Genômica aplicada ao melhoramento animal: presente e futuro

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Ferramentas genômicas aplicadas ao melhoramento animal (Genomic Tools Applied to Animal Breeding)

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Since the 1980's large efforts have been devoted by several international research groups to identify informative molecular markers and build genetic maps for animal species with economic importance. Genetic maps were built using different techniques with the objective of developing the necessary tools for identifying and characterizing the underlying genes responsible for the genetic variation observed in traits related to productivity, product quality, disease resistance, etc. Several resource populations were generated by crossing breeds with extreme phenotypes, and also by using structured populations found in standard genetic evaluation programs, to map Quantitative Trait Loci (QTL) for eventual identification of the underlying genes by positional cloning. Research objectives aimed at identifying DNA markers for use as breeding tools in Marker Assisted Selection (MAS) procedures and also at the development of innovative biotechnological tools (transgenics, knock-outs, etc) based on the physiological role of newly identified genes. However, over two decades of work resulted in the identification of only a small number of major genes that affect production traits and a few genes responsible for heritable diseases. Commercial molecular marker panels were assembled with the generated information and marketed as breeding tools for cattle and pigs but, at the most, can explain only a small fraction of the estimated additive genetic variance for any given trait, hindering their use as highly questionable. The Bovine Genome Project, starting in 2003, spearheaded efforts to massively identify and use SNP (Single Nucleotide Polymorphisms) markers in agricultural species. The identification of hundreds of thousands of SNPs and the assembly of a reference sequence allowed for the application of then newly developed genotyping methods that can provide data for hundreds of thousands of SNPs in parallel, which brought about a revolution in methods and objectives of molecular breeding research. Methods have been developed to simultaneously estimate the effects of all genomic regions that affect a particular trait (termed Genomic Selection) which have shown correlations >70% with EBVs (Estimated Breeding Values) estimated with traditional methods. In addition, these new tools have also made a great contribution to research aiming at identifying genes responsible for heritable diseases, turning projects that would cost hundreds of thousands of dollars and last for years into experiments that can be carried out in weeks at a fraction of the costs and that require little to no investment in laboratory infrastructure. These innovations have created the potential for higher rates of genetic gains at reduced costs and great improvements are still expected in the near future as new methods that use Next Generation Sequencing technologies are fully incorporated into genetic evaluation and breeding programs. We will show how Embrapa's animal genetics and improvement research groups have been at the forefront of these developments and have acted to pioneer research activities in the country.

Quantitative genomic methods applied to animal breeding

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Major advances have been made in technologies for prospecting genes related to complex biological traits such as disease resistance, production efficiency and product quality. The aim of this work is to present quantitative methods applied to animal breeding by Embrapa's Animal Genomics Research Network, using two distinct approaches: structural and functional. The structural approach is based on using molecular markers to relate DNA sequence changes (polymorphisms) to population structure and to observed variation in phenotypes of interest. Currently, Single Nucleotide Polymorphisms (SNP), a single base change in the genetic sequence of an individual with respect to a reference genome, due to their abundance in the genome and suitability for automated large scale processing are the most powerful markers for genomic studies. Methods to use dense SNP genotypes to estimate linkage disequilibrium (LD), to infer effective population size and to design whole genome association studies and genomic evaluation schemes are presented and demonstrated with livestock data. Additionally, from a functional perspective, gene expression profiling using oligonucleotide microarrays represents another large scale alternative to identify genes that contribute to economically important phenotypic variation in livestock. In these experiments, the effect of a treatment, condition or genotype on transcript abundance is simultaneously measured for thousands of genes, facilitating the identification of gene regulatory networks and metabolic pathways. The processing of samples to assess gene expression involves several steps and there are embedded procedures to verify the quality of the RNA sample and experimental procedures. Initially, quality control criteria are used to evaluate array images for artifacts, raw data distributions consistency, correlations between arrays, percentage of detected genes, background and noise values, scale factors and control probes signals. Next, robust multiarray average (RMA) is employed for background adjustment, quantile normalization, log2-transformation and summarization of the multiple corrected probes intensities to a single signal value. Finally, the differentially expressed genes identification is based on a two-step single-gene mixed model analysis and a modified F test combining information across genes, using permutations to calculate significance and false discovery rate to adjust p-value for multiple testing. Despite using different methodology, structural and functional approaches are both of prospective nature, providing insights for the associations between groups of genes and physiological traits, links between the genome and the biological processes involved in the manifestation of the phenotype and may generate direct information for the genetic background of economically important traits or new hypotheses to be tested in subsequent studies, using more specific or targeting approaches.