Noelle E. Cockett, Chittaranjan Kole (Editors)

Genome Mapping and Genomics in Domestic Animals

With 49 Illustrations, 12 in Color

Springer
Preface to the Series

The deciphering of the sequence of a gene for the first time, the gene for bacteriophage MS2 coat protein to be specific, by Walter Fiers and his coworkers in 1972 marked the beginning of a new era in genetics, popularly known as the genomics era. This was followed by the complete nucleotide sequence of the same bacteriophage in 1976 by the same group; DNA sequencing of another bacteriophage (Φ-X174) in 1977 by Fred Sanger, Walter Gilbert, and Allan Maxam, working independently; and first use of any DNA marker in gene mapping in 1980 for the human system by David Botstein. These landmark discoveries were immediately embraced by the life science community and were followed by an array of elegant experiments leading to the development of several novel concepts, tools, and strategies for elucidation of genes and genomes of living organisms of academic and economic interests to mankind.

The last two decades of the twentieth century witnessed the invention of the polymerase chain reaction; several types of molecular markers; techniques of cloning large DNA segments in artificial chromosomes; approaches to isolate and characterize genes; and tools for high-throughput sequencing, to name just a few. Another noteworthy development had been the formulation of different computer software to analyze the huge amount of data generated by genome mapping experiments, and above all deployment of information technology to store, search, and utilize enormous amounts of data particularly of cloned genes, transcripts, ESTs, proteins, and metabolites. This sweet and swift marriage of biology and information technology gave birth to bioinformatics and the new “omics” disciplines such as genomics, transcriptomics, proteomics, and metabolomics.

The tide of genome mapping and genomics flooded all phyla of the animal kingdom and all taxa of the plant kingdom and most obviously the prokaryotes. In the animal systems, we already had the gene sequence for the CFTR protein in humans in 1989; genome sequence of the model organism Caenorhabditis elegans in 1998; genetic maps of many higher animals with map positions of genes and gene-clusters during the nineties. We also happily witnessed the beginning of genome sequencing projects of three domestic animals (cow, dog, and horse) and poultry in 1993. All these achievements and endeavors culminated in the whole-genome sequence of the fruit-fly Drosophila, the garden pea of the animal system, in 2000 declaring a successful and pleasant ending of the genome science efforts of the twentieth century. The new millennium in 2001 started with the publication of the draft sequence of the human genome on February 15th by The International Human Genome Mapping Consortium and on February 16th by The Celera Genomics Sequencing Team.

A flurry of new concepts and tools in the first few years of the first decade of the twenty-first century has enriched the subject of genomics and the field has broadened to include the young and fast-growing disciplines of structural genomics, functional genomics, comparative genomics, evolutionary genomics, and nutraceutical genomics, to name just a few. We now have more, faster, cheaper, and cleverer mapping and sequencing strategies, association mapping and the 454 for example; several tools, such as microarrays and cDNA-AFLP to
isolate hundreds of known and unknown genes within a short period, elegantly assisted by transcript-profiling and metabolic-profiling; identifying new genes from the knowledge-base of homologous genomes; and precise depiction of the road map of evolution of human and other members of the animal kingdom and their phylogenetic relationships with members of other species or genera. Within less than a decade of the deciphering of the first complete genome sequence for an animal species in 1998, we have complete sequences of some seventeen species of the animal kingdom including nematodes (2), arthropods (4), domestic animals and poultry (2), marsupial (1), wild animals (2), aquatic animals (4), human (1), and non-human primate (1). Many more genome mapping projects are progressing rapidly and their results are expected to be published soon.

The list of achievements in the fields of genome mapping and genomics in human and other members of the animal kingdom is enormous. It is also true that in today's world, in the global village of the new millennium, we have access to almost all information regarding the initiation, progress, and completion of all endeavors of animal genome sciences and can enrich our knowledge of the concepts, strategies, tools, and outcomes of the efforts being made in animal genome mapping and genomics. However, all this information is dispersed over the pages of periodicals, reviews on particular types of animals or their specific groups in hard copy versions, and also in electronic sources at innumerable links of web pages for research articles, reports, and databases. But we believe that there should be a single compilation, in both hard copy and electronic versions, embodying the information on the work already done and to be done in the fields of genome mapping and genomics of all members of the animal kingdom that are of diverse interests to mankind: academic, health, company, or environment.

We, therefore, planned for this series on Genome Mapping and Genomics in Animals with five book volumes dedicated to Arthropods; Fishes and Aquatic Animals; Domestic Animals; Laboratory Animals; and Human and Non-Human Primates. We have included chapters on the species for which substantial results have been obtained so far. Genomes of many of these species have been sequenced or are awaiting completion of sequencing soon. Overview on the contents of these volumes will be presented in the prefaces of the individual volumes.

It is an amazingly interesting and perplexing truth that only four nucleotides producing only twenty amino acids in their triplet combination could create anywhere between five to thirty million species of living organisms on the earth. An estimated number of about a half million vertebrate animal species have been described so far! Genomes of the few animal species from this enormous list that we know today are also too diverse to elucidate. It is therefore daring to edit a series on depiction of the diverse genomes we are presenting in over sixty chapters in the five volumes. Seven globally celebrated scientists with knowledge and expertise on different groups of animal systems, and human and non-human primates provided me with the inspiration and encouragement to undertake the job of the series editor. Wayne (Wayne B. Hunter), Tom (Thomas D. Kocher), Noelle (Noelle E. Cockett), Paul (Paul Denny), Ravi (Ravindranath Duggirala), Tony (Anthony G. Comuzzie), and Sarah (Sarah Williams-Blangero) were always available for consultations and clarifications on any aspect while editing the manuscripts of this series. During working on this series, I have been a student first, a scientist second, and an editor third and last, with the mission to present a comprehensive compilation of animal genome mapping and genomics to the students, scientists, and industries currently involved and to be involved in the study and practice of animal genome sciences.
I express my thanks and gratitude as a humble science worker to these seven volume editors for giving me an opportunity to have an enriching and pleasant view of the wide canvas of animal genome mapping and genomics. I also extend my thanks and gratitude to all the scientists who have generously collaborated with their elegant and lucid reviews on the rationale, concepts, methodologies, achievements, and future prospects of the particular systems they are working on, and for the subtle touches of their own experiences and philosophies.

As expected, the editing jobs of this series comprised communication with the volume editors, authors, and publishers; maintenance of the files in hard and soft copies; regular internet searches for verification of facts and databases; and above all maintenance of an environment to practice and enjoy science. My wife Phullara, our son Sourav, and our daughter Devleena were always with me on my travels as a small science worker on a long road of “miles to go before I sleep,” not only for the successful completion of this series but also in all my efforts for teaching, research, and extension wherever I worked and stayed in my life.

