

Farm animal genomics and informatics: an update

Ahmed Fadiel*, Ifeanyi Anidi and Kenneth D. Eichenbaum¹

Yale University School of Medicine, Yale Center for Research On Reproductive Biology, New Haven, CT 06511, USA and ¹Mount Sinai School of Medicine, New York, NY 10029, USA

Received July 7, 2005; Revised August 15, 2005; Accepted October 10, 2005

ABSTRACT

Farm animal genomics is of interest to a wide audience of researchers because of the utility derived from understanding how genomics and proteomics function in various organisms. Applications such as xenotransplantation, increased livestock productivity, bioengineering new materials, products and even fabrics are several reasons for thriving farm animal genome activity. Currently mined in rapidly growing data warehouses, completed genomes of chicken, fish and cows are available but are largely stored in decentralized data repositories. In this paper, we provide an informatics primer on farm animal bioinformatics and genome project resources which drive attention to the most recent advances in the field. We hope to provide individuals in biotechnology and in the farming industry with information on resources and updates concerning farm animal genome projects.

PRELUDE

The omics and bioinformatics

Genomics is the scientific study of structure, function and interrelationships of both individual genes and the genome in its entirety (1). The field has evolved from identifying short nucleotide strings of DNA to the sequencing of an organism's complete genome. Current progress in genomics research has facilitated comprehensive mapping of the building blocks of biology (2). Ultimately, researchers hope to gain mastery over the fundamental description of cellular function at the DNA level (3). This would encompass gene regulation, in which proteins often regulate their own production or that of other proteins in a complex web of interactions. Databases can be developed to provide solutions to problems that people encounter when dealing with massive amounts of data. However, the abundance and growing complexity of the data tools and resources required for analysis are overwhelming (<http://www.ncbi.nlm.nih.gov/About/primer/bioinformatics.html>). The same is true of researchers focusing on the study of

function and structure of proteins and protein–protein interactions.

Proteomics, or the science of protein structure and function, is now a hot spot in biomedicine. A key component to the next revolution in the 'post-genomic' era will be the increasingly widespread use of protein structure in rational experimental design. New computational methodologies now yield structure models that are, in many cases, quantitatively comparable to crystal structures, at a fraction of the cost (4). The technical challenge is the complete coverage of physicochemical properties for thousands of proteins (5). Thus, by analytically investigating genes and proteins, researchers have developed the umbrella study of bioinformatics, the science of analyzing biological data using cutting-edge computing techniques.

Bioinformatics deals with methods for storing, retrieving and analyzing biological data, such as nucleic acid (DNA/RNA) and protein sequences, structures, functions, pathways and genetic interactions: the computational management of all kinds of biological information (<http://www.ncbi.nlm.nih.gov/About/primer/bioinformatics.html>). Rather than merely a mixture of computer science, data management and genome sciences, Bioinformatics now encompasses both conceptual and practical tools for the propagation, generation, processing and understanding of scientific ideas and biological information (6).

DNA and protein sequences data banks

The availability of many complete genome sequences from different species can bring insight into the function of conserved non-coding regions of DNA sequence (7). Organization of the data into coding (genes) and non-coding sequences, in addition to organizing these data into databases for 'DNA databases' and proteins (Table 1), is central for bioinformatics (6,8,9). Parsing the sequence of DNA or protein is a first step, followed by curation then analysis and sometimes re-curation based on the analysis. The presence of these databases and derivative search engines gave rise to programs, such as FASTA (10) and PSI-BLAST (11), which are DNA and protein sequence analysis tools, respectively (12). These tools facilitate searches for sequences that resemble one another and homologous relationship inferences. Utilization

*To whom correspondence should be addressed. Tel: +1 203 737 1218; Fax: +1 203 785 5294; Email: afadiel@yale.edu

Table 1. General genomics and proteomics databases: comprised of resources for human, goat, mouse, deer, rat, and horse genomes

DB name	DB type	URL address and geographical location	Major contents
General utility databases			
GenBank	Sequence DB (for all organisms)	http://www.ncbi.nlm.nih.gov/Genbank/ NCBI, USA	DNA/protein
PDB	The Protein Data Bank proteins structure	http://www.rcsb.org/pdb/index.html USA	Experimentally determined 3D structure of proteins
EMBL	The EMBL nucleotide sequence database. Nucleic sequences	http://www.ebi.ac.uk/embl/ USA	Nucleotide sequences of loci
Codon usage DB	Codon usage frequency	http://www.kazusa.or.jp/codon/ Japan	Codon usage in animals and other organisms
OMIA	Online mendelian inheritance in animals	http://www.angis.org.au/Databases/BIRX/omia/ Australia	Mendelian inheritance in animals
Entrez gene	Curated sequence and descriptive information about genetic loci. Genes—human	http://www.ncbi.nih.gov/entrez/query.fcgi?db=gene USA	Loci sequences
OMIM	Online mendelian inheritance in man. Genes—human	http://www3.ncbi.nlm.nih.gov/Omim/ USA	Catalog of human genes
GOBASE	The organelle genome database. Nucleic sequences mitochondrial	http://megasun.bch.umontreal.ca/gobase/gobase.html Canada	Mitochondrial genes
IMGT	The international immunogenetics database. Genes of multi-species	http://imgt.cines.fr:8104/home.html France	Genes evolving in immunology
Swiss-Prot	Annotated protein sequence database. Proteins—sequences	http://us.expasy.org/sprot EMBL, Europe (China mirror)	Annotated sequences of proteins
Special genomic region databases			
ISIS	Introns of genes. Genes of multi-species sequences introns	http://isis.bit.uq.edu.au/front.html Europe	Introns of genes
Loci-specific databases			
Deerbase	The deer genome database. Genomic mapping	http://www.thearkdb.org/browser?species=deer UK	Loci homologies with deer
Goatmap	Mapping the goat genome. Genomic mapping	http://locus.jouy.inra.fr/cgi-bin/lgbc/mapping/common/intro2.pl?Base=goat France	Loci homologies with goat
MGD	The mouse genome database. Genomic mapping	http://www.informatics.jax.org/ USA	Loci homologies with the mouse
Ratmap	The rat genome DB. Genomic mapping	http://ratmap.gen.gu.se/ USA	Loci homologies with rat
Comparative genomic databases			
Homology form	The mammalian comparative map	http://www.informatics.jax.org/searches/homology_form.shtml Jackson Lab, USA	Comparative maps
HomoloGene	The homologue database	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=homologene NCBI, USA	Gene homology

of similarity search programs, which operate on sequences, has helped in augmenting annotated databases, which house information about sequence domains. Information recording, retrieval and cataloging continue to advance further database capabilities (13). Collaborating research centers, particularly in the US, Japan and the UK, have been actively collecting sequence data and making it accessible to public (14) (Table 1).

