GENETIC BASIS AND IMPROVEMENT OF REPRODUCTIVE TRAITS

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Keywords: gene, genome, reproduction, livestock, SNP, candidate, QTL, gene expression, GWAS, genetic selection, genomic selection

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Summary

This chapter summarizes the knowledge about genetic factors affecting reproduction in livestock and available methods for studying the genetic influence on reproductive traits. Identification of the genetic basis of reproductive processes is in general complicated by their complex and quantitative nature. In the last decades, two main approaches have been widely applied for this goal in different domestic species: candidate gene studies and genome scans.

Both approaches have been useful respectively in the identification of associations of specific gene polymorphisms or genomic regions with reproductive traits. Nevertheless, the identification of the specific causal mutations affecting the traits remains a challenging task. More recently the availability of high throughput platforms for the study of the genome at structural (SNP chips) and functional (expression microarrays) levels offer new possibilities for the dissection of the genetic variation and metabolic pathways influencing reproductive efficiency.

Merging the available results of different approaches allows for the identification of new functional and positional candidate genes for future studies and candidate molecular pathways to control reproductive processes. Massive sequencing methodologies will probably improve in the near future the power and resolution for the identification of specific genetic variants influencing reproductive physiology.

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1. Introduction

Reproduction is essential for all species as it is the key for survival and evolution. Overall processes of sexual reproduction are relatively conserved and well defined, but the underlying molecular and genetic basis of each of the numerous steps involving these general processes is much less known. The complexity and transient nature of specific reproductive processes are the cause of reduced knowledge concerning their molecular basis.

From a productive point of view, reproductive efficiency is one of the most important factors affecting productivity in livestock industries. Reproductive traits, especially those related with fertility, litter size and pre-weaning viability, are important components for reducing the costs of producing animal meat (de Vries, 1989; Rothschild and Bidanel, 1998). Therefore, much effort is made to identify the ways for improving these traits. This improvement of reproductive traits is related to different fields, with management, nutrition and genetics having a great impact.

Regarding genetic improvement, available work has mainly focused on phenotypic selection, that is, reproductive animals have been selected using observable and measurable information on productive traits, rather than using information on specific genetic factors (genotypic information) affecting these productive traits. Nevertheless, reproductive traits are characterized by low heritabilities and a complex genetic basis and are thus difficult to improve using traditional selection methods. Moreover, these traits are recordable only in one sex and late in the animal’s life.

While numerous improvements have been made in other economic traits such as growth or feed efficiency using genetic and selection management advances, reproductive efficiency has not been very successfully improved in most livestock species. These limitations have led to a growing interest in the identification and characterization of specific genes and genomic regions implicated in the variability and regulation of reproductive processes.

Understanding the genetic control of female reproductive performance would offer the opportunity to utilize natural variation and improve selective breeding programs through the inclusion of molecular genetics information for evaluation of candidates for reproduction.

Molecular genetics and genomics are the field of biology that studies the structure and function of genes and genomes at a molecular (nucleic acids) level. In recent years, the extraordinary development of molecular genetics and genomics methods and platforms has opened the possibility for the identification and characterization of markers, genes and pathways responsible for the genetic complexity of quantitative traits in domestic animals.

The dissection of this complex genetic architecture will increase our understanding of the underlying physiology and could probably allow the efficient genetic improvement of reproductive traits through the use of gene and/or marker assisted selection.
2. Reproductive Traits

In the field of genetics, the main research area in relation to animal reproduction is the identification of genes or genomic regions influencing reproductive phenotypes.

The reproductive function consists of a complex mosaic that combines different male and female processes, and interactions among them. The first process is the development of competent gametes. Interaction between male and female cells starts with the ability of the female tract to transport, select and prepare spermatozoa for fertilization, then to ensure a maternal environment that facilitates fertilization and early embryo development. The cross talk between an embryo and its maternal environment leads then to successful early embryo development and implantation. In the whole reproductive process it is difficult to isolate and measure precise events and functions involved in pregnancy success or failure.