We have already completed a seven-volume series on Genome Mapping and Molecular Breeding in Plants with Springer that has been very popular among students, scientists, and industries. We are also working on a series on Genome Mapping and Genomics in Microbes with Springer. It was, is, and will be enriching and entertaining to work with the experienced and wonderful people involved in the production of this series, including Sabine (Dr. S. Schwarz) and Jutta (Dr. J. Lindenborn) among many from the Springer family. I record my thanks and gratitude to them, here (and also submit in the databanks for future retrieval) for all their timely co-operation and advice when publishing these volumes.

I trust and believe that we must have missed deliberations on many significant animal species and left many mistakes on the pages of these volumes. All these lapses are surely mine, and all the credits must go to the volume editors, the authors, and the publisher. In the future these errors will be rectified on receipt of suggestions from the readers, and also there will be further improvement of the contents and general set-up of the volumes of this series.

Clemson Chittaranjan Kole

January 10, 2008
Preface to the Volume

Over the past century, humans have used an expanding knowledge of genetics to improve the functionality and wellbeing of animals. The field of quantitative genetics has led to the selection and breeding of domesticated animals possessing superior genes for desirable traits. Enhanced animal selection, as well as a clearer understanding of the genes and genetic regulation underlying traits, is now possible through the study of genomics.

The nine chapters in this volume focus on genome mapping and genomics research that has been conducted in domesticated and farm species. Topics include the development of genome maps, descriptions of available genomic resources, phylogenetic analyses, domestication patterns, and genetic control of traits. While each chapter serves as a stand-alone description of genomics for that particular species, when read as a whole, the breadth of the research in domesticated and farm species is remarkable, particularly in the light of the limited funding, resources, and personnel as compared to the investment on humans and laboratory species. These limitations have resulted in the development of collaborations and consortiums that cross the globe. Clearly, the pooling of funding and expertise has expanded genomic resources for these species, and allowed prioritization of needs through a collective and iterative process.

While not all domesticated and farm species are included in the volume, the ones that are described here allow a comparison of the outcomes and approaches that were used across the various species. To encapsulate, the amount of genomics research that has occurred to date differs dramatically across the species. For example, there are only a limited number of molecular markers and a rudimentary genome map in cervids and water buffalo while full genome sequences are publicly available for cattle, chickens and dogs. And while there are limited outcomes from the research in some species, the impact of genomics research in livestock and domestic species has resulted in critical information. Direct outcomes have been the identification of genetic regions and in some cases, the causative mutation, that control a spectrum of traits including fertility, reproduction, growth rate and efficiency, milk production, carcass quality and composition, fitness, immune function, and disease traits. This progress is remarkable given that it has only been since the early 1990s, when genome linkage maps containing molecular markers were developed, that genome-wide studies for economic trait loci became feasible.

Comparative genomics is a critical component in the advancement of genomics for livestock and domesticated species. Anchoring the genome of one species to another has allowed an exchange of information and resources, particularly important when one of the species has limitations in funding and researchers, or is at an earlier stage in the discovery process. In addition to leveraging resources across species, an equally important outcome of the comparative genomic efforts is the comparison of locus order in mammalian species, providing additional information for understanding chromosomal evolution.

As mentioned, whole genome sequences for several species are now available or soon to be available, including cattle, dogs, chickens, horses and swine. Certainly
a fully sequenced genome will advance the progress of research in every species but the utilization and impact of genomics resources is tempered by the number of active scientists working on that particular species. The economic impact of a species is also a major determinant of the emphasis placed on genomics resources. Several farm species, such as sheep and rabbits, are now used as models for biomedical studies, which has increased attention on securing genomics information.

It is important to note that the genomics research being conducted on these species is not static. With each passing week, more information is added. Therefore, the chapters included in this volume serve as a “snapshot” of the existing information available at the time that the chapter was written. Each author has included a section that highlights areas of future work and needs.

It has been a pleasure to work with the 23 authors who have contributed the chapters in this volume. These authors were invited to participate because they are experts within their field of study. As expected, they have added their own style and interpretation to the work conducted in their assigned species. The authors are affiliated with institutions from around the world, highlighting the global impact of the work being conducted. We appreciate the hard work and perseverance of the authors in the preparation of their chapters and contribution to the volume.

Logan, UT, USA
Clemson, SC, USA
April 15, 2008

Noelle E. Cockett
Chittaranjan Kole
Contents

Contributors

1 Cattle
M. D. MacNeil, J. M. Reecy, D. J. Garrick

1.1 Introduction
1.1.1 History
1.1.2 Economic Importance
1.2 Molecular Genetics
1.2.1 Genetic-Mapping Resources
1.2.2 Quantitative Trait Loci
1.2.3 Using Genotypes in Breeding Cattle
1.3 Future Scope of Work

References

2 Water Buffalo
L. Iannuzzi and G. P. Di Meo

2.1 Introduction
2.1.1 Taxonomic Description
2.1.2 Economic Importance
2.1.3 Breeding Objectives
2.2 Molecular Genetics
2.2.1 Classical Mapping Efforts
2.2.2 Construction of Genetic Maps and Comparative Mapping
2.3 Future Scope of Work

References

3 Sheep
C. A. Bidwell, N. E. Cockett, J. F. Maddox and J. E. Beever

3.1 Introduction
3.1.1 Economic and Biomedical Importance
3.1.2 History
3.1.3 The Sheep Karyotype
3.2 Molecular Genetics
3.2.1 Linkage Maps
3.2.2 Mapped Traits in Sheep
3.2.3 Resources for Mapping and Sequencing the Ovine Genome
3.3 Future Scope of Work

References

4 Deer
Richard J. Hall

4.1 Introduction
4.1.1 Taxonomic Description
4.1.2 Economic Importance
4.1.3 Karotype of Cervids
5 Poultry
Michael N. Romanov Alexei A. Sazanov, Irina Moiseyeva, and Aleksandr F. Smirnov

5.1 Introduction
5.1.1 Brief History and Zoological Description
5.1.2 Chickens
5.1.3 Economic Importance and Nutritional Value
5.1.4 Breeding Objectives

5.2 Classic Genetics
5.2.1 Brief History of Poultry Genetics
5.2.2 Early Classical Mapping Efforts
5.2.3 First Chicken Map
5.2.4 Subsequent Classical Mapping

5.3 Molecular Genetics and Whole-Genome Sequence
5.3.1 First-generation Molecular Maps
5.3.2 Physical Maps
5.3.3 Whole-Genome Sequence
5.3.4 Chicken Genome and Sequence Features
5.3.5 Genetics and Molecular Mapping in Other Birds