Farm animals: an unexploited gold mine for biotech

Farm animals are quite valuable as resources, often notable as models for pathology and physiology studies. Magnussen (15) discusses how a variety of these farm animal models are used.

The reproductive physiology of farm animals is more similar to humans than that of rodents because farm animals have longer gestation and pre-pubertal periods than mice (16). Specific farm animal physiology, such as the digestive system of the pig is similar to that of humans (17). These attributes of farm animals reveal that they are an unparalleled resource for research replicating human physiological function (15).

For decades, breeders have altered the genomes of farm animals by first searching for desired phenotypic traits and then selecting for superior animals to continue their lineage into the next generation (18). This genomic work has already facilitated a reduction in genetic disorders in farm animals, as many disease carriers are removed from breeding populations by purifying selection (19). By studying diverse phenotypes

over time, researchers can now monitor mutations that occur as wild species become domesticated (20). Farm animal food safety will remain a concern for some time; however, advancements such as the discovery of *Escherichia coli* resistant genes in the pig (21) can mediate most of the problems. Moreover, resources devoted to investigating the genomes of farm animals can bring eventual economic benefits. For example, isolation of DNA from animal tissue can be used as an inexpensive method for tracking the origin of a meat sample, providing the recipient with the quality assurance of that food (22).

2005: the year of the chicken

There has been significant interest in the first complete analysis of the draft genome sequence of the chicken. This sequence has given rise to chicken genome array chips and a number of web based mapping tools. The great importance of the chicken as a scientific resource can be seen from the research on avian leucosis virus, which has led to developments in the areas of proviral insertion-mediated oncogenesis and vertebrate viral-host interactions (23,24). Still, many chicken lines are being lost due to facility downsizing and closings (<http://www.grcp.ucdavis.edu/publications/doc20/full.pdf>).

The release of the first draft of the chicken genome in March 2004 spawned the current boom in chicken genomic research (25) (Table 2). From an evolutionary standpoint, investigation of the chicken genome will provide significant information needed to understand the vertebrate genome evolution, since the chicken is between the mammal and fish on the evolutionary tree (26). Furthermore, the chicken remains significant as a food animal which comprises 41% of the meat produced in the world and serves as a reliable model for the study of diseases and developmental biology (26). With this sequenced genome, chicken breeders will have a framework for investigating polymorphisms of informative quantitative traits to continue their directed evolution of these species. The chicken genome is also effective as a comparative genomic tool that sheds additional light on various aspects of our own genome (27). In addition, complementary DNA microarrays for the chicken have already been produced for the study of metabolic and other systemic processes (27,28).

The swine sequence

The sequencing of the pig genome generated an invaluable resource for advancements in enzymology, reproduction, endocrinology, nutrition and biochemistry research (29,30). Since pigs are evolutionarily distinct to both humans and rodents, but have co-evolved with these species, the diversity of selected phenotypes make the pig a useful model for the study of genetic and environmental interactions with polygenic traits (31). The sequencing of the pig genome is also instrumental in the improvement of human health. Clinical studies in areas such as infectious disease, organ transplantation, physiology, metabolic disease, pharmacology, obesity and cardiovascular disease have used pig models (32) (Table 3). In the near future, the sequencing of the porcine genome will allow gene markers for specific diseases to be identified, assisting breeders in generating pig stocks resistant to infectious diseases (33). Furthermore, as researchers investigate the swine genome and isolate genes that may impact

the economics of breeding, members of the commercial pig industry are able to use this information to garner benefits (30).

The *Bos taurus* genome

The mammalian order Cetartiodactyla (possessing *B.taurus* or cattle) is of great interest since it represents a group of eutherian mammals phylogenetically distant from primates (34,35). Working with the cow species, *B.taurus*, is significant because the cow is such an economically important animal. This form of livestock makes up the beef and milk production industry, which is one of the largest industries in the United States. The identification of numerous single-nucleotide polymorphisms (SNPs) makes it possible for geneticists to find associations between certain genes and cow traits that will eventually lead to the production of superior-quality beef (36). After the completion of the September 2004 *B.taurus* draft assembly (Table 4), this genome has functioned as a vehicle for studies on non-primate and non-rodent genomes as well as in comparative genomics (37). Similar to the pig, the cow also serves as a good animal model for obesity, infectious diseases and female health (34,38).

Sheep (*Ovis aries*) genome project

Bioinformatics researchers from New Zealand, US, UK and Australia have come together to work on the sheep genome map. The focal point of interest in sheep is based on the quest to maximize sheep meat and cotton wool production. This sector of the corporate farming industry is so intent on this biotechnology project that AWI, Meat and Livestock Australia and nine other partners are investing \$50 million into the Sheep Genome Project to ensure its completion (<http://www.wool.com.au/LivePage.aspx?pageId=116>). As a resource in biological science, researchers have mapped a subset of genes that have also been mapped in humans and mice (39). These studies have revealed the existence of mutations that yield phenotypes unique to the sheep, demonstrating that genetic analysis of the sheep can enhance our knowledge of biological pathways in other mammalian species (39,40). Table 5 provides information on current genome informatics resources available on the Internet related to sheep.

The fish genome project

Fish are one of the most studied organisms. Researchers have investigated the genome of zebrafish, medaka, pufferfish (*Fugu rubripes* and *Tetraodon nigroviridis*) and sticklebacks. The zebrafish genome has attracted the attention of various pharmaceutical and biotech companies owing to the ease with which scientists can use this fish to study the gene function (<http://www.wellcome.ac.uk/en/genome/genesandbody/hg05f006.html>). The number of databases and informatics resources related to fish genomic study on the Internet is consistently growing (Table 6). Japanese researchers are interested in medakas from an evolutionary standpoint (40). Other fish genome sequences, such as the pufferfish genome are similar to the Fugu genome in size and are ~7.5 times smaller than the human genome. This has led many to believe that the genes conserved between these two species would reveal the minimal number of genes required for a vertebrate organism (41). Further investigation of the Fugu genome supported this