Thus, in the genetic study of reproduction, these complex reproductive processes are measured in the form of objective records, which reflect the success/efficiency of the several stages of the reproductive process. These reproductive phenotypic records are diverse and the common feature is that all the processes measured correlate in some way with reproductive efficiency. Phenotypic records include endocrine measures (plasmatic hormonal levels), litter measures (embryo survival, counts of live, dead, mummified, weaned descendants), morphologic measures of reproductive organs (weights of testicles or ovaries, scrotal circumference, teat number, length and placement, udder characteristics, uterine capacity and length), semen quality (sperm, semen and ejaculation characteristics), fertility related traits (calving ease and interval, heat intensity, fertilization rate, non-return rate, ovulation rate, inseminations per conception) and other general reproductive traits as age at puberty or gestation length.

The relevance of the different reproductive traits is not the same and also differs among species. For this reason, most genetic studies have focused on some reproductive traits of utmost relevance. In cattle, low female fertility has a very negative impact on production as it causes economic losses by increasing the need for additional inseminations, higher veterinary costs, longer than optimal lactations, fewer calves, and higher replacement costs. Also, calving ease and incidence of dystocia are two measures narrowly related to reproductive success and mother and descendant’s viability. Calving difficulty has an obvious negative impact on the profitability of a herd through increased calf and heifer mortality, slower re-breeding performance and considerable additional labour and veterinary expense. Therefore, improving these kinds of traits is important for dairy cattle breeders. In meat sheep production, litter size and days to lambing are two of the most important traits (Olesen et al., 1994), but its inclusion in selection schemes has been limited because of its low heritability (Fogarty, 1995).

Although fertility is considered the most important reproductive factor affecting farm profitability there are many others with obvious relevance such as age at puberty or calving interval. Also, other less evident reproductive traits are receiving increasing attention such as scrotal size (SS) or gestation length (GL). Scrotal size is positively associated with increased semen production and quality; and decreased age at puberty in heifer progeny. Additionally, the genetic correlation between this trait and growth are
positive suggesting that selecting heavier cattle at any age will increase scrotal circumference. Gestation length - the number of days from mating until birth of the calf - has a positive genetic correlation with days to next calving suggesting that a decrease in gestation length would be associated with a decrease in calving interval. The genetic correlation between gestation length and birth weight is positive. Selection for a decrease in gestation length would result in heifers with shorter gestation lengths, lowered calf birth weights and a lesser likelihood of difficult births.

In pig breeding, as in other polytocous species such as rabbits, the litter size is probably the most relevant and easily measured reproductive trait, and the one to which most attention is devoted. The usual measures of litter size used are the total number of piglets born (TNB) and the number of piglets born alive (NBA). TNB is the sum of NBA and the number of stillborn piglets (NSB). Litter size is determined by the interaction of numerous physiological components, such as the number of ovulated eggs (ovulation rate, OR) which determines the maximum number of possible offspring, and the rate of prenatal survival (Haley and Lee, 1993).

3. Quantitative Genetics

Quantitative Genetics is the branch of genetics that studies quantitative traits and has as main objective the study of their inheritance. Any phenotypic trait that takes different values in different individuals and does not follow a pattern of simple mendelian inheritance is a quantitative or polygenic trait. Most of the traits of interest in livestock are included in this category (e.g. growth, physiological functions, milk production). Other traits, such as litter size or conception vs. non-conception, present only few discrete categories, and are named “threshold traits”. However we can assume that there is an underlying continuous distribution, such that they can be treated as continuous traits.

Phenotypic variation is due to underlying genetic complexity from multiple interacting genes or loci (positions of genes or DNA sequences on a genetic map). For each gene or position, each animal has two copies (alleles) received from the parental gametes, with allelic effects that are susceptible to the particular environmental conditions (Falconer and MacKay, 1996). The phenotype value for a specific individual is the result of genetic factors, environmental factors, and the interaction between both.

Phenotype = Genetic Factors + Environmental Factors + G x E

Genetic factors affecting quantitative traits can show Additive (each allele has a specific metric value that is added to the phenotype), Dominant (homozygous dominant and heterozygous genotypes contribute the same to the phenotype) or Epistatic (interaction of two genes controlling a trait) gene action, with the Additive action being the most important. To genetically improve a specific quantitative trait it is necessary to know its heritability, which can be expressed as the ratio of additive genetic variance to the total phenotypic variance:
Heritability indicates the resemblance between parents and their offspring. For a specific trait, high heritability implies a strong resemblance between parents and offspring while low heritability implies a low level of similarity. Given its definition as a ratio of variance components, the value of the heritability always lies between 0 and 1. For traits associated with fitness, such as the main reproductive traits, heritability is typically between 0.1–0.2 (Visscher et al., 2008).

