

Review

Is quantitative genetics still necessary in this age of genomics?

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Quantitative genetics and genomics are two different disciplines that have separate evolutions. The quantitative genetics has enormous applications and has contributed a lot in four main distinct fields of plant breeding, animal breeding, evolutionary genetics and human genetics. This field is based on study of inheritance patterns and their underlying mechanisms using biometrical or statistical methods. The analysis of genome aims to identify genes of interest and understand gene expression profile and gene function. This analysis exploits different molecular biology approaches. This review discusses the quantitative genetics and molecular approaches in studies of quantitative traits. It also tries to find out the connection and complementation between approaches of quantitative genetics and molecular biology in the studies of quantitative traits. The information gathered in this review will assist breeders and geneticist in their regular research works.

Key words: Gene, genome, genotype, phenotype, trait.

INTRODUCTION

Quantitative genetics and genomics are two different disciplines that have separate evolutions. Quantitative genetics provides the means to estimate heritability, genetic correlations and predicted responses to various selection schemes (Keurentjes et al., 2008). Genomics offers powerful tools for mass screening of desired traits (Holland and Cardinal, 2008). Both disciplines are currently applied as tools for crop and animal improvement and for human and evolution genetics (Ellgren and Galtier, 2016). This paper discusses the quantitative genetics and molecular approaches in studies of quantitative traits and also tries to find out the connection and complementation between approaches of

quantitative genetics and molecular biology in the studies of quantitative traits. Then, it gave a general view.

QUANTITATIVE GENETICS

Genetic traits can be qualitative or quantitative and each category has its own specificity. Qualitative traits are controlled by single genes and characterized by clear phenotypic classes. Inversely, quantitative traits are controlled by many genes and they present continuous variations in phenotypes. Moreover, these traits are extremely affected by non-genetic effects and their

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complexity is enhanced by interactions between genes and environment (Holland, 2007; Keurentjes et al., 2008; Kroymann and Mitchell-Olds, 2005). The study of inheritance patterns of quantitative traits and their underlying mechanisms by using biometrical or statistical methods is named quantitative genetics (Falconer et al., 1996).

The quantitative genetics has enormous applications and has contributed a lot in four main distinct fields of plant breeding, animal breeding, evolutionary genetics and human genetics. The general objective of studies related to these fields is to determine the contribution of genetic and non-genetic factors to the phenotype. However, the specific objectives of each field differ from one another. Plant and animal geneticists focus on development of new lines and identify among these lines, individuals which present desirable and stable traits. The human geneticists focus on identification of genotype associated with diseases and contribution of non-genetic factors for the disease development (Wray and Visscher, 2015). On the side of evolutionary genetics, geneticists concentrate on pinning out the genetic makeup of specific phenotype and try to understand its past and its probable future evolutions (Kearsey et al., 2003; Walsh, 2001).

Even though the quantitative genetics has contributed to solve different problems in agriculture and animal breeding, human genetics and evolution genetics, it presents some drawbacks. Quantitative genetics does not provide facility to study effects of isolate genes on variation of a specific variation (Kearsey et al., 2003). In addition, with quantitative genetics, it is not easy to understand the genetic basis of quantitative traits and their mechanisms of maintenance during evolution and to understand the relationship between genetic variation and phenotypic variation (Mackay et al., 2009). This is a particularity of molecular approaches which facilitate following and localizing the transmission of small pieces of chromosomal region from parents to offspring (Kearsey et al., 2003). Therefore, the progress in molecular approaches including genomics could have a positive effect on evolving the quantitative genetics.

Molecular approaches

Currently, many studies in molecular biology aim to understand the gene function and gene expression profile. To achieve this goal, different molecular approaches such as analysis of genome, transcriptome, metabolome and proteome were developed (Carpentier, 2007; Lappalainen, 2015).

The analysis of an organism's genome is a complex study and this discipline is known as genomics. The origin of genomics is genetics on which, there is aim to understand the structure, function and the evolution of genomes. Genomics is based on a complete genome analysis and involves DNA sequencing, assembly of

sequences, annotation and mapping of genes (Arabidopsis, 2000).