Table 2. Chicken-based internet genomic resources

Database	Site content	URL
Poultry and avian research resources	A detailed stock and curator listing of available avian research stocks are provided	http://animalscience.ucdavis.edu/AvianResources/index.htm
Chicken variation database	An integrated information system for storage, retrieval, visualization and analysis of chicken variation data	http://chicken.genomics.org.cn/index.jsp
Chicken genome browser	The genome browser zooms and scrolls over chromosomes, showing the work of annotators worldwide	http://genome.ucsc.edu/cgi-bin/hgGateway?org=Chicken&db=0&hgsid=30948908
NCBI chicken genome resources	Provides information on chicken-related resources from NCBI and the chicken research community	http://www.ncbi.nlm.nih.gov/genome/guide/chicken/
Wellcome trust chicken genome browser	This site presents an annotation of the first draft chicken genome assembly	http://www.ensembl.org/Gallus_gallus/
WUGSC chicken genome site	Possesses helpful information on the chicken genome	http://genome.wustl.edu/genome.cgi?GENOME=Gallus%20gallus
Chicken genome array	The GeneChip [®] chicken genome array is a key research tool for the study of chicken genomics and chicken viral pathogens	http://www.affymetrix.com/products/arrays/specific/chicken.affx
ChickCmap	ChickCmap allows the alignment of the different available maps in chicken	http://www.animalsciences.nl/cmapp/
ChickFPC	Search using a sequence name, gene name, locus or other landmark	http://www.animalsciences.nl/ChickFPC/
Chicken database AvianNet	Online public database browser A portal to information on the chicken genome and chicken biology	http://www.thearkdb.org/browser?species=chicken http://www.chicken-genome.org/information/about.html
ChickEst	Provides access to 339 314 <i>Gallus gallus</i> ESTs	http://chick.umist.ac.uk/
US poultry genome project	Supported national animal genome research programme to serve the poultry genome mapping community	http://poultry.mph.msu.edu/index.html
ChickAce	Mainly intended to store mapping information in chicken	https://acedb.asg.wur.nl/
University of Delaware ChickEST database	Contains over 40 000 EST sequences from the chicken cDNA libraries in the UD collection	http://www.chickest.udel.edu/
TIGR <i>G.gallus</i> gene index	Integrates research data from international <i>G.gallus</i> EST sequencing and gene research projects	http://www.tigr.org/tigr-scripts/tgi/T_index.cgi?species=g_gallus
Bacterial artificial chromosome (BAC)-based physical and genetic map	A genome-wide, BAC-based, integrated genetic and physical map of the chicken genome	http://hbz7.tamu.edu/homelinks/phymap/chicken/chick_home.htm
Consensus linkage map of chicken genome	Wageningen University chicken consensus linkage map	http://www.zod.wau.nl/abg/hs/research/molecular/intro.html
Chick RH server	RH mapping on INRA chicken radiation hybrid panel	http://chickrh.toulouse.inra.fr/
Chicken-IMAGE	Improvement of chicken immunity resistance to disease based upon analysis of genome	http://www.vjf.cnrs.fr/image/chicken/
Chickmap	Aim to construct an integrated genetic and physical map of the chicken genome	http://www.projects.roslin.ac.uk/chickmap/about_chickmap.html
Chicken genome array	Key research tool for the study of chicken genomics and chicken viral pathogens	http://www.servicexs.com/products/
Chicken genome browser	Ensembl home ensembl chicken exportview	http://atlas.cnio.es/Gallus_gallus/exportview
Chicken chromosome linkage map	Provides comparative mapping information	http://poultry.mph.msu.edu/resources/Resources.htm#Chicken%20Chromosome%20Linkage%20Map
Chicken BAC library	A BAC library of the chicken genome has been constructed	http://www.zod.wau.nl/vf/research/chicken/body_bac_library.html
GEISHA	<i>G.gallus</i> (chicken) EST and <i>in situ</i> hybridization analysis database	http://geisha.biosci.arizona.edu/
NCBI chicken genome map viewer	<i>G.gallus</i> (chicken) genome	http://www.ncbi.nlm.nih.gov/mapview/map_search.cgi?taxid=9031

hypothesis and showed the ability of the Fugu genome to aid in the study of vertebrate functional non-coding sequences (41). Other studies of fish have focused on the stickleback, for its variable body shapes, ecology or its behavior ([\[www.genome.gov/Pages/Research/Sequencing/SeqProposals/SticklebackSEQ.pdf\]\(http://www.genome.gov/Pages/Research/Sequencing/SeqProposals/SticklebackSEQ.pdf\)\). In general, fish genomic work is of interest to the commercial fish farming community. Based on transgenic studies, antifreeze protein and fish](http://</p>
</div>
<div data-bbox=)

Table 3. Genomic and proteomic internet sites devoted to the study of the swine genome

Database	Site content	URL
NCBI pig genome resources	Brings together information on porcine-related resources from NCBI	http://www.ncbi.nlm.nih.gov/projects/genome/guide/pig/
Pig EST database	Pig EST database accommodates 98 988 pig ESTs, which were obtained from various sources	http://pigest.genome.iastate.edu/
Genomic targets for comparative sequencing	Genomic targets of the pig	http://www.nisc.nih.gov/projects/zooseq/comp_seq_org_targets.cgi?org=pig
Pig QTL database	The database makes it possible to compare on pig chromosomes the most feasible location for a gene responsible for quantitative trait important to pig production	http://www.animalgenome.org/QTLdb/
Swine genome maps	Swine gene mapping information	http://www.marc.usda.gov/genome/genome.html
Porcine genome physical mapping project	A physical map of the porcine genome has been generated by an international collaboration of four laboratories	http://www.sanger.ac.uk/Projects/S_scrofa/
Cytogenetic map of the pig	List of genes mapped on pig cytogenetic map	http://www.toulouse.inra.fr/lgc/pig/cyto/cyto.htm
PigBase	PigBase is a computer database that includes information on papers published about gene mapping in the pig	http://www.thearkdb.org/browser?species=pig
The US pig genome project	US pig gene mapping	http://www.animalgenome.org/pigs/
Pig genome mapping	Listing of pig genome databases	http://projects.roslin.ac.uk/pigmap/
Blast pig genome	Blast pig sequences	http://www.ncbi.nlm.nih.gov/genome/seq/SscBlast.html
Pig genome sequencing project	Porcine genome project	http://www.piggenome.dk/
Monsanto swine genome project	Produce genetic information from cDNA libraries made from swine tissue	http://ascswine.rnet.missouri.edu/Description.html
Animal genome research program	Contains pig EST data explorer	http://animal.dna.affrc.go.jp/agp/index.html
ArkDB-pig mapping database	A genome database of the pig	http://bioresearch.ac.uk/browse/mesh/D013552.html
Animal genome database	Contains available pig cDNA clones	http://ws4.niai.affrc.go.jp/jgbase.html
ARK-genomics	Collaborative center for functional genomics in farm animals	http://www.ark-genomics.org/index.php

growth hormone have been introduced into fish genomes, creating fish with greater cold tolerance and faster growth rates (42).

The forgotten rabbit

Little genomics attention is paid to rabbits in comparison with other animal models, such as the mouse, rat and fruit fly in the pre- and post-genomic era. However, experimental models, such as the Alba or the 'mighty lighting rabbit', were developed as glowing mutants that shine under special light for commercial reasons. French scientists created Alba using a process called zygote microinjection. In this process, the scientists plucked a fluorescent protein from the fluorescent jellyfish *Aequorea victoria*. Then, they modified the gene to make its glowing properties twice as powerful. This gene, called EGFG (enhanced green fluorescent gene, was then inserted into a fertilized rabbit egg cell that eventually grew into Alba (*Amanda onion*). Debates about the project itself and about the practice of manipulating genes in animals for research have quickly arisen in the research community. The French National Institute of Agronomic Research hesitated to release these rabbits owing to protests over its development.

