GENOMIC APPROACHES TO ECONOMIC TRAIT LOCI AND APPLICATION TO MUSCLE BIOCHEMISTRY

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In livestock species, significant advances in the selection process for economically important characters have been achieved over the past decades (Dekkers and Hospital, 2002) : such progress was based on the phenotypical recording of individual performances for traits of interest and on the compilation of these observations, together with the genealogical information concerning a certain "breeding value" of candidates for selection. Most of the economic traits considered in animal selection are quantitative traits, for which genetic variation is thought to be based on the cumulative interaction of different alleles of several genes along with environmental factors : indeed for quantitative trait loci a generally accepted hypothesis is that the genetic architecture of a QTL consists of a large number of genes, each having a small effect on the phenotype (Flint and Mott, 2001). Therefore to attain a reasonable understanding of the relevant genes controlling a specific phenotype and of their interaction remains an impossible challenge with traditional methods although recent studies have demonstrated that in some cases, a small number of genetic loci contribute to a large proportion of the variance of the trait of interest (Hilbert et al., 1991; Jacob et al., 1991). Moreover, several limitations of these methods for genetic improvement based on population genetics and statistics are becoming evident with time : first, efficiency decreases when the traits are difficult to measure or have a low heritability, second, animal selection has been generally limited to traits that can be correctly measured in a large number of animals and third, new selection criteria have to be integrated in the selection process such as adequacy of the processed product (i.e. milk for cheese production, carcasses for meat production ...), quality and acceptance of the final product by the consumer, and animal welfare.

With the rapid advancement in elucidating the mechanisms of heredity and in technologies giving direct access to the blueprint of an organism, the basis for a new discipline called "genomics" was established. Phenotype differences between different animals, and therefore differences in a final product, can now be studied from a completely different point of view, namely the nucleotide sequence. A major goal of genomics is to gain an exhaustive understanding of the structure and the function of genomes through a detailed molecular characterization of whole genomes. Therefore genomic approaches can help to biological problems like the dissection of the genetic components of a qualitative, quantitative and complex trait and thus new possible applications for animal selection can be considered in the near future (i.e. marker assisted selection). In this presentation, current genomic approaches available to reseachers and strategies to study economic trait loci in livestock will be described, and some applications to muscle biochemistry will be indicated. These efforts will lead to a better understanding of the relationship between genetic variation and biological function.

Genomic approaches :

Genomics is divided into two basic areas, the characterization of the physical nature of whole genomes (structural genomics) and the characterization of the overall patterns of gene expression (functional genomics). Both approaches are relevant to the mapping, the detailed characterization of economic trait loci and the identification of the relevant gene(s) controlling the trait of interest.

Structural genomics :

Starting with a phenotype of interest in an animal population and postulating that no prior knowledge could lead to the direct discovery of the underlying gene(s), identification of the genetic determinants of a particular phenotype will most often start with the identification of pedigrees in which the traits of interest are segregating in order to develop a positional cloning approach. This strategy takes advantage of the structural knowledge of the genome namely cytogenetics, genetics, radiation hybrids and physical maps of a genome : a trait of interest will be mapped to a particular chromosomal region through the identification of linked markers and genes. This approach is often combined with a candidate gene approach where potential functional candidate genes are investigated in the defined interval of localization of the studied trait.

As genomic approaches are emerging in different species, data from several genomes are produced and combined into a relatively new discipline, namely comparative genomics : through comparative mapping, chromosome similarities among species are identified making it possible to extrapolate mapping data from genomes with high resolution gene maps (human and mouse) to genomes with low resolution gene maps (i.e. livestock species). Another step in comparative genomics is comparative sequencing, where sequence comparisons could prove very useful to confirm functional annotations or computational gene-finding results and to identify novel genes in a genome [Thomas & Touchman, 2002 ; Roest et al., 2000]. Beside the comparison of coding regions, comparative sequencing has the potential of identifying conserved sequences outside the coding regions that could control gene expression (Hardisson, 2000). One can hypothetize that part of the conserved sequences should be of potential functional significance.

Functional genomics:

A major effort in genomics is the identification of coding sequences or transcript units on a whole genome basis and the discovery of those that are trait-associated and expressed in a specific organ or tissue and therefore responsible for a particular function and/or phenotype. One recent technological advance in this area is DNA microarray. In this technique, DNA containing known and undefined genes is spotted at a very high density to generate a microarray (DNA chip). Samples of messenger RNA are then reversed transcribed and hybridized to the microarray followed by the quantification of the amount of material per spot : the result will give a gene expression "fingerprint" and by comparing samples from two or more tissues or the same tissue with different treatments, it is possible to associate the expression of particular genes with the phenotype. This technology has recently been tested and several papers have successfully demonstrated that this methodology can provide insights on complex biological systems.

Other approaches based on the combination of structural, functional and comparative genomics could prove very useful in the near future :

1. Accessing metabolic pathways : physiological and biochemical expertise of a trait of interest (phenotype) could lead to the identification of candidate pathways and therefore candidate genes involved in the entire pathway. Taking the human genome as master genome, human gene sequences for all known genes of a pathway make it possible to identify species specific coding sequences and therefore species specific large insert clones (BAC) for which polymorphism, namely Single Nucleotide Polymorphism (SNP) could be detected : this polymorphism would then be used to test a putative association for each gene of the pathway and the trait of interest.

2. Making use of model organisms : in order to identify potential genes involved in meat quality, a model organism like *Caenorhabidtis elegans* could help identify all the genes involved in the development of the muscle tissue since the complete genome is now sequenced and cell differentiation is well known.

Finally, as new tools and methodologies are now available to researchers for the study of the genetic determinants of specific traits and phenotypes, particular efforts have to be made on the characterisation and the dissection of specific phenotypes into simple biological units for which the genetic determinants are easier to identify : a complex trait would then be the interaction of several "simple" biological units.