The study of gene expression and its regulation is another approach to understanding the gene function. This approach is known as transcriptome. The most efficient tools to carry out the transcriptome analysis include microarray analysis, cDNA fragment fingerprinting and serial analysis of gene expression (SAGE) (Brown and Botstein, 1999; Schena et al., 1998).

Metabolome represents the collection of all metabolites in a biological organism at a specific time point and under specific conditions. These metabolites are the end products of the biological organism genes expression. The study of metabolome (metabolomics) is the comprehensive, qualitative and quantitative study of all small molecules (less than or equal to 1500 daltons) participating in important metabolic functions and fulfilling critical roles such as signalling molecules or secondary metabolites in an organism (Oliver et al., 1998). The main methods for metabolome analysis are metabolite profiling and metabolite fingerprinting (Hall, 2006).

The last approach towards understanding the gene function and gene expression profile is proteomics. Proteomics focuses on the characterization of the cellular proteome which is defined as a set of protein species present in a biological unit at a specific developmental stage and under determined external biotic and abiotic conditions (Jorrín et al., 2006; Klug et al., 2000; Prescott et al., 2005). Proteomics involves protein biochemistry and bioinformatics to determine the spatial and temporal expression of proteins in cells and tissues of a living organism (Karr, 2007). Expression measurements of mRNA levels show the dynamics of gene expression and show what might occur in the cell, whereas, proteomics discovers what is actually happening (Prescott et al., 2005; Ghatak et al., 2017). The main tool of proteome analysis is a two dimensional gel electrophoresis (2-DE).

All these approaches (genomics, transcriptomics, metabolomics and proteomics) are powerful tools for massive screening of several genes and aim to reveal the changes of what might be occurring in a cell (Rute et al., 2016). However, each approach has its own strength and weakness.

The comparisons of mRNA expression and protein expression revealed a poor correlation between RNA transcription and protein abundance (Greenbaum et al., 2003). This observation was attributed to the fact that there are many complicated and varied regulation mechanisms of gene expression and post-transcriptional mechanisms. Therefore, the expressed proteins of the same gene may differ significantly in their abundance and structures (Giavalisco et al., 2005).

A genome project provides information on the number and kinds of genes present in an organism (Klug et al., 2000). Sequencing has revealed that the link between gene and gene product is often complex and one gene can produce several types of transcripts as a result of an

alternative splicing (Celotto and Graveley, 2001). It is estimated that 40 to 60% of human genes produce more than one protein because of the alternative splicing and post-translational modification (Klug et al., 2000; Kwon et al., 2006). These variations of end products of the same genes have effects on variation of phenotypes.

The transcriptomics and the proteomics studies are based on the available information of genome sequence. Therefore, transcriptomics studies are still hindered by the lack of full sequence of genome of many living things (Greenbaum et al., 2003). The sequences of genes are infrequently identical between species. On the contrary, functional protein domains are well conserved. Therefore, it is possible to identify the function of new gene product by its comparison with well-known homologous proteins (Carpentier et al., 2008).

These molecular approaches are powerful tools to identify candidates with desired traits but the manifestation of these traits depends on non-genetic factors. This requires the investigation of appearance of those traits in different environments before taking a final conclusion on identified candidates. From this observation, it is also evident that the quantitative genetics assists the molecular approaches to reconfirm their findings. Therefore, there is a close link between quantitative genetics and molecular approaches.

LINK BETWEEN QUANTITATIVE GENETICS AND GENOMICS

In the quantitative genetics, a trait is controlled by many genes. In the past, there was a gap of knowledge on a theoretical work of individual genes determining the quantitative trait. Currently, a method to study these genes is available and these genes are known as quantitative trait loci (QTLs). The identification of individual genes leads to several applications. It can facilitate the selection process for traits with low heritability and allow their applications in a genetic engineering of quantitative traits. In the medical field, the identification of individual genes responsible for hereditary diseases can assist to improve the prevention methods. This discovery has also a positive effect in the understanding of evolution process (Falconer et al., 1996).