Chinese scientists have placed rabbit genes in cotton plants, producing cotton fibers as bright and soft as rabbit hair but stronger and warmer. This indicates not only the rise of the rabbit in experimental models for genetics engineering, but also for future medical experimentation models. Despite the controversy that the 'shining rabbit' and the 'cotton rabbit' raised, it is clear that this type of genetic engineering is at an

early stage. Currently available sources of information about the rabbit on the web can be seen in Table 7.

Farm animal genomics: current statistics

As researchers delve into the composition of farm animal genome sequences, new functional and biological data emerge. Table 8 is compiled from the Ensembl database (<http://www.ensembl.org/>) and illustrates a summary of current analysis on coding regions within genomes for selected farm animals. For example, in the cow genome, ~239 000 exon regions and just over 29 000 transcripts have been tallied from among the 565 million bp found in the genome.

One of the major sources of information on farm animal genomics is the ArkDB (43), which is available through the Roslin Institute (UK) and Texas A&M University (USA). The ArkDB provides detailed genomic mapping data on sheep, chicken, cow and pig genomes (44), including data on PCR primers, genetic linkage map assignments of specific loci and markers, and cytogenetic map assignments. Information about farm animals in this database is displayed in Table 9 and provides a snapshot of current resources available for each genome. Quantitative functional information, such as the number of clones, microsatellites and associated mapping assignments, can lend insight into the complexity of the models available. For example, the number of primers tabulated in the swine genome currently far exceeds that known for the cow, indicating more varieties of genes are available for study in the swine. Much of this information remains at an early stage and with increasing experimentation, compilation and analysis, will be refined.

Table 4. Cow genomics and proteomics resources on the Internet

Database	Site content	URL
NCBI cow genome resources	Brings together information on cow-related resources from NCBI	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=10708
Bovine genome sequencing	Aim to produce a draft assembly of the genomic sequence of cow <i>B.taurus</i>	http://www.genome.gov/12512284
Ensembl genome browser	Produces and maintains automatic annotation on selected eukaryotic genomes	http://www.ensembl.org/Bos_taurus/index.html
Blast cow sequence	Perform sequence comparisons for cow-specific sequences	http://www.ncbi.nlm.nih.gov/genome/seq/BtaBlast.html
CowBase	The cow genome database	http://www.thearkdb.org/browser?species=cow
Baylor bovine genome project	Working to sequence <i>B.taurus</i> using a whole genome shotgun approach	http://www.hgsc.bcm.tmc.edu/projects/bovine/
Cattle genome database	The CGD is part of an international collaboration to map the bovine genome	http://www.cgd.csiro.au/
The interactive bovine <i>in silico</i> SNP (IBISS) database	IBISS creates an <i>in silico</i> SNP database by harnessing the vast number of bovine EST sequences	http://www.livestockgenomics.csiro.au/ibiss/
The US cattle genome project	National cattle genome coordination program	http://www.genome.iastate.edu/cattle/community/
Bovmap database	Cattle and cattle on human chromosomes physical mapping	http://locus.jouy.inra.fr/cgi-bin/bovmap/intro.pl
Bovine QTL viewer	Contains all available public domain bovine QTL data for both dairy and beef traits	http://bovineqtl.tamu.edu/
Dairy cattle QTL map database	Combined QTL map of dairy cattle traits	http://www.vetsci.usyd.edu.au/reprogen/QTL_Map/
TIGR cattle gene index	Integrates research data from international <i>B.taurus</i> EST sequencing and gene research projects	http://www.tigr.org/tigr-scripts/tgi/T_index.cgi?species=cattle
NCBI SNP database	Cattle single nucleotide polymorphism database	http://www.ncbi.nlm.nih.gov/SNP/snp_batchSearch.cgi?org=9913&type=SNP
Beef genomics initiative	Uses structural and functional genomics approaches to study the bovine genome	http://www.afns.ualberta.ca/Hosted/Bovine%20Genomics/Index.asp?Research
Bovine genome browser	Aligns all features to the bovine genome scaffolds from baylor college bovine genome project	http://www.livestockgenomics.csiro.au/cattle.shtml
Cattle EST gene family database	EST family database through Gbrowse	http://www.genome.iastate.edu/cattle/maps/db.html
Unigene: <i>B.taurus</i>	UniGene is an experimental system for automatically partitioning GenBank sequences into a non-redundant set of gene-oriented clusters	http://www.ncbi.nlm.nih.gov/UniGene/UGOrg.cgi?TAXID=9913
Cow (<i>B.taurus</i>) genome browser	UCSC genome browser created by the genome bioinformatics group of UC Santa Cruz	http://genome.ucsc.edu/cgi-bin/hgGateway?clade=vertebrate&org=Cow

Table 5. Internet informatics resources pertaining to the sheep genome

Database	Site content	URL
UK sheep genome mapping project	The genome database of the sheep	http://www.projects.roslin.ac.uk/sheepmap/front.html
US sheep genome mapping project	Public database browser section of the sheep database	http://www.thearkdb.org/browser?species=sheep
Sheep genome resources	Genome effort will generate an important resource for gene discovery, affecting health and biology and the growing	http://www.ncbi.nlm.nih.gov/genome/guide/sheep/
Australian sheep gene mapping site	Sheep genome database	http://rubens.its.unimelb.edu.au/%7Ejillm/jill.htm
Genomic targets for comparative sequencing	Targets for organism: sheep	http://www.nisc.nih.gov/projects/zooseq/comp_seq_org_targets.cgi?org=sheep
Mendelian inheritance in sheep	A compiled annotated trait/locus list	http://www.angis.org.au/Databases/BIRX/mis/
Blast sheep sequences	Blast your sequence against sheep sequences	http://www.ncbi.nlm.nih.gov/genome/seq/OarBlast.html
Only cytogenetics of animals (OCA)	OCA contains references to the literature on the cytogenetics of animals	http://www.angis.org.au/Databases/BIRX/oca/