5.4 QTL and Functional Genomics
5.4.1 QTL Analysis
5.4.2 QTL: Growth, Meat Quality, and Productivity
5.4.3 QTL: Egg Quality and Productivity
5.4.4 QTL: Disease Resistance
5.4.5 QTL: Behavior
5.4.6 Toward Functional Genomics of Poultry

5.5 Other Molecular Applications
5.5.1 Biodiversity Studies
5.5.2 Molecular Sexing

5.6 Conclusions

References
6.2 Construction of Genetic Maps ........................................... 148
6.2.1 Genetic Markers .................................................. 148
6.2.2 Primary Genetic Linkage Maps .................................. 151
6.2.3 Second-generation Linkage Map ................................. 151
6.2.4 Integrative Mapping ............................................... 153
6.2.5 Comparative Mapping ............................................. 154
6.2.6 Other Comparative Studies ..................................... 155
6.2.7 Physical Mapping .................................................. 157
6.2.8 The Next-Generation Physical Maps ......................... 157
6.3 Advanced Works, Functional Genomics ............................... 158
6.3.1 ESTs, Microarrays, and SAGE .................................. 158
6.3.2 Candidate Gene Mapping ......................................... 159
6.4 Conclusion ............................................................ 160
References ................................................................. 160

7 Rabbit
Claire Rogel-Gaillard, Nuno Ferrand, and Helene Hayes .......... 165
7.1 Introduction .......................................................... 165
7.1.1 History ............................................................ 165
7.1.2 Taxonomic Position ............................................... 165
7.1.3 Physical Characteristics ......................................... 166
7.1.4 Breeds ............................................................. 166
7.1.5 Domestication, Phylogeny, and Genetic Diversity .............. 167
7.1.6 Economic Importance ............................................ 171
7.2 Molecular Genetics .................................................... 175
7.2.1 Cytogenetics ...................................................... 175
7.2.2 Genetic Molecular Markers ..................................... 176
7.2.3 Physical Mapping Tools ......................................... 204
7.2.4 Sequencing Data ............................................... 204
7.2.5 Bioinformatics Tools ............................................. 205
7.2.6 Expected Tools and Development .............................. 206
7.2.7 Genome Mapping ............................................... 206
7.3 Future Scope of Work ............................................... 220
7.3.1 Using Rabbits to Study the Domestication Process .......... 220
7.3.2 Using Rabbits to Study Color Patterns ......................... 220
7.3.3 Using Rabbits to Study Early Embryonic Development .... 220
7.3.4 Using Rabbits to Produce Embryonic Stem Cells and Validate Candidate Genes ............................................ 221
7.3.5 Perspectives of the Rabbit as a Farm Animal ............... 221
References ................................................................. 223

8 Dog
D.S. Mosher, T.C. Spady, and E.A. Ostrander ...................... 231
8.1 Introduction .......................................................... 231
8.1.1 Dog Breeds ...................................................... 231
8.1.2 Genetic Diversity and Dog Breeds .............................. 233
8.1.3 The Superfamily Canoidae ..................................... 234
8.1.4 Mitochondrial DNA (mtDNA) Analysis of Canids ............ 234
8.1.5 The Domestic Dog Population ................................ 236
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.2</td>
<td>Molecular Genetics of Dogs</td>
<td>237</td>
</tr>
<tr>
<td>8.2.1</td>
<td>Canine Linkage and Radiation Hybrid Maps</td>
<td>237</td>
</tr>
<tr>
<td>8.2.2</td>
<td>Comparative Maps</td>
<td>238</td>
</tr>
<tr>
<td>8.2.3</td>
<td>Survey Sequence and a Canine Gene Map</td>
<td>239</td>
</tr>
<tr>
<td>8.2.4</td>
<td>The 7.5x Canine Genome Sequence</td>
<td>240</td>
</tr>
<tr>
<td>8.2.5</td>
<td>Single Gene Traits</td>
<td>241</td>
</tr>
<tr>
<td>8.2.6</td>
<td>Complex Traits</td>
<td>244</td>
</tr>
<tr>
<td>8.2.7</td>
<td>Resources</td>
<td>249</td>
</tr>
<tr>
<td>8.3</td>
<td>Future Scope of Work</td>
<td>250</td>
</tr>
<tr>
<td>References</td>
<td></td>
<td>251</td>
</tr>
</tbody>
</table>

9 Pig

9.1 Introduction | 257
9.1.1 History and Description | 257
9.1.2 Economic Importance | 258
9.1.3 Breeding Objectives | 258
9.2 Molecular Genetics of Pigs | 259
9.2.1 Genetic Maps | 259
9.2.2 Physical and RH Maps | 260
9.2.3 Pig–Human Comparative Maps | 260
9.2.4 Quantitative Trait Loci | 261
9.2.5 Candidate Gene Discovery | 262
9.2.6 Marker-Assisted Breeding | 264
9.3 Functional Genomics | 265
9.3.1 Expressed Sequence Tags | 265
9.3.2 DNA Microarrays | 265
9.4 Future Scope of Work | 266
9.4.1 Swine Genome Sequencing | 266
9.4.2 Expression QTL | 266
9.4.3 Conclusion | 268
References | 268
Contributors

J.E. Beever
Department of Animal Sciences
University of Illinois
220 Edward R. Madigan Laboratory
1201 West Gregory Drive
Urbana, IL 61801, USA

C.A. Bidwell
Purdue University
Department of Animal Sciences
125 South Russell Street
West Lafayette
IN 47907–2042, USA
cbidwell@purdue.edu

N.E. Cockett
Department of Animal Dairy & Veterinary Sciences
Utah State University
Logan, UT 84322–4700, USA

c.W. Ernst
Department of Animal Science
3385 Anthony Hall
Michigan State University
East Lansing, MI 48824, USA
ernstc@msu.edu

N. Ferrand
CIBIO, Centro de Investigação em Biodiversidade e Recursos Genético
Campus Agrário de Vairão
4485-661 Vairão, Portugal

and
Departamento de Zoologia e Antropologia
Faculdade de Ciências, Universidade do Porto
Praça Gomes Teixeira, 4099-002 Porto
Portugal

D.J. Garrick
Department of Animal Science
Iowa State University
Ames, IA 50011, USA

R.J. Hall
AgResearch Ltd.
Invermay
Agricultural Centre
Private Bag 50034, Mosgiel 9053
New Zealand
Richard.Hall@esr.cri.nz