The main methods of quantitative genetics to identify the genes underlying quantitative traits are multimodal distribution, backcrossing with selection, non-normal distribution, heterogeneity of variance, offspring parent resemblance and complex segregation analysis. However, these methods do not give any information on how the individual genes contribute to the traits. Therefore, the new approach to study these individual genes is to identify all individual genes that have effect on the trait, try to set up their linkage map and finally use molecular cloning of relevant sequences of DNA

(Falconer et al., 1996).

The difference between individuals is mainly due to variation at a genomic level and this variation affects the quantitative traits. The variation observed in these traits are derived specifically from the variation in DNA sequences and this polymorphism at DNA level is the most excellent marker of variation between individuals (Keurentjes et al., 2008). Nevertheless, this polymorphism needs a careful analysis because in some cases, they are meaningless. On one hand, the polymorphisms in coding DNA sequences and in regulatory sequences can result in variations in protein expression, function and stability. Consequently, these variations affect strongly the phenotypes. On the other hand, effects of polymorphism on non-coding DNA sequence are extremely low when affecting the phenotype. The study of these polymorphisms could assist to predict quantitative traits in breeding programs (Borevitz and Nordborg 2003; Keurentjes et al., 2008).

Quantitative genetics uses mainly the variance to evaluate different traits in the population, whereas, genomics uses precise markers. In quantitative genetics, there are challenges because genotypes are generally unknown and their appearance in population is a random process. On the side of genomics, there are tools for quantitative genetics to overcome this challenge. These tools include molecular markers mainly established from single nucleotide polymorphisms (SNPs) and or microsatellites. These genomic tools for quantitative genetics assist to identify a QTL mapping and to estimate the degree of relatedness between individuals (Walsh, 2001). These tools are the results of progress of molecular biology.

The progress in molecular biology techniques has changed the focus of quantitative genetics from one characteristic to a broad analysis. These techniques permit geneticists to identify the relationship between gene, its product and its biological function. The combination of these molecular techniques and progress in the statistics through quantitative genetics permitted the establishment of regulatory network that put together diverse stages of biological information from gene to function (Keurentjes et al., 2008).

The study on connection between genetics and genomics was first carried out on yeast in 2002 and this work opened the window for other similar studies (Brem et al., 2002). The progress in genome sequence offers the possibilities to compare genomic positions of genes with the map positions of QTLs that affect the expression of these genes. This comparison gives information on cis- and trans- regulation of gene expression (duplication, transcription and translation). In this process of gene expression, transcription is the initial stage of connection of sequences of genotype to phenotype. The variation in quality and quantity of successive products (proteins and metabolites) resulting from this expression process are responsible for variation in phenotype. These were also

confirmed by high analysis of proteome and metablome of physiologically stressed individuals and between individuals with different genetic makeup (Chevalier et al., 2004; Fiehn et al., 2000; Keurentjes et al., 2008).

Even though proteomics and metablomics are good candidates to study the functional consequences of natural genetic variation, they present some limitations. The complete analysis of proteome or metablome which is equivalent to full genomics analysis is impossible. This impossibility is due to the complexity and diversity of proteins and metabolites in a living organism and their analysis requires different and many protocols. Moreover, even for full sequenced genome, it is not possible to precisely predict proteins or metabolites that a living organism can express. This is because of variation in gene expression where one gene can be expressed in products varying in quality and quantity (Fiehn, 2002; Jansen, 2003).

The progress of findings in genomics has positive effects on quantitative genetics. After having a complete genome sequence, it is possible to scan the potential variations among individuals. These variations can be used to choose microsatellite makers and to construct different DNA chip microarrays for identified DNA sequences. In addition, other techniques such as DNA probing, *in situ* hybridization and others are based on the availability of full genome sequence. With full genome sequence, it is possible to propose candidates presenting genes for the traits of interest (Walsh, 2001). All these improvements in genomics have positive effects by shortening the screening process in the specific studies of quantitative traits. Therefore, it seems that in addition to the link between quantitative genetics and genomics, these two fields complement one another.

