkage map that has been developed. With the previous sheep linkage map, marker data for 550 additional loci were created. The new map has 1093 markers representing 1062 distinct loci, covers 3500 cM (sex-averaged) for the autosomes, and 132 cM (female) on the X chromosome. There are 941 anonymous loci and 121 genes in the new map. The sheep linkage map consists strong links to both the cattle and goat maps. There are 572 loci on the sheep linkage map that have also been mapped using linkage analysis in cattle, and there are 209 loci on the sheep linkage map that have also been mapped using linkage analysis in goats. In accordance with ruminant linkage maps, the current sheep linkage map's genomic coverage is comparable to that of the available cattle maps. The sheep map is a vital resource for the global sheep, cow and goat gene mapping community.

### **Goat gene mapping**

One of the first species of livestock to be domesticated, the goat is significant on both a cultural and economic level around the world. ARS1 known as the current goat reference genome, is reported as the first nonhuman genome assembly using 69x PacBio sequencing. However, the X and Y



chromosome scaffolds of ARS1 have become incomplete and highly fragmented. The first goat reference genome (CHIR\_1.0) was created from a female Yunnan black goat in 2013 (Dong *et al.*, 2013), followed by minor (CHIR\_1.1) and major (CHIR\_2.0) changes in 2014 (Du *et al.*, 2014). Gene mapping and marker-assisted breeding in goats have benefited greatly from the use of CHIR\_1.0, which is the first application of optical mapping technology being applied to genome assembly scaffolding. This genome assembly further enabled the design of the first 50K GoatSNP50 chip (Tosser-Klopp *et al.*, 2014). The chip has been extensively used to study genetic diversity and its effect on phenotypic variation in domestic goats (Bertolini *et al.*, 2018; Nazari-Ghadikolaei *et al.*, 2018).

### **Pig gene mapping**

Over 98% of the euchromatin of the 18 pig autosomes with the X chromosome along with localized coverage on Y is represented in 172 contigs, with chromosome 13 (218 Mb) represented by a single contig. The map is accessible through pre-Ensembl, where it links to marker and sequence data can be found.

### **Cattle gene mapping**

Construction of the cattle genome in recent published reports has ~90% of the cattle genome sequence placed on 29 autosomes and chromosome X, where 2.87 Gb is the estimated amount of the cattle genome. Moderate-resolution cattle linkage maps were extensively used in an entire genome investigation for QTL governing milk production traits in Holstein cattle (Georges *et al.*, 1995; Keele *et al.*, 1999). Furthermore, utilizing dairy cattle from the Finnish Ayrshire breed, 31 chromosomal areas impacting milk production QTLs were discovered (Viitala *et al.*, 2003). A number of monogenic disorders were identified by combining data from genetic linkage maps with genome-wide association analyses. For instance, a missense mutation in the bovine ATP2A1 gene has been linked to congenital pseudomyotonia in Chianina cattle, and it could be conceivable to use this species as a model for human Brody disease (Drögemüller *et al.*, 2008). In order to connect radiation hybrid linkage groupings to cow chromosomes, the USDA-MARC map was also utilised (Everts-van der Wind *et al.*, 2004).

### **Gene annotation in the livestock genomes**

Annotating the genetic elements under each genome is necessary for building a genomic map. The first features to be mapped to the genomes were the protein-coding genes. Currently, most animal genomes have almost all of their protein-coding genes annotated. Exception is the chicken genome, where 360 genes are still missing in the current annotation, which most likely map to unassembled microchromosomes (Warren *et al.*, 2017). Wherein, the mapping of non-coding (nc) genes is still at



its initial stages, particularly in farm animals. ncRNAs can be classified into small ncRNAs (usually <200 nucleotides long) and long ncRNA (usually >200 nucleotides long) molecules based on the length of the transcripts. Small ncRNA can be divided into further categories, although probably the best characterized are the family of microRNA (miRNA) genes (Wright, 2014). These genes comprise a group that, after being transcribed and processed, produces brief dsRNA structures, typically 21 nucleotides long. Up to ten miRNAs can co-express from polycistronic clusters where over 80% of miRNA genes map (Hausser and Zavolan, 2014). They are likely the best annotated class of nc-genes in the farm animal genomes as a result of this helping with their mapping. Another type of gene mapped to the genome is pseudogenes. In total, there are many transcripts produced by protein-coding genes, non-coding genes and pseudogenes (20,000-50,000 in farm animals, but close to 200,000 in humans). The information on alternative transcripts and projected proteins produced by each gene is also included in the most recent genomic maps.

### Conclusion

Genetic mapping is an illustration of how genes and other genetic elements are distributed throughout the genome of a single species. Two methods namely physical and genetic linkage mapping are used to identify gene location. Additionally somatic cell hybrid maps also provide information about the chromosomal assignments of gene marker. The current gene mapping status of chicken, sheep, goat, pig and cattle were mentioned above. Most animal genomes have almost all of their protein-coding genes annotated. Wherein, the mapping of nc-genes is still at its initial stages, particularly in farm animals. Advancement in genomic technologies, such as next-generation sequencing and high-throughput genotyping have enabled the generation of high-density genetic maps for various livestock species. These maps have made it easier for researchers to pinpoint the parts of the genome linked to critical characteristics like growth, the quality of meat, and resistance to disease.