H. Hayes
INRA, UR339 Unité de Génétique biochimique et Cytogénétique
F-78350 Jouy-en-Josas, France

L. Iannuzzi
National Research Council (CNR)
Institute of Animal Production Systems in the Mediterranean Environments (ISPAAM)
Laboratory of Animal Cytogenetics and Gene Mapping
Naples, Italy
leopoldo.iannuzzi@ispaam.cnr.it

M.D. MacNeil
USDA
Agricultural Research Service
Miles City, MT 59301, USA
mike@larrl.ars.usda.gov

J.F. Maddox
Department of Veterinary Science
University of Melbourne, Victoria 3010
Australia
I. Moiseyeva  
N.I. Vavilov Institute of General Genetics  
Russian Academy of Sciences  
Gubkin Street 3  
Moscow, GSP-1, 119991, Russia  

D.S. Mosher  
National Human Genome Research Institute,  
National Institutes of Health  
50 South Drive  
MSC 8000, Building 50, Room 5334  
Bethesda, MD 20892-8000, USA  

E.A. Ostrander  
National Human Genome Research Institute,  
National Institutes of Health  
50 South Drive MSC 8000,  
Building 50, Room 5334  
Bethesda, MD 20892-8000, USA  
eostrand@mail.nih.gov  

G. Pia Di Meo  
National Research Council (CNR)  
Institute of Animal Production Systems in the Mediterranean Environments (ISPAAM)  
Laboratory of Animal Cytogenetics and Gene Mapping  
Naples, Italy  

A.M. Ramos  
Department of Animal Science  
3385 Anthony Hall  
Michigan State University  
East Lansing, MI 48824, USA  

J.M. Reecy  
Department of Animal Science  
Iowa State University  
Ames, IA 50011, USA  

K.M. Reed  
Department of Veterinary and Biomedical Sciences  

College of Veterinary Medicine  
University of Minnesota  
St. Paul, MN 55108, USA  
reedx054@tc.umn.edu  

C. Rogel-Gaillard  
INRA CEA, UMR314 Laboratoire de Radiobiologie et Etude du Génome  
F-78350 Jouy-en-Josas, France  
claire.rogel-gaillard@jouy.inra.fr  

M.N. Romanov  
CRES – Conservation and Research for Endangered Species  
Zoological Society of San Diego  
Arnold and Mabel Beckman Center for Conservation Research  
15600 San Pasqual Valley Road  
Escondido, CA 92027-7000, USA  
mromanov@sandiegozoo.org  

A.A. Sazanov  
All-Russian Institute of Animal Genetics and Breeding  
Russian Academy of Agricultural Science  
Moskovskoye shosse 55A, St Petersburg, Pushkin 189620  
Russia  

A.F. Smirnov  
Biological Research Institute  
St Petersburg State University  
Oranienbaumskoye shosse 2  
St Petersburg, Stary Petergof 198504  
Russia  

T.C. Spady  
National Human Genome Research Institute,  
National Institutes of Health  
50 South Drive  
MSC 8000, Building 50, Room 5334  
Bethesda, MD 20892-8000, USA
CHAPTER 1

Cattle

Michael D. MacNeil¹, James M. Reecy, and Dorian J. Garrick²

¹ USDA, Agricultural Research Service, Miles City, MT 59301, USA, mike.macneil@ars.usda.gov
² Department of Animal Science, Iowa State University, Ames, IA 50011, USA

1.1 Introduction

1.1.1 History

All contemporary cattle are thought to have been domesticated from the now extinct aurochs, *Bos primigenius*. Evidence from mitochondrial DNA indicates divergence of two cattle taxa, *Bos indicus* and *Bos taurus*, more than 100,000 years ago (Loftus et al. 1994; Bradley et al. 1996). These two taxa were likely domesticated independently (Grigson 1980; Loftus et al. 1994) some 10,000 years before present. Mehrgrarh, in modern-day Pakistan, is a strong candidate for the site of domestication of *Bos indicus* cattle. Catal Hüyük, Anatolia, in modern-day Turkey, is a likely site of the Near-Eastern domestication of *Bos taurus* cattle. There is further but less secure evidence for additional domestications of aurochs in the Nile Valley (Bradley et al. 1996; Troy et al. 2001) and in North East Asia (Mannen et al. 2004). These domestications are postulated to give rise to the *Bos taurus* cattle of Africa and contribute to the gene pool of cattle in Mongolia, North China, Korea, and Japan, respectively.

Immigration of *Bos indicus* cattle into Africa appears to radiate from the Horn and East Coast (Hannotte et al. 2002). This immigration may result from local Arabian contacts. Alternatively, it may have been a consequence of long-distance trade on the Indian Ocean that was also responsible for introducing other domestic species into Africa (Clutton-Brock 1993). *Bos primigenius* was distributed throughout Europe at the end of the last Ice Age, and it remains unclear whether or not all European cattle are derived from the stock domesticated in western Asia (Bailey et al. 1996). However, the dominant mitochondrial DNA haplotype in European cattle is consistent with their being of Anatolian origin (Troy et al. 2001; Kühn et al. 2005). Genetic relationships among European *Bos taurus*, African *Bos taurus*, African *Bos indicus*, and Indian *Bos indicus* are illustrated in Fig. 1 (Bradley et al. 1998).

Cattle are not indigenous to Australia, North America, and South America. Importations of cattle to these countries followed the respective patterns of human exploration and colonization. Early importations to Australia and North America were predominantly British breeds, whereas early importations to South America were mainly of Spanish origin (Rouse 1970). Subsequently, *Bos indicus* cattle were brought to the more tropical areas of these continents (Rouse 1970) and still later there were substantial importations of *Bos taurus* cattle from continental Europe (Willham et al. 1993).

1.1.2 Economic Importance

Cattle have had a central role in the evolution of human cultures with significant numbers of cattle produced in every continent except Antarctica. From an economic perspective cattle are the most important domestic animal species (Cunningham 1992). In various parts of the world, cattle provide traction, milk, and meat. Worldwide production in 2004 of beef and veal, nonfat dry milk, butter, and cheese were predicted to be 51,191; 3,486; 6,676; and 13,373 thousand metric tons, respectively (USDA 2005).

Following Lush (1945), modern paradigms for genetic improvement of livestock are commonly traced to Robert Bakewell (1725–1795) whose admonitions included: “Like produces like or the likeness of some ancestor; inbreeding produces prepotency and refinement; breed the best to the best.” Historical
breeding objectives for cattle have focused primarily on increasing yield of milk or milk components in dairy breeds and growth rate, carcass weight, and composition in beef breeds. Success of these efforts in bringing about genetic change can be illustrated by genetic trends in fluid milk production by Holstein cattle in the US (Fig. 2) and growth to weaning by Hereford cattle in Canada (Fig. 3).