Table 6. Fish genomic resources on the internet

Database	Site content	URL
Queen Mary University of London	The fugu genomics project	http://fugu.biology.qmul.ac.uk/
Genoscope (the french national sequencing center)	Tetraodon genome browser	http://www.genoscope.cns.fr/externe/tetranew/
Institute of molecular and cell biology	Fugu genome project blast	http://www.fugu-sg.org/BLAST/Blast2.htm
Joint genome institute	Fugu genome browser	http://genome.jgi-psf.org/fugu6/fugu6.home.html
Broad institute	<i>Tetraodon nigroviridis</i> database	http://www.broad.mit.edu/annotation/tetraodon/
NCBI entrez genome	Blast the fugu genome	http://www.ncbi.nlm.nih.gov/BLAST/Genome/fugu.html
NCBI entrez genome	Blast zebrafish sequences	http://www.ncbi.nlm.nih.gov/genome/seq/DrBlast.html
Ensembl tetraodon	Tetraodon genome browser	http://www.ensembl.org/Tetraodon_nigroviridis/
Ensembl fugu	Fugu genome browser	http://www.ensembl.org/Fugu_rubripes/
UCSC genome browser	Tetraodon genome browser gateway	http://genome.ucsc.edu/cgi-bin/hgGateway?org=tetraodon
UCSC genome browser	Fugu genome browser gateway	http://genome.ucsc.edu/cgi-bin/hgGateway?clade=vertebrate&org=Fugu&db=0&hgsid=42757856
Roslin institute	Salmon public database browser	http://www.thearkdb.org/browser?species=salmon
Zebrafish gene	Characterization of mapped zebrafish genes. Genomic mapping	http://zfin.org/cgi-bin/webdriver?MVal=aa-ZDB_home.apg
FishBase	Description of fish species. Zoology	http://www.fishbase.org/search.cfm

Table 7. Rabbit informatics databases

Database	Site content	URL
HRS articles	Information/articles pertaining to many rabbit diseases written by veterinarians	http://www.hrschicago.org/articleslay.html
INRA RabbitMap database	Mapping the rabbit genome. The site contains data about loci, genes, microsatellites, polymorphisms in rabbit	http://locus.jouy.inra.fr/cgi-bin/lgbc/mapping/common/intro2.pl?BASE=rabbit
Online mendelian inheritance in animals (OMIA)	Genes and phenes that have been documented in a wide range of animal species (other than human, rat and mouse). Complementary to human's OMIM	http://omia.angis.org.au/
PIR non-redundant reference protein database	Provide an integrated public resource of functional annotation of protein data	http://www-nbrf.georgetown.edu/cgi-bin/nfspecies.pl

Table 8. Ensemble (gene build July 2005) and NCBI statistics of available farm animal genomes^a

No.	Information source/type	Chicken	Cow	Pig	Sheep	Fish (zebrafish)
Ensembl (e)						
1	eGene predictions	17 784	22 013	NA	NA	22 877
2	Genscan predictions	77 600	103 597	NA	NA	49 697
3	egene exons	185 326	239 889	NA	NA	231 799
4	egene transcripts	28 491	29 363	NA	NA	32 143
5	Base pairs	1 054 180 845	565 382 643	NA	NA	1 688 467 974
NCBI (entrez 2005 records)						
1	Nucleotide	923 899	1 961 869	628 750	28 716	912 447
2	Protein	29 634	51 726	8835	3160	47 458
3	UniSTS	2936	13 320	7851	2408	27 616
4	Gene	18 449	39 815	2388	625	18 429
5	HomoloGene	14 433	12 909	10 795	1016	11 026
6	EST	554 084	624 652	461 891	10 960	651 991

^aThe ESTs in this table are based on the dbEST release 082605-August 26, 2005 (http://www.ncbi.nlm.nih.gov/dbEST/dbEST_summary.html) BLAST alignment data, associated Human UniGene and RH maps (EBI GenomeMap'99 and NCBI GeneMap'99), pig-human comparative map information and mapped pig genes in the pig genome database (PigBase).

Expression sequence tags

Expression sequence tags (ESTs) are small pieces of cDNA sequence (usually 200–500 nt long), which are useful as markers for a desired portion of RNA and DNA that can be used for

gene identification and positional mapping within a genome (<http://www.ncbi.nlm.nih.gov/About/primer/est.html>). The NCBI provides the most comprehensive EST database for many farm animals. Tabulation of chicken EST information, including quantities of ESTs and their tissue sources can

Table 9. Current status summary provided by the ArkDB

No.	Element	Chicken	Pig	Cow	Sheep
Markers					
1	Loci	2530	4081	2725	2030
2	Designated genes	765	1588	746	543
3	5 3 Sine-PCR	47	18	146	3
4	Microsatellite	1277	1673	1219	2257
5	RFLP	255	258		250
6	Clones	316	602	1	206
Map assignments					
1	Linkage	3400	5141	2209	14 909
2	Cytogenetic	307	1927	659	843
3	Total	3707	7068	2868	15 752

be found in the BBSRC ChickEST Database (<http://chick.umist.ac.uk/>) (45,46). ChickEST provides access to ~339 000 Gallus ESTs, generated from 21 different embryonic and adult tissues. Cow EST information is available on ArkDB, Ensembl (http://www.ncbi.nlm.nih.gov/mapview/map_search.cgi?taxid=9031) and the NCBI Cow genome EST. A collection of pig ESTs is also available through the pig EST database (<http://pigest.genome.iastate.edu/index.html>) (47) in two versions. The first version contains ~14 000 EST sequences obtained from porcine whole embryo, term placenta, anterior pituitary, hypothalamus and ovary. The second, newer version of the database accommodates 99 000 pig ESTs. Pig sequence homology comparisons can be readily studied on the Iowa State University's website. However, database updates were carried out only until January 2002. Among farm animals, there is sparse information about rabbit ESTs. NCBI does not provide comprehensive EST information, with virtually no physical maps on the rabbit. However, NCBI is still the central source for information about rabbit ESTs, mining 2275 GenBank rabbit ESTs (dbEST release 082605).

Physical mapping

Genome maps in livestock species have been under development for the last decade. Mapping, which involves understanding the relative distances between genes on a chromosome, has been performed for the many farm animals. The NCBI provide comprehensive mapping information for many farm animal species. Mapping information is available at http://www.ncbi.nlm.nih.gov/mapview/map_search.cgi?taxid=?, with specific animal links available by substituting the '?' sign in the previous URL with the species' taxonomic number, such as 9031 for the chicken, 9913 for the cow, 9823 for the pig, 7955 for the zebrafish and 9940m for the sheep. For example, the chicken mapping site can be found at NCBI MapView website (http://www.ncbi.nlm.nih.gov/mapview/map_search.cgi?taxid=9031). The US Livestock Species Genome Projects (<http://www.animalgenome.org/>) suggest using ArkDB (mentioned above), for mapping information on farm animals. The Laboratory of Biochemistry and Cytogenetics (Jouy-in-Josas, France) at the National Institute for Agricultural Research (INRA) provides the rabbit 'Lepine' genome mapping database (<http://dga.jouy.inra.fr/cgi-bin/lgbc/main.pl?BASE=rabbit>). The database provides access to information about rabbit genomic information which includes so far

410 loci with 1327 homologue loci on 129 species, 21 polymorphisms, 314 genes and their physical location on chromosomes. Other information about primers, probes and enzymes are also included. Genes in the RabbitMap database are hyperlinked to a separate page that provides locus information. Physical mapping of the zebrafish is available through the Ensembl database at http://www.ensembl.org/Danio_rerio/index.html. The Ensembl database also provides a comprehensive map viewer for zebrafish and the chicken (http://www.ensembl.org/Gallus_gallus/index.html). High-resolution maps for sheep chromosomes are available at <http://www.ncbi.nlm.nih.gov/genome/guide/sheep/index.html>.