COMPLEMENT BETWEEN QUANTITATIVE GENETICS AND GENOMICS

Quantitative genetics and genomics have different levels of screening process but both levels contribute to the availability of good results. In the quantitative genetics, the selection of complex traits in the animal and plant breeding is totally based on phenotypes. Currently, genomics allows a direct selection to genotype level. This facilitates and shortens the selection process (Walsh, 2001). However, this selection at genome level has some shortcomings. In breeding process, specifically for horizontal resistance, the frequencies of genes controlling quantitative traits increase with time under selection pressure. The probability that the frequencies of these genes will increase in population with selection to genotype level is extremely low. Moreover, the expression of gene depends on many factors. Therefore, the presence of a gene does not mean the presence of a phenotype.

The ability to screen plant cells in tissue culture and then grow the identified and surviving individuals to

develop whole and fertile plants greatly increases the efficiency of selection process for certain characters. However, results from the controlled artificial environment need to be confirmed in natural environment because many studies revealed divergent results in these two different environments (Walsh, 2001). This shows the need for the phenotype evaluation to be part of the screening process. Therefore, genomics can be used to check the presence of the genes and then the quantitative genetics intervenes to explore the end products of genes expression.

The French breeding program of daily sheep is a good practical case that combines the genomics and quantitative genetics. This program was able to develop very good French daily sheep breeds using conventional phenotypic selection for milk production and other valuable traits. To emphasize the disease resistance in this program, genomic tools were incorporated in the breeding program for the management of the PrP gene associated with spongiform encephalopathies. These new tools were used for PrP genotyping of one year old rams and allowed to identify the status of PrP gene in young ram before sending them into pipeline of breeding program (Barillet, 2010).

Currently, some developed molecular makers are available and applied in selection. The study of fatty acid biosynthesis pathway in plants and sequencing of genes in that pathway make DNA markers to assist in the selection for specific change in fatty acid traits in soybean (Holland and Cardinal, 2008). The molecular makers associated with diseases and pest resistance, drought and frost tolerance and others have been developed and are under use in the breeding program, but all these markers are used at the initial stages of the screening process (Mohan et al., 1997; Staub et al., 1996; Tanksley, 1983). The identified individuals undergo other studies with quantitative genetic approaches. This process of current breeding program shows the manner in which both genomics and quantitative genetics are important in the breeding works.

CONCLUSION

Quantitative genetics provide the methods to measure heritability and genetic correlation, and to predict the responses in selection process and assist the breeders to improve crops and livestock. This selection is mainly based on phenotypic variation which is determined by the combination of genetic makeup of individuals and environments. The main challenge of quantitative genetics is to understand the connection between genetic makeup (variation at DNA sequence) and variation in phenotype (quantitative traits), the mechanisms of maintenance and evolution of quantitative traits in population. At this point, quantitative genetics is effectively supported by genomics due to the availability of DNA sequencing, abundant markers, fingerprinting,

reverse genetic methods, studies on gene expression, development of statistical method for analyzing quantitative trait locus mapping and others. In combination with other molecular approaches (transcriptome, metabolite and proteome analysis) based on the availability of full genome sequence, genomics evolved the quantitative genetics. Moreover, information on quality and quantity of variation in proteins and metabolites, understanding the cis- and trans-regulation in the process of gene expression assist in understanding and obtaining a complete picture of genetic and phenotypic variation within the same and between different populations. However, in some cases, there is a contradiction between results from molecular approaches and those from quantitative genetics approaches.

In many molecular works, sometimes, cells or small tissues are used as a living organism mode. Results from this living organism mode are useful specifically in the screening process of breeding program. However, unexpected results are frequent when identified and selected individuals at cell level are tested in natural environment. This recalls the power of quantitative genetics on which the final conclusion is based on phenotypes. Therefore, both quantitative genetics and genomics approaches could complement each other to generate conclusive results.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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