Genetic selection for increased production usually, although not always, leads to increased consumption of feed and gross efficiency, while some aspect of fertility is usually impaired (Roberts 1979; MacNeil et al. 1984; Wall et al. 2003). Technology for efficient multiple-trait selection was developed by Hazel (1934) more than 70 years ago and classical applications of multiple-trait selection for dairy and beef production were put forth in the early 1970s (Norman and Dickinson 1971; Cunningham and McClintock 1974; Dickerson et al. 1974). In regions, where feed costs and land prices are high, breeding objectives have been developed and implemented for dual-purpose cattle that are raised for both milk and meat production (e.g., Niebel 1986; Bekman and van Arendonk 1993). VanRaden (2004) reviewed the changing application of multiple-trait breeding objectives to US dairy production from the early 1970s to the present. Application of multiple-trait breeding objectives and selection indexes to beef production has been relatively more recent (e.g., Ponzoni and Newman 1989; Graser et al. 1994; MacNeil et al. 1994).
Genetic improvement of cattle is complicated by relatively late attainment of puberty and low reproductive rate, long generation interval, genetic antagonisms, manifestation of economically important phenotypes late in life, and valuable phenotypes that can only be observed post-harvest. Genomic science and its application to selection have the potential to partially overcome several of these obstacles by facilitating selection decisions being made earlier in life without the usual erosion of accuracy. Objectives of this chapter are to review: (1) the current state of genetic mapping in cattle, (2) assignment of economically important phenotypes to those maps, and (3) ongoing development of breeding programs that have been implemented using molecular genetic technologies.

1.2 Molecular Genetics

1.2.1 Genetic-Mapping Resources

The first bovine genetic maps were generated using somatic cell hybrid (SCH) panels and fluorescent in situ hybridization (FISH). Heuertz and Hors-Cayla (1981) and Womack and Moll (1985, 1986) were the first reports on the use of somatic cell hybrids to develop maps of conserved synteny between bovine genes and previously mapped human homologs of these genes. A bovine/hamster somatic cell radiation hybrid panel was recently developed and used to assign 1,303 previously unassigned expressed sequence tags (ESTs) to chromosome segments (Itoh et al. 2003). Itoh et al. (2005) also used a bovine radiation hybrid panel to map 3,216 microsatellites and 2,377 ESTs. ZOO-FISH mapping has been completed, in which human chromosome-specific painting probes were hybridized to cattle chromosomes (Hayes 1995; Solinas-Toldo et al. 1995; Chowdhary et al. 1996) to produce comparative maps. However, as with somatic cell hybrid panels, gene order could not be addressed with these chromosome pairs.

There are numerous reports on the development of chromosome-specific linkage maps (e.g., Barendse et al. 1993). However, Bishop et al. (1994) were the first to report a genetic linkage map for a majority of the bovine genomes. That map was shortly followed by second-generation medium density maps (Barendse et al. 1997; Kappes et al. 1997). At present, over 3,800 simple tandem repeat polymorphisms have been mapped in cattle by linkage analysis (Ihara et al. 2004). This most recent map comprised 29 sex-averaged autosomal linkage groups and a sex-specific X-chromosome linkage group covering 3,160 centiMorgans (cM). The average interval between markers was 1.4 cM.

Radiation hybrid (RH) mapping (Goss and Harris 1975) has recently been rediscovered as an effective approach to building ordered maps of sequence-tagged sites, regardless of allelic variation. Womack et al. (1997) reported on the generation of a 5,000-rad bovine whole-genome RH panel. This RH panel has served as a resource for mapping the
expanding pool of bovine EST, for integrating the existing bovine linkage maps, and for the construction of ordered comparative maps relating the cattle genome to those of the human and mouse (Yang and Womack 1998). The main advantage of RH mapping over other methods is the straightforward positive/negative polymerase chain reaction (PCR) genotyping of RH panel clones. In addition, one can map genes without the need for polymorphisms, which is important when mapping sequences with a low rate of polymorphism (O'Brien et al. 1993). Numerous cattle chromosome-specific RH maps have been published (e.g., Womack et al. 1997; Yang et al. 1998; Rexroad and Womack 1999; Amarante et al. 2000). Subsequently, there have been several efforts to develop whole-genome radiation hybrid maps for cattle. To date, more than 4,000 microsatellites and 2,400 genes have been placed on bovine radiation hybrid maps (Band et al. 2000; Williams et al. 2002; Everts-van der Wind et al. 2004; Itoh et al. 2005). These resources will prove invaluable in the assembly of the bovine genome, which is ongoing in 2008. In addition, efforts are underway to integrate RH and linkage maps (Snelling et al. 2004).

In order to facilitate bovine gene sequencing, both bacterial artificial chromosome (BAC) and yeast artificial chromosome (YAC) libraries have been generated. Cai et al. (1995) reported construction of the first bovine BAC library. Subsequently, several other libraries have been generated (Zhu et al. 1999; Buitkamp et al. 2001; Eggen et al. 2001; http://bacpac.chori.org). Similarly, the first bovine YAC library was produced by Libert et al. (1993). Since that time, at least three other YAC libraries have been generated (Smith et al. 1996; Takeda et al. 1998; Hills et al. 1999). Over the course of the last couple of years the International Bovine BAC Map Consortium has developed a BAC fingerprint map that contains 257,912 clones in 655 contigs, and 32,885 singleton clones (http://www.ncbi.nlm.nih.gov/Genbank). The current (release 2) assembly provides 6.2x coverage of the bovine genome. Sequence data are publicly available at the following databases: GenBank (www.ncbi.nlm.nih.gov/Genbank), EMBL Bank (www.ebi.ac.uk/embl/index.html), and DNA Data Bank of Japan (www.ddbj.nig.ac.jp). The data can be viewed via NCBI's Map Viewer (www.ncbi.nlm.nih.gov), UCSC Genome Browser (www.genome.ucsc.edu), and the Ensembl Genome Browser (www.ensembl.org). Complementary single nucleotide polymorphism (SNP) discovery is ongoing by sequencing DNA from one cow from each of the Holstein, Jersey, Norwegian Red, Angus, Limousin, and Brahman breeds. As of 2008, chips to assay more than 50,000 SNP are commercially available to estimate genetic variation within and between populations of cattle. These resources will allow bovine researchers to leverage infrastructure and expertise of the broader genome research community and provide greater opportunities for biomedical research (S. Kappes, personal communication).