Quantitative trait loci and genetic linkage

One of the primary challenges in modern biology is the understanding of the genetic basis of phenomic diversity within and among species (20). The foundation for this diversity lies in genetic governance of both how traits are expressed and the associated linkage maps. Genes mapped in some farm animals serve as 'anchors' across the comparative maps of other species (39). Quantitative trait loci (QTLs) play a major role in farm animals and the related biotechnology industry, as they can further the identification of traits related to meat and milk production. A number of studies have been conducted to detect QTLs that can be used for determining gene variances (48,49). The third generation of sheep linkage map (50) contains 1062 loci (941 anonymous loci and 121 genes) and is a compilation of genotype data generated by 15 laboratories using the IMF population (<http://rubens.its.unimelb.edu.au/~jillm/jill.htm>). The ArkDB provides current summaries of linkage and cytogenetic map assignments, polymorphic marker details, PCR primers and two point linkage data (see Table 9). The ArkDB also is a major source for mapped sheep loci, with SheepBase containing almost 1500 loci. The Roslin Institute has developed the 'resSpecies' (<http://www.respecies.org/>) database to study genetic linkage maps, QTLs, alleles and other markers (44,51). Bovine QTL databases are available from several sources (52,53). Various traits, such as milk yield and composition, are available along with QTL dot maps, which provide varied positional and statistical information. The pig QTL (<http://www.animalgenome.org/QTLdb/>) includes two release versions from NCBI in May 2004 and from NAGRP in December 2004. The pig QTL database, or pig QTLdb, contains all published pig QTL data from the past decade. The user can locate genes responsible for quantitative traits central to pig production. To date, 791 QTLs from 73 publications, representing 219 different traits are incorporated into the database in the first release and 1129 QTLs, from 86 publications representing 235 different traits in the second release. The project also provides maps at <http://www.animalgenome.org/cgi-bin/QTLdb/viewmap> and links to the NCBI pig EST Map database (<http://pigest.genome.iastate.edu/index.html>).

FARM ANIMAL GENOMICS: THE LEGAL SIDE

Genome protections: lessons from the human genome

Similar to other areas of scientific research, the field of farm animal genomics is ingrained with various issues requiring

ethical consideration. Although a number of gene-based technological advances, such as the prediction of illnesses or adverse drug response are beneficial for commercial interests (54), many look to protect how genetic information is used. The corollary in human genomics is the recent Genetic Information Nondiscrimination Act of 2005 (<http://www.genome.gov/PolicyEthics/>). This bill, which is pending in the US Congress, prohibits among other things 'a health insurance issuer from: adjusting premiums on the basis of genetic information' (<http://thomas.loc.gov/cgi-bin/bdquery/z?d109:SN00306:@@L&summ2=m&>). Concerns over such actions reveal the understanding by the US government that the use of human genomic data must be closely regulated in order to hinder any commercial abuses. Although genetic discrimination and health insurance might not be issues relevant to farm animal genomics, a great need exists to establish a similar legal framework for farm animals in order to ensure the proper use of farm animal genomic information.

Genome policies for transgenic animals

The federal government's role as a legal authority for protecting the environment from scientifically introduced transgenic organisms has not been clearly outlined (55). This underscores the need for greater governmental attention to address legal problems that will arise as animal biotechnology continues to grow. Many argue that it is not only a moral imperative to respect the intrinsic sentience of animals but also a legal one (<http://www.foodethicscouncil.org/library/consultations/BBSRCgenomics.pdf>). The European Union's Treaty of Amsterdam states that animals must be treated humanely, as sentient beings, which some argue implies respect for their intrinsic nature and protection against such infringements of that respect in studies such as transgenic animal experiments (<http://www.eurotreaties.com/amsterdamtext.html>). Furthermore, US food regulatory agencies, such as the United States Department of Agriculture and the Food Safety and Inspection Service, charged with the duty of making sure that transgenic animals anticipated for human consumption are correctly labeled and wholesome, have already moved forward to institute policies regulating the slaughtering of non-transgenic animals created from transgenic animal experiments (56).

Ethical reservations of farm animal genomic study

As farm animal species continue to be sequenced (one of the latest being the cow, *B.taurus*), farming companies are using this information to perform genetic profiles of traditionally bred animals and to genetically engineer or clone other animals (57). Although many farmers may enjoy access to greater genetic resources, animal rights organizations oppose the use of animals such as transgenic goats that produce silk proteins used to make Biosteel fibers because of the allegedly inhumane treatment of animals during these studies (58). Proponents of such experiments point to the ability of transgenic mouse mammary glands to assemble and secrete recombinant human fibrinogen (59). These studies raise many concerns about research ethics and species integrity (60,61).

The potential of farm animal genomics

Farm animal genomic studies continue to attract audiences excited by the multitude of applications (62). The meat industry can now use cow and chicken genomic data to confirm the quality of meat products. For example, meat producers can now confirm the parentage of an Angus cattle breed by performing a genetic blood test or attempt to identify the SNPs associated with high-quality beef (57). Other companies are using genomic information to determine disease-resistant genes in shrimp and then are selectively mating the shrimp that carry them in order to create disease resistant strains (57). In the healthcare arena, farm animal genomic work will aid in enterprises such as xenotransplantation (the transfer of animal tissues or organs into humans). Though animal organs may be used someday to satiate organ donor shortage, genomic work in this area is still in its early stage (63). Many of the immediate practical applications of farm animal genomics show potential for growth in this field.

ACKNOWLEDGEMENTS

We thank Professor William Dynan, Medical College of Georgia for helpful discussions and careful editing of the manuscript. We thank Ms J. Wade and T. Scalise for assistance during the processing of this manuscript. Special thanks goes to the reviewers for their valuable comments and suggestions. The Open Access publication charges for this article were waived by Oxford University Press.

Conflict of interest statement. None declared.