\[ h^2 = \frac{va}{vp} \]

Genotypes are not passed on from parents to progeny but the alleles at the loci that influence the traits are. The additive genetic value of an individual - their breeding value - is the sum of the average effects of all the alleles the individual carries (Falconer & Mackay, 1996). The use of the BLUP (Best lineal Unbiased Prediction) statistical methodology is the best one to obtain the breeding values. All records and genetic relationships available are used in order to estimate simultaneously genetic and environmental effects. BLUP-animal model allows for an evaluation of all animals of both sexes, either with or without performance, leading to increases in selection accuracy, particularly for traits with low heritability such as reproductive traits. For example, in polytocous species such as pigs or rabbits, the estimated heritability of litter size at birth and at weaning ranges between 0.10 and 0.15. These low heritabilities hinder the improvement of these traits but this problem can be improved using models with permanent environment effects. Usually, repeated measures are available for the same individual across its lifetime, and these repeated measures can readily be accommodated within the animal model framework by including a further random effect defining the permanent environment common to all observations on the same individual (Lynch & Walsh 1998). Consequently all available measurements can be exploited, rather than using a single average value for each animal.

In cattle, heritabilities for nearly all measures of fertility are only 1–5% (Cammack et al., 2009), and are negatively genetically correlated with milk production traits. Genetic improvement of reproductive traits is also hampered by the fact that an individual record is not available for maternal reproductive traits when selecting among boars and is not available for females when selecting among young gilts. Traditional selection for these traits is based on relative’s performance and therefore animals from the same litter have an equal estimated breeding value. Other reproductive traits, such as age at puberty, have an estimated heritability of 35%, thus animals with genetic potential to reach puberty at an earlier age can contribute to improved conception rates and lower costs associated with feeding.

It is necessary to point out that the heritability estimate is specific not only for the population in question but also for the environment it was estimated in; and can change over time. Genetic variance can change if allele frequencies change (if there is selection or inbreeding) or when new variants come into the population by migration or mutation. There are other effects that can be taken into account for most reproductive traits, such as maternal effects. Maternal effects occur when the phenotype of the mother affects the phenotype of her offspring. In mammals, these effects may be either genetically or environmentally determined. For example, lactation has a critical effect on offspring
growth rate and performance, and may be determined by both the mother’s genotype and her environment. In the case of weight at birth, its variance is influenced by the maternal uterine environment.

Moreover the same trait measured at different ages may be influenced by different genetic and environmental factors. For some traits we could get repeated measures for the same individual across its lifetime. In the animal model framework this is not a problem but an advantage, because all available measurements can be exploited, rather than using a single average value for each animal (Lynch & Walsh, 1998).

The biological constraints that limit the success of traditional selection for reproductive traits can potentially be ameliorated by the application of molecular genetics methods, particularly the inclusion of genetic markers in selection strategies. The essence of using genetic markers in breeding programs is that they mark chromosomal regions (and sometimes individual genes), and thus make it possible to follow the inheritance of these regions from parents to offspring. Thus, if we know which chromosomal segments contain alleles of value, markers may be used to help identify animals that have inherited these alleles and hence the best of the genetic variation, whether or not we have phenotypic records or progeny information on the animals (Visscher et al., 1998).

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ANIMAL REPRODUCTION IN LIVESTOCK - Genetic Basis and Improvement of Reproductive Traits - Cristina Óvilo, Carmen Rodríguez Valdovinos


Biographical Sketches

Cristina Óvilo was born in Spain in 1969. She graduated in Veterinary Medicine in 1993 (Animal Production) and got her Ph.D. degree in Animal Genetics (1999) at the Universidad Complutense de Madrid. Currently she is senior researcher at the Department of Animal Breeding and Genetics of the National Institute of Agricultural and Food Research (INIA) in Madrid, Spain. Her background is molecular geneticist and her main research interest is the study of Genetic Basis of productive and reproductive traits in swine. Specific research projects are related with the identification of markers, genes and metabolic pathways associated with phenotypic traits (growth, fatness, quality and reproductive traits) by means of QTL, candidate gene and transcriptome studies. Other research lines include nutrigenomics and prenatal programming studies. She has participated in several important research projects with national and international founding. She has authored or coauthored more than 50 scientific articles published at relevant journals, has participated as speaker in several national and international conferences, works as referee for numerous journals and as scientific consulter for several institutions.

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