### References

- Cohen-Zinder, M., Seroussi, E., Larkin, D.M., Loor, J.J., Everts-van der Wind, A., Lee, J.H., Drackley, J.K., Band, M.R., Hernandez, A.G., Shani, M., Lewin, H.A., Weller, J.I. and Ron, M. (2005). Identification of a missense mutation in the bovine ABCG2 gene with a major effect on the QTL on chromosome 6 affecting milk yield and composition in Holstein cattle. *Genome Research*, **15**(7): 936-944.
- Heuertz, S. and Hors-Cayla, M.C. (1978). Bovine chromosome mapping with the cell hybridization technic. Localization on the X chromosome of glucose-6-phosphate dehydrogenase, phosphoglycerate kinase, alpha-galactosidase A and hypoxanthine phosphoribosyltransferase. *Annales de Genetique*, **21**: 197-202.
- Womack, J.E. and Moll, Y.D. (1986). Gene map of the cow: conservation of linkage with mouse and man. *Journal of Heredity*, **77**: 2-7.





- Itoh, T., Takasuga, A., Watanabe, T. and Sugimoto, Y. (2003). Mapping of 1400 expressed sequence tags in the bovine genome using a somatic cell hybrid panel. *AnimalGenetics*, **34**: 362-370.
- Kappes, S.M., Keele, J.W., Stone, R.T., McGraw, R.A. and Sonstegard, T.S. (1997). A second-generation linkage map of the bovine genome. *GenomeResearch*, **7**: 235-249.
- Laurent, P., Elduque, C., Hayes, H., Saunier, K. and Eggen, A. (2000). Assignment of 60 human ESTs in cattle. *Mammalian Genome*, **11**: 748-754.
- Bishop, M.D., Kappes, S.M., Keele, J.W., Stone, R.T. and Sunden, S.L. (1994). A genetic linkage map for cattle. *Genetics*, **136**: 619-639.
- Georges, M., Nielsen, D., Mackinnon, M., Mishra, A. and Okimoto, R. (1995). Mapping quantitative trait loci controlling milk production in dairy cattle by exploiting progeny testing. *Genetics*, **139**: 907-920.
- Ma, R.Z., Beever, J.E., Da, Y., Green, C.A. and Russ, I. (1996). A male linkage map of the cattle (*Bos taurus*) genome. *Journal of Heredity*, **87**: 261-271.
- Ihara, N., Takasuga, A., Mizoshita, K., Takeda, H. and Sugimoto, M. (2004). A comprehensive genetic map of the cattle genome based on 3802 microsatellites. *Genome Research*, **14**: 1987-1998.
- Arias, J.A., Keehan, M., Fisher, P., Coppieters, W. and Spelman, R. (2009). A high density linkage map of the bovine genome. *BMC Genetics*, **10**: 18.
- Warren, W.C., Hillier, L.W., Tomlinson, C., Minx, P., Kremitzki, M., Graves, T., Markovic, C., Bouk, N., Pruitt, K.D., Thibaud-Nissen, F., Schneider, V., Mansour, T.A. and Cheng, H.H. (2017). A new chicken genome assembly provides insight into avian genome structure. *G3 (Bethesda, Md.)*, **7**(1): 109-117.
- Dong, Y., Xie, M., Jiang, Y., Xiao, N., Du, X. and Zhang, W. (2013). Sequencing and automated whole-genome optical mapping of the genome of a domestic goat (*Capra hircus*). *Genetics Selection Evolution*, **31**: 135-41.
- Du, X., Servin, B., Womack, J.E., Cao, J., Yu, M. and Dong, Y. (2014). An update of the goat genome assembly using dense radiation hybrid maps allows detailed analysis of evolutionary rearrangements in Bovidae. *BMC Genomics*, **15**: 625.
- Tosser-Klopp, G., Bardou, P., Bouchez, O., Cabau, C., Crooijmans, R. and Dong, Y. (2014). Design and characterization of a 52K SNP chip for goats. *PLoS One*, **9**: e86227
- Bertolini, F., Cardoso, T.F., Marras, G., Nicolazzi, E.L., Rothschild, M.F. and Amills, M. (2018). Genome wide patterns of homozygosity provide clues about the population history and adaptation of goats. *Genetics Selection Evolution*, **50**: 59.
- Nazari-Ghadikolaei, A., Mehrabani-Yeganeh, H., Miarei-Aashtiani, S.R., Staiger, E.A., Rashidi, A. and Huson, H.J. (2018). Genome-wide association studies identify candidate genes for coat color and mohair traits in the Iranian Markhoz goat. *Frontiers in Genetics*, **9**: 105.
- Keele, J.W., Shackelford, S.D., Kappes, S.M., Koohmaraie, M. and Stone, R.T. (1999). A region on bovine chromosome 15 influences beef longissimus tenderness in steers. *Journal of AnimalScience*, **77**: 1364-1371.
- Viitala, S.M., Schulman, N.F., de Koning, D.J., Elo, K. and Kinoshita, R. (2003). Quantitative trait loci affecting milk production traits in Finnish Ayrshire dairy cattle. *Journal of Dairy Science*, **86**: 1828-1836.
- Drögemüller C, Drögemüller M, Leeb T, Mascarello F, Testoni S. (2008). Identification of a missense mutation in the bovine ATP2A1 gene in congenital pseudomyotonia of Chianinacattle: an animal model of human Brody disease. *Genomics*, **92**: 474-477.
- Everts-van der Wind, A., Kata, S.R., Band, M.R., Rebeiz, M. and Larkin, D.M. (2004). A 1463 gene



cattle human comparative map with anchor points defined by human genome sequence coordinates. *Genome Research*, **14**: 1424-1437.

Wright, M.W. (2014). A short guide to long non-coding RNA gene nomenclature. *Human Genomics*, **8**: 7.

Hausser, J. and Zavolan, M. (2014). Identification and consequences of miRNA-target interactions--beyond repression of gene expression. *Nature Reviews Genetics*, **15**(9): 599-612.