REFERENCES

1. Bazer, F.W. and Spencer, T.E. (2005) Reproductive biology in the era of genomics biology. *Theriogenology*, **64**, 442–456.
2. Bilello, J.A. (2005) The agony and ecstasy of 'OMIC' technologies in drug development. *Curr. Mol. Med.*, **5**, 39–52.
3. Chan, E.Y. (2005) Advances in sequencing technology. *Mutat. Res.*, **573**, 13–40.
4. Maggio, E.T. and Ramnarayan, K. (2001) Recent developments in computational proteomics. *Trends Biotechnol.*, **19**, 266–272.
5. Drake, R.R., Deng, Y., Schwegler, E.E. and Gravenstein, S. (2005) Proteomics for biodefense applications: progress and opportunities. *Expert Rev. Proteomics*, **2**, 203–213.
6. Rhee, S.Y. (2005) Bioinformatics. Current limitations and insights for the future. *Plant Physiol.*, **138**, 569–570.
7. Koyanagi, K.O., Hagiwara, M., Itoh, T., Gojobori, T. and Imanishi, T. (2005) Comparative genomics of bidirectional gene pairs and its implications for the evolution of a transcriptional regulation system. *Gene*, **4**, 169–176.
8. Bernstein, F.C., Koetzle, T.F., Williams, G.J., Meyer, E.F.Jr, Brice, M.D., Rodgers, J.R., Kennard, O., Shimanouchi, T. and Tasumi, M. (1977) The Protein Data Bank. A computer-based archival file for macromolecular structures. *J. Mol. Biol.*, **112**, 535–542.
9. Berman, H.M., Westbrook, J., Feng, Z., Gilliland, G., Bhat, T.N., Weissig, H., Shindyalov, I.N. and Bourne, P.E. (2000) The Protein Data Bank. *Nucleic Acids Res.*, **28**, 235–242.
10. Pearson, W.R. and Lipman, D.J. (1988) Improved tools for biological sequence comparison. *Proc. Natl Acad. Sci. USA*, **85**, 2444–2448.
11. Altschul, S.F., Madden, T.L., Schaffer, A.A., Zhang, J., Zhang, Z., Miller, W. and Lipman, D.J. (1997) Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. *Nucleic Acids Res.*, **25**, 3389–3402.