To aid in the assembly of the bovine genome, a composite RH/linkage map is being constructed using information from the Shirakawa-Meat Animal Research Center (MARC) linkage map (Ihara et al. 2004), Shirakawa RH map (Itoh et al. 2005), ComRad RH map (Williams et al. 2002), and the ILTX-2004 RH map (Everts-van der Wind et al. 2004). The RH/linkage composite map is constructed using CarthaGene (de Givry et al. 2005), following procedures described by Snelling et al. (2004). The current composite map represents...
9,112 markers, of which 3,919 markers are in at least two data sets, and 297 markers are common to all four data sets. The composite RH/Linkage map will be integrated with the BAC maps and assembled genomic sequence (W. Snelling, personal communication).

1.2.2 Quantitative Trait Loci

A primary objective of quantitative trait loci (QTL) detection studies in cattle is to identify markers that can be used in breeding programs through marker-assisted selection. Most QTL identification efforts have focused on milk production in dairy cattle and on carcass traits in beef cattle. There have been numerous whole-genome scans that have been implemented in both dairy and beef cattle. Investigation of candidate genes based on physiological pathways that control phenotypic expression has provided an alternative to whole-genome scans to detect genes corresponding to QTL (Rothschild and Soller 1997). Results for QTL-mapping studies may also identify critical biochemical pathways affecting various phenotypes for further investigation and manipulation.

Dairy Cattle

Geldermann (1975) and Weller et al. (1990) proposed daughter and granddaughter designs for QTL identification. These designs have been widely employed in dairy cattle, beginning with Georges et al. (1995). Populations studied originate from Finland (Elo et al. 1999; Viitala et al. 2003; Schulman et al. 2004), France (Biochard et al. 2003), Germany (Freyer et al. 2003a; Kuhn et al. 2003), the Netherlands (Spelman et al. 1996), Israel (Weller et al. 2003; Ron et al. 2004), New Zealand (Spelman et al. 1999), Norway (Klungland et al. 2001; Olsen et al. 2002), Sweden (Holmberg and Andersson-Eklund 2004), and North America (e.g., Georges et al. 1995; Zhang et al. 1998; Ashwell and Van Tassell 1999; Heyen et al. 1999; Ashwell et al. 2001, 2004). Recently, methods have been used that relax the pedigree constraints of the daughter and granddaughter designs (Chamberlain et al. 2002).

In a comprehensive review, Khatkar et al. (2004) found QTL that affected milk production identified on 20 of the 29 bovine chromosomes. Significant numbers of the detected QTL had pleiotropic effects, as may be expected given well-established genetic correlations among the phenotypes (Freyer et al. 2002, 2003b; Schrooten et al. 2004). Whether the pleiotropic QTL arise from pleiotropy at the gene level or from tight linkage is the subject of recent investigation (Freyer et al. 2004). In addition, any genetic change in milk yield without concomitant changes in protein and fat yields will result in changes in the percentages of these components. Thus, QTL identified for milk yield may have concomitant effects on composition.

Georges et al. (1995) observed that bovine chromosome 6 (BTA6) contained a QTL that influenced milk production. The presence of QTL on BTA6 associated with milk production and composition was subsequently confirmed by Kuhn et al. (1996), Spelman et al. (1996) (Fig. 4), Velmala et al. (1999), and

![Fig. 4 Interval mapping of BTA6 marker effect on milk, fat and protein yields for six families of Dutch Holstein-Friesian cattle (Spelman et al. 1996). Arrows on the X-axis indicate positions of markers](image-url)
others. As a consequence, BTA6 has been the subject of intense investigation to define the genetic basis for the QTL. These investigations have established the presence of multiple QTL regions indicating potential for several functional genes located on BTA6 to influence milk production (Ron et al. 2001; Freyer et al. 2002). Fine-mapping studies have further localized QTL on BTA6 affecting milk production (Olsen et al. 2004, 2005), and positional and functional candidate genes have been postulated (osteopontin, Schnabel et al. 2005; peroxysome proliferator-activated receptor-gamma coactivator-1 alpha, Weikard et al. 2005; ABCG2, Cohen-Zinder et al. 2005).

Coppieters et al. (1998) identified a QTL near the centromere on BTA14 with major effects on fat and protein percentages as well as milk yield (Fig. 5). The location of this QTL was subsequently resolved to a chromosome segment of approximately 5 cM (Riquet et al. 1999) and confirmed in independent populations (Heyen et al. 1999; Ashwell et al. 2001). Looft et al. (2001) found strong linkage between the QTL on BTA14 and an expressed sequence tag (EST) derived from mammary gland. Grisart et al. (2002) constructed a BAC contig corresponding to the BTA14 QTL marker interval and identified a nonconservative missense mutation in the positional candidate gene AcylCoA:diacylglycerol acyltransferase (DGAT1). Winter et al. (2001) described the association of a lysine/alanine polymorphism (K232A) in DGAT1 with milk fat content and postulated that this mutation was directly responsible for variation in milk fat content at the QTL. The effect of this polymorphism on milk production and/or composition was subsequently validated in New Zealand Jersey, Holstein-Friesian, and Ayrshire by Spelman et al. (2002), in Israeli Holstein by Weller et al. (2003), and in German Fleckvieh and Holstein by Thaller et al. (2003a). Recently, Grisart et al. (2004) presented genetic and functional data that confirmed the causality of the DGAT1 K232A mutation.

Georges et al. (1995) identified a centrally located QTL affecting milk yield on BTA20. This QTL was subsequently confirmed, the interval that contained the QTL was refined, and genes coding for the receptors of growth hormone and prolactin were proposed as positional candidate genes (Arranz et al. 1998). Additional conformation of a QTL on BTA20 that affects milk yield was provided by Mäki-Tanila et al. (1998) and Olsen et al. (2002). Subsequent dissection of the QTL revealed a substitution of tyrosine for phenylalanine in the transmembrane domain of the bovine growth hormone receptor protein that is associated with a strong effect on milk yield (Blott et al. 2003). There is also evidence to support additional QTLs for milk yield and composition that are linked to the growth hormone receptor (GHR) gene (Arranz et al. 1998; Blott et al. 2003).

Recent work has suggested additional sources of genetic variation in fat and protein yields and percentages, independent of the lysine/alanine polymorphism in DGAT1, but that are closely linked to it (Bennewitz et al. 2004). Kuhn et al. (2004) showed that alleles from the DGAT1 promoter derived from a variable number tandem repeat (VNTR) polymorphism were associated
with milk fat content in animals that were homozygous for the 232A allele and suggested that variation in the number of tandem repeats might result in variability in the transcription level of \textit{DGAT1}.

