Agricultural Sciences, 2015, 6, 1033-1038
Published Online September 2015 in SciRes. http://www.scirp.org/journal/as
http://dx.doi.org/10.4236/as.2015.69098

Recent Advances in Understanding Plant Heterosis

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Received 16 July 2015; accepted 20 September 2015; published 23 September 2015

Abstract

Although heterosis is widely utilized in crop production, its genetic and molecular basis is still elusive. It is arguably that heterosis arises in crosses between genetically and/or epigenetically distinct individuals. Various genetic models have been proposed to explain heterosis, such as dominance and overdominance hypothesis. With the recent advancements in functional genomics, epigenetics, transcriptomics, proteomics, and metabolomics-related technologies, systems-level approaches have been adopted to understand the molecular basis of heterosis. In this review, we gather a brief account of findings from various studies in order to better understand the genetic and molecular basis of heterosis.

Keywords

Heterosis, Genetic Factor, Epigenetic Factor

1. General View of Heterosis

Heterosis is a common phenomenon in many plants. Heterosis is formed by crossing different strains or varieties. Heterosis refers to the super performance of a hybrid exhibiting increased biomass, size, yield, growth rate, or fertility relative to its parents [1]. Joseph Koelreuter (1776) described that some plant hybrids displayed superior growth over their parents [2]. In 1876, Charles Darwin concluded that "the crossed plants when fully grown were plainly taller and more vigorous than the self-fertilised ones". Then he observed the growth patterns in more than 60 plant species [3]. The phenomenon was rediscovered by George H. Shull, and he firstly introduced the term heterosis in 1914 [4]. Since then, heterosis has been widely utilized in crop breeding, especially in maize. In the late 1990s, it was estimated that 65% of the worldwide maize (Zea mays) area was planted as hybrids,

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How to cite this paper: Feng, S.Q., Chen, X.L., Wu, S.J. and Chen, X.S. (2015) Recent Advances in Understanding Plant Heterosis. *Agricultural Sciences*, **6**, 1033-1038. http://dx.doi.org/10.4236/as.2015.69098

and the yield of maize had increased six fold since the use of hybrids started in the 1930s [5]. The economic importance of heterosis has led to extensive research to understand its basis. However, the genetic and molecular mechanisms for heterosis are still poorly understood. In this review, we present a brief account of findings in various heterosis studies (**Table 1**).

2. Genetic Analysis of Heterosis

Although the genetic basis for heterosis has been studied for over a century and several hypotheses have been advanced to explain the phenomenon, less progress has been made for the genetic basis of heterosis. Conventionally, dominance and overdominance were the two most prominent genetic hypotheses for heterosis [6]. The dominance hypothesis proposes that complementation of corresponding deleterious alleles lead to heterosis in hybrids [7] [8]. The overdominance hypothesis proposes that heterozygous allelic interactions result in heterosis in hybrids [1]. In summary, both the two genetic hypotheses describe genetic differences between hybrids and inbred lines. However, it is difficult to directly associate the favorable alleles that "dominant" and "overdominant" predict with the phenotypic traits in crop breeding (including maize) [9].

3. Transcriptomic and Proteomic Analysis of Heterosis

Various transcriptomic analyses have been carried out to explore the gene expression changes between hybrid and its parents to correlate the changes to heterosis. Based on the modes of gene action in the hybrid, the genes have mainly been classified as additive, dominance and over-dominance (non-additive) expression patterns [6]. Additive expression represents mid-parental expression patterns in the hybrid, whereas the dominance model suggests both low and high parent-like expression. In the case of over-dominance, the gene expression level in hybrid is either higher or lower than the level in parent. Various aspects of plant development and different organs have been analyzed at the transcriptome level. In summary, there is no uniform global expression detected in these studies.

Several studies indicated that non-additive gene expression was prevalent between parent and hybrid [10]-[13], while additive gene expression was detected in other studies [14] [15]. In addition, a similar number of genes followed additive and non-additive expression model was also observed [16]. Interestingly, of the two heterotic rice hybrid, non-additive gene expression was prevalent in one hybrid, while additive gene expression in another at the younger stages of development [11]. Although the modes of gene expression vary from different studies, the global trends are similar. For example, heterosis is a genome-wide phenomenon involves global

Table 1. Heterosis related studies.

Scope of the research	Results or factors related to heterosis	References
Genetics	Dominance	[7] [8]
Genetics	Over-dominance	[1]
Transcriptomics	Global expression trend (additive, non-additive and dominance)	[11]-[13] [16]
Transcriptomics	Genomic imprinting	[10]
Transcriptomics	Parent-of-origin effects	[19] [20] [21]
Transcriptomics	Dosage-sensitive factors	[22]
Transcriptomics	Altered expression of circadian and flowering genes	[25]
Proteomics	Global expression trend (additive and non-additive)	[27]
Proteomics	Altered expression of isoforms and modifications proteins	[28]
Epigenetics	DNA methylation	[18] [23] [24]
Epigenetics	Small RNAs	[17]
Energies	Energy utilization efficiency	[31]

changes in gene expression. More significant expression differences are found in the related species than those within species [6].

Allelic expression variation was further detected in many plant hybrids, such as maize and rice [17] [18]. Some genes in maize showed maternal or paternal like expression patterns