12. Chen, Z. (2003) Assessing sequence comparison methods with the average precision criterion. *Bioinformatics*, **19**, 2456–2460.
13. Wheeler, D.L., Barrett, T., Benson, D.A., Bryant, S.H., Canese, K., Church, D.M., DiCuccio, M., Edgar, R., Federhen, S., Helmberg, W. *et al.* (2005) Database resources of the National Center for Biotechnology Information. *Nucleic Acids Res.*, **33**, D39–D45.
14. Kanz, C., Aldebert, P., Althorpe, N., Baker, W., Baldwin, A., Bates, K., Browne, P., van den Broek, A., Castro, M., Cochrane, G. *et al.* (2005) The EMBL Nucleotide Sequence Database. *Nucleic Acids Res.*, **33**, D29–D33.
15. Magnusson, U. (2005) Can farm animals help to study endocrine disruption? *Domest. Anim. Endocrinol.*, **29**, 430–435.
16. Rhind, S.M. (2002) Endocrine disrupting compounds and farm animals: their properties, actions and routes of exposure. *Domest. Anim. Endocrinol.*, **23**, 179–187.
17. Sweeney, T. (2002) Is exposure to endocrine disrupting compounds during fetal/post-natal development affecting the reproductive potential of farm animals? *Domest. Anim. Endocrinol.*, **23**, 203–209.
18. Harlizius, B., van Wijk, R. and Merks, J.W. (2004) Genomics for food safety and sustainable animal production. *J. Biotechnol.*, **113**, 33–42.
19. Andersson, L. (2001) Genetic dissection of phenotypic diversity in farm animals. *Nature Rev. Genet.*, **2**, 130–138.
20. Andersson, L. and Georges, M. (2004) Domestic-animal genomics: deciphering the genetics of complex traits. *Nature Rev. Genet.*, **5**, 202–212.
21. Edfors-Lilja, I., Gustafsson, U., Duval-Iflah, Y., Ellergren, H., Johansson, M., Juneja, R.K., Marklund, L. and Andersson, L. (1995) The porcine intestinal receptor for *Escherichia coli* K88ab, K88ac: regional localization on chromosome 13 and influence of IgG response to the K88 antigen. *Anim. Genet.*, **26**, 237–242.
22. Brem, G. (2004) Techniques and possibilities of traceability of food: genotyping of the domestic animal population as an innovative contribution to food safety. *Dtsch Tierarztl Wochenschr.*, **111**, 273–276.
23. Neimann, P.E., Ruddell, A., Jasoni, C., Loring, G., Thomas, S.J., Brandvold, K.A., Lee, R.M., Burnside, J. and Delrow, J. (2001) Analysis of gene expression during myc oncogene-induced lymphomagenesis in the bursa of Fabricius. *Proc. Natl Acad. Sci. USA*, **98**, 6378–6383.
24. Crittenden, L.B., Provencher, L., Santangelo, L., Levin, I., Abplanalp, H., Briles, R.W., Briles, W.E. and Dodgson, J.B. (1993) Characterization of a red jungle fowl by white leghorn backcross reference population for molecular mapping of the chicken genome. *Poult. Sci.*, **72**, 334–348.
25. Antin, P.B. and Konieczka, J.H. (2005) Genomic resources for chicken. *Dev. Dyn.*, **232**, 877–882.
26. Dequeant, M.L. and Pourquie, O. (2005) Chicken genome: new tools and concepts. *Dev. Dyn.*, **232**, 883–886.
27. Burt, D. and Pourquie, O. (2003) Genetics. Chicken genome—science nuggets to come soon. *Science*, **300**, 1669.
28. Cogburn, L.A., Wang, X., Carre, W., Rejto, L., Porter, T.E., Aggrey, S.E. and Simon, J. (2003) Systems-wide chicken DNA microarrays, gene expression profiling, and discovery of functional genes. *Poult. Sci.*, **82**, 939–951.
29. Wernersson, R., Schierup, M.H., Jorgensen, F.G., Gorodkin, J., Panitz, F., Staerfeldt, H.H., Christensen, O.F., Mailund, T., Hornshøj, H., Klein, A. *et al.* (2005) Pigs in sequence space: a 0.66X coverage pig genome survey based on shotgun sequencing. *BMC Genomics*, **6**, 70.
30. Rothschild, M.F. (2003) From a sow's ear to a silk purse: real progress in porcine genomics. *Cytogenet. Genome Res.*, **102**, 95–99.
31. Blakesley, R.W., Hansen, N.F., Mullikin, J.C., Thomas, P.J., McDowell, J.C., Maskeri, B., Young, A.C., Benjamin, B., Brooks, S.Y., Coleman, B.I. *et al.* (2004) An intermediate grade of finished genomic sequence suitable for comparative analyses. *Genome Res.*, **14**, 2235–2244.
32. Rothschild, M.F. (2004) Porcine genomics delivers new tools and results: this little piggy did more than just go to market. *Genet. Res.*, **83**, 1–6.
33. Klymiuk, N. and Aigner, B. (2005) Reliable classification and recombination analysis of porcine endogenous retroviruses. *Virus Genes*, **3**, 357–362.
34. Larkin, D.M., Everts-van der Wind, A., Rebeiz, M., Schweitzer, P.A., Bachman, S., Green, C., Wright, C.L., Campos, E.J., Benson, L.D., Edwards, J. *et al.* (2003) A cattle–human comparative map built with cattle BAC-ends and human genome sequence. *Genome Res.*, **13**, 1966–1972.
35. Kumar, S. and Hedges, S.B. (1998) A molecular timescale for vertebrate evolution. *Nature*, **392**, 917–920.
36. Adam, D. (2002) Draft cow genome heads the field. *Nature*, **417**, 778.
37. Barendse, W., Armitage, S.M., Kossarek, L.M., Shalom, A., Kirkpatrick, B.W., Ryan, A.M., Clayton, D., Li, L., Neibergs, H.L., Zhang, N. *et al.* (1994) A genetic linkage map of the bovine genome. *Nature Genet.*, **6**, 227–235.
38. Wilson, H.L., Aich, P., Roche, F.M., Jalal, S., Hodgson, P.D., Brinkman, F.S., Potter, A., Babiuk, L.A. and Griebel, P.J. (2005) Molecular analyses of disease pathogenesis: application of bovine microarrays. *Vet. Immunol. Immunopathol.*, **105**, 277–287.
39. Cockett, N.E., Shay, T.L. and Smit, M. (2001) Analysis of the sheep genome. *Physiol. Genomics*, **7**, 69–78.
40. Mouchel, N., Tebbutt, S.J., Broackes-Carter, F.C., Sahota, V., Summerfield, T., Gregory, D.J. and Harris, A. (2001) The sheep genome contributes to localization of control elements in a human gene with complex regulatory mechanisms. *Genomics*, **76**, 9–13.
41. Ahituv, N., Rubin, E.M. and Nobrega, M.A. (2004) Exploiting human–fish genome comparisons for deciphering gene regulation. *Hum. Mol. Genet.*, **R261–R266**.
42. Zbikowska, H.M. (2003) Fish can be first—advances in fish transgenesis for commercial applications. *Transgenic Res.*, **12**, 379–389.
43. Hu, J., Mungall, C., Law, A., Papworth, R., Nelson, J., Brown, A., Simpson, J., Leckie, S., Burt, D., Hillyard, A. *et al.* (2001) The ARKdb: genome databases for farmed and other animals. *Nucleic Acids Res.*, **29**, 106–110.
44. Law, A.S. and Archibald, A.L. (2000) Farm animal genome databases. *Brief. Bioinform.*, **1**, 151–160.
45. Boardman, P.E., Sanz-Ezquerro, J., Overton, I.M., Burt, D.W., Bosch, E., Fong, W.T., Tickle, C., Brown, W.R., Wilson, S.A. and Hubbard, S.J. (2002) A comprehensive collection of chicken cDNAs. *Curr. Biol.*, **12**, 1965–1969.
46. Hubbard, S.J., Grafham, D.V., Beattie, K.J., Overton, I.M., McLaren, S.R., Croning, M.D., Boardman, P.E., Bonfield, J.K., Burnside, J., Davies, R.M. *et al.* (2005) Transcriptome analysis for the chicken based on 19,626 finished cDNA sequences and 485,337 expressed sequence tags. *Genome Res.*, **15**, 174–183.
47. Tuggle, C.K., Green, J.A., Fitzsimmons, C., Woods, R., Prather, R.S., Malchenko, S., Soares, B.M., Kucaba, T., Crouch, K., Smith, C. *et al.* (2003) EST-based gene discovery in pig: virtual expression patterns and comparative mapping to human. *Mamm. Genome*, **14**, 565–579.
48. Page, G.P., George, V., Go, R.C., Page, P.Z. and Allison, D.B. (2003) 'Are there yet?': Deciding when one has demonstrated specific genetic causation in complex diseases and quantitative traits. *Am. J. Hum. Genet.*, **73**, 711–719.
49. Phillips, T.J. and Belknap, J.K. (2002) Complex-trait genetics: emergence of multivariate strategies. *Nature Rev. Neurosci.*, **3**, 478–485.
50. Maddox, J.F., Davies, K.P., Crawford, A.M., Hulme, D.J., Vaiman, D., Cribs, E.P., Freking, B.A., Beh, K.J., Cockett, N.E., Kang, N. *et al.* (2001) An enhanced linkage map of the sheep genome comprising more than 1000 loci. *Genome Res.*, **11**, 1275–1289.
51. Walling, G.A., Visscher, P.M., Andersson, L., Rothschild, M.F., Wang, L., Moser, G., Groenen, M.A., Bidanel, J.P., Cepica, S., Archibald, A.L. *et al.* (2000) Combined analyses of data from quantitative trait loci mapping studies. Chromosome 4 effects on porcine growth and fatness. *Genetics*, **155**, 1369–1378.
52. Khatkar, M.S., Thomson, P.C., Tammen, I. and Raadsma, H.W. (2004) Quantitative trait loci mapping in dairy cattle: review and meta-analysis. *Genet. Sel. Evol.*, **36**, 163–190.
53. Thomson, P. (2003) A generalized estimating equations approach to quantitative trait locus detection of non-normal traits. *Genet. Sel. Evol.*, **35**, 257–280.
54. Guttmacher, A.E. and Collins, F.S. (2002) Genomic medicine—a primer. *N. Engl. J. Med.*, **347**, 1512–1520.
55. Howard, T.H., Homan, E.J. and Bremel, R.D. (2001) Transgenic livestock: regulation and science in a changing environment. *J. Anim. Sci.*, **79**, E1–E11.
56. Basu, P., Masters, B., Patel, B. and Urban, O. (1993) Food safety and inspection service update on food safety of animals derived from biotechnology experiments. *J. Anim. Sci.*, **71**, 41–42.
57. Dove, A.W. Clone on the range: what animal biotech is bringing to the table. [Erratum (2005) *Nat. Biotechnol.* **23**, 488.]. *Nat. Biotechnol.*, **23**, 283–285.
58. Van Cott, K.E. and Velander, W.H. (1998) Transgenic animals as drug factories: a new source of recombinant protein therapeutics. *Expert Opin. Investig. Drugs*, **7**, 1683–1690.

59. Butler, S.P., O'Sickey, T.K., Lord, S.T., Lubon, H., Gwazdauskas, F.C. and Velander, W.H. (2004) Secretion of recombinant human fibrinogen by the murine mammary gland. *Transgenic Res.*, **13**, 437–450.
60. Christiansen, S.B. and Sandoe, P. (2000) Bioethics: limits to the interference with life. *Anim. Reprod. Sci.*, **60–61**, 15–29.
61. Smith, T.J. (1994) Commercial exploitation of transgenics. *Biotechnol. Adv.*, **12**, 679–686.
62. Appels, R., Francki, M., Cakir, M. and Bellgard, M. (2004) Looking through genomics: concepts and technologies for plant and animal genomics. *Funct. Integr. Genomics*, **4**, 7–13.
63. Cascalho, M. and Platt, J.L. (2001) Xenotransplantation and other means of organ replacement. *Nature Rev. Immunol.*, **1**, 154–160.