Mastitis is an inflammatory disease of the mammary gland that has considerable economic impact on dairying through treatment cost, lost production, decreased longevity, disposal of milk due to treatment with antibiotics, and additional labor. Numerous studies have mapped and confirmed QTL for somatic cell score and(or) mastitis resistance on BTA11 (Holmberg and Andersson-Eklund 2004; Schulman et al. 2004), BTA14 (Klungland et al. 2001; Schulman et al. 2002), BTA18 (Ashwell et al. 1997; Schrooten et al. 2000; Rodriguez-Zas et al. 2002; Schulman et al. 2002; Bennewitz et al. 2003; Kuhn et al. 2003), BTA21 (Rodriguez-Zas et al. 2002; Khatib et al. 2005), BTA23 (Ashwell et al. 1997; Heyen et al. 1999), and BTA27 (Klungland et al. 2001; Schulman et al. 2004). Additional QTL affecting either somatic cell score or mastitis resistance have been identified on BTA1, 3, 4, 5, 6, 7, 10, 15, 20, and 22. Schwerin et al. (2003) used mRNA differential display to identify DNA sequences that were differentially expressed in noninfected and infected quarters of a cow. The results of mRNA differential display combined with RH mapping led to the identification of four candidate genes affecting resistance to mastitis: \textit{OSTF1} on BTA8, \textit{AHCY} on BTA13, \textit{PRKDC} on BTA14, and \textit{HNRPU} on BTA16 (Schwerin et al. 2003).

In addition, other studies have evaluated potential for QTL to influence phenotypes related to reproductive rate (Kirpatrick et al. 2000; Lien et al. 2000; Ashwell et al. 2004; Cruickshank et al. 2004; Gonda et al. 2004; Ron et al. 2004), dystocia (Grupe et al. 1998), longevity (Ron et al. 2004), dairy type (Spelman et al. 1999; Connor et al. 2004; Van Tassell et al. 2004), behavior (Hiendleder et al. 2003), udder conformation (Hiendleder et al. 2003), and other diseases (Georges et al. 1993; Hanotte et al. 2003; Zhang et al. 2004). Ashwell and Van Tassell (1999) and Schrooten et al. (2000) evaluated 30 and 27 phenotypes descriptive of conformation and function, respectively. In a majority of these cases, there has yet to be substantial independent confirmation of the reported QTL. Exceptions include a putative QTL on BTA5 affecting ovulation rate or twinning which has been fine mapped by Meuwissen et al. (2002).

**Beef Cattle**

Backcross and F$_1$ designs using diverse breeds have predominated QTL identification studies in beef cattle, and several studies using the genome scan approach have successfully identified QTL that affect body composition traits, carcass yield and quality, and growth (Keele et al. 1999; Stone et al. 1999; Schmutz et al. 2000; Casas et al. 2000, 2003, 2004; MacNeil and Grosz 2002; Kim et al. 2003a, b; Li et al. 2004). These designs were developed for use with inbred lines, each homozygous for different alleles at marker loci and assumed QTL (Soller et al. 1976; Zhuchenko et al. 1979). Until recently, it was unknown to what extent these experiments were relevant within breeds. Thallman et al. (2003) reported that QTL influenced meat quality and carcass composition traits, which were identified in a two-breed backcross also segregated within breeds. Further, the resolution of these QTL was only on the order of several tens of centiMorgans. Unfortunately, to date, only one causal mutation for QTL in beef cattle (discussed later) has been identified. While comparative maps between cattle and humans can be used to identify candidate genes for testing, current maps obtained from linkage and radiation hybrid panel analyses contain numerous gaps that limit their utility. Determining the bovine genome sequence (http://www.usda.gov/news/releases/2003/12/0420.htm) will alleviate this problem.

The phenotype commonly referred to as double muscling, or more correctly as muscular hypertrophy, was first documented by Culley (1807) and has been the subject of considerable investigation in cattle (see reviews by Hanset 1981; Arthur 1995; Bellinge et al. 2005). This phenotype was mapped by Charlier et al. (1995) to within 2 cM of a marker locus on BTA2 using microsatellites genotyped across a backcross family. Smith et al. (1997) mapped the myostatin gene to a locus in the interval that was previously shown to contain the muscular hypertrophy locus and that was cytogenetically indistinguishable from it, suggesting that myostatin may be the gene causing muscular hypertrophy in cattle. Mutations in myostatin alleles common to the Belgian Blue and Piedmontese breeds were shown to confer the characteristic increase in muscle mass (Grobet et al. 1997; Kambadur et al. 1997; McPherron and Lee 1997). Pleiotropic effects on other agronomic phenotypes have also been reported (Casas et al. 1998; Short et al. 2002).
Building on previous results related to QTL for fat content of milk, a role in triglyceride synthesis (Cases et al. 1998), expression of sequence tags in bovine adipose tissue (Fries and Winter 2002), and radiation hybrid mapping to BTA14 (Womack et al. 1997), DGAT1 was suggested as a positional and functional candidate gene for intramuscular fat deposition in cattle (Thaller et al. 2003b). The chromosome regions flanking bovine DGAT1 are gene rich (Winter et al. 2004), and results from fine-mapping analyses are suggestive of yet to be identified polymorphisms affecting fat deposition (Moore et al. 2003). Also linked with DGAT1 is the gene encoding thyroglobulin (TG), whose product is a precursor of hormones affecting lipid metabolism (Barendse 1999). In the beef cattle industry, commercial tests have been designed to evaluate polymorphisms in TG and used to aid genetic improvement of marbling.

Inconsistent tenderness of beef is frequently identified by US consumers as a primary reason for dissatisfaction with beef (e.g., Huffman et al. 1996). Casas et al. (2000) and Morris et al. (2001) independently identified a QTL for shear force, an objective measure that is highly correlated with tenderness as perceived by consumers, to BTA29. The gene encoding micromolar calcium-activated neutral protease (CAPN1), which degrades myofibrillar proteins under postmortem conditions and appears to be the primary enzyme in the postmortem tenderization process (Koohmaraie 1992, 1994, 1996), was colocated with the QTL (Smith et al. 2000). Page et al. (2002) presented evidence that SNPs predicted to result in amino acid changes in the CAPN1 gene were associated with variation in meat tenderness. The utility of these markers was subsequently validated and has been developed into a commercial test to improve tenderness of beef (Page et al. 2004).

1.2.3 Using Genotypes in Breeding Cattle

Numerous simulation studies have documented theoretical potential for use of genotypic information for marker-assisted selection (MAS) to increase rate of response to selection (e.g., Soller 1978; Soller and Beckmann 1983; Lande and Thompson 1990). Results of MAS are expected to be especially favorable in multiple ovulation and embryo transfer schemes where selection can be practiced within full-sib families (Kashi et al. 1990; Ruane and Colleau, 1996; Gomez-Ray and Klemetsdal 1999). However, negative covariance between QTL and polygenes results from selection (Bulmer 1971) and may compromise response resulting from MAS in comparison with traditional selection (Gomez-Ray and Gibson 1993; Gibson 1994; Spelman and Garrick 1997). Schulman and Dentine (2005) suggested within-family two-stage selection using MAS will result in more rapid genetic gain than traditional selection and that this advantage will persist over several generations. To date, demonstrated gain in rate of genetic improvement from use of DNA-based tests for QTL is limited, because selection without markers is already quite accurate, very few QTL have been identified as of yet, and genotyping is relatively expensive (Goddard 2003).

The B-variant of the milk protein β-lactoglobulin is associated with a DNA polymorphism resulting in decreased synthesis of this protein variant in milk, leading to a decrease in whey protein concentration and an increase in casein concentration, which results in an increase in cheese yield. Tests have long been available for milk protein variants, originally based on testing for the presence of each variant in milk protein and more recently from direct DNA tests. From 1995 onward, 28 suppliers (representing 8,500 cows) belonging to a small cheese manufacturing cooperative preferentially bred females to bulls that were homozygous for the B allele at the β-lactoglobulin locus (Boland et al. 2000).

Some studies have found association between consumption of the A1 variant of β-casein and onset of insulin-dependent diabetes. In addition, there is epidemiological evidence to suggest a relationship between consumption of milk (and therefore the A1 variant of β-casein) and coronary heart disease. Subsequent studies have been unable to consistently confirm these associations (Hill et al. 2002). The studies showing a benefit of milk containing the A2 variant of β-casein have led to the formation of a New Zealand company to market milk obtained from cows that are homozygous for the A2 allele, presumably with claims as to the health benefits with regard to diabetes and heart disease. A recent agreement was reached between the New Zealand Company and a US corporation to test some 100,000 cows in the US with the aim of marketing A2 milk in 5,000 US health food stores.
Causal mutations have been identified for more than 28 genetic disorders that affect cattle (Nicholas 2003). Molecular genetic tests have been developed for several of these disorders including: bovine leukocyte adhesion deficiency (Schuster et al. 1992), uridine monophosphate synthase deficiency (Schwenger et al. 1993), and complex vertebral malformation (Grzybowski 2003). Given that every animal likely carries a few deleterious recessive alleles, it is unlikely that culling carrier bulls will be an effective solution for eliminating all genetic defects. The general philosophy has shifted from trying to eliminate carrier animals as rapidly as possible to one of a controlled reduction in allele frequency at the population level and avoidance of matings between carriers. Unpublished simulations show net industry benefit from continued use of proven carrier bulls if their genetic merit is sufficiently high, with future carrier males being discarded before progeny testing in favor of noncarrier sibs.

It has been envisioned that phenotypic and genotypic data will be combined in future genetic evaluation systems to produce marker-assisted estimates of genetic merit (Fig. 6; Thallman 2004). Cornell University currently produces a marker-assisted genetic evaluation for shear force, a quantitative measure of meat tenderness, for the American Simmental Association using phenotypes from progeny testing and genotypes at SNP316 in the CAPN1 gene (E. J. Pollak and R. L. Quaas, personal communication). In an evaluation of 120 progeny tested sires, average accuracy of the resulting estimated predicted difference (EPD) was increased from 0.26 to 0.28 by including the genotypic information. However, accuracy of a genetic evaluation computed using only the genotypic information from this single marker would be on the order of 0.05. Thus, collection of phenotype data is still a critical requirement for accurate evaluation of genetic potential.

1.3 Future Scope of Work

Over the past several years, tremendous progress has been made with respect to cloning/obtainment of putative embryonic stem cells and targeted genetic modification/homologous recombination in somatic cells (e.g., see reviews by Tian et al. 2003; Wang and Zhou 2003; Saito et al. 2004). When coupled with the sequencing of the bovine genome, it will be possible to manipulate the bovine genome in ways only previously possible in laboratory species. It is expected that these advancements will dramatically facilitate our understanding of the biology of beef and dairy cattle.

Hand in hand with these advancements are numerous bovine-specific functional genomic resources that are either available or being developed (e.g., full-length complementary DNA or cDNA clones; cDNA and long-oligo microarrays). Recent development of these resources has dramatically increased the need for bioinformatic resources, and several efforts are underway (e.g., http://www.ncbi.nlm.nih.gov/genome/guide/cow/index.html; http://bovinegenome.org/; http://www.livestockgenomics.csiro.au/; http://locus.jouy.inra.fr/cgi-bin/bovmap/intro.pl; http://www.tigr.org/microarray/; http://www.animalgenome.org/
cattle). Together these genomic, functional genomic, and bioinformatic resources will facilitate defining molecular mechanisms underlying phenotypes of interest.

Ultrahigh-throughput SNP genotyping with modest cost and mapping of haplotypes may allow association-based approaches to be applied to candidate genes, QTL regions, or serve as a basis for genome-wide scanning of cattle in a manner analogous to that envisioned by The International HapMap Consortium (2003). However, there is only marginal improvement in precision of traditional QTL mapping by linkage analysis through the use of a dense marker map (Darvasi et al. 1993). Thus, a shift from the present paradigm of searching for causative mutations underlying QTL to a breeding strategy based on molecular biology may be anticipated. Meuwissen et al. (2001) demonstrated that accurate estimates of breeding value could be obtained for animals that have no phenotypic record of their own and no progeny using a dense and complete marker map and phenotypic information from the parental and grandparental generations. This approach also facilitates shortening the generation interval and thus accelerating genetic improvement.

Dekkers and Hospital (2002) concluded that genotype-environment interaction, pleiotropy, and epistasis would make selection for complex traits solely on the basis of molecular information risky unless consequent response was confirmed by phenotypic evaluation. Mapping traits to chromosomal locations is a concomitant requirement for accurately and precisely assessing phenotypic variation. Daughter and granddaughter designs use the law of averages to reduce environmental variance in mapping QTL in dairy cattle. QTL-mapping strategies for beef cattle have relied on crosses of phenotypically diverse breeds to increase statistical power by magnifying the smallest true difference to be detected. Functional approaches are also inherently dependent on accurate and precise phenotypes.

References


Quantitative trait loci affecting clinical mastitis and somatic cell count in dairy cattle. Mamm Genom 12:837–842


Norman HD, Dickinson FN (1971) An economic index for determining the relative value of milk and fat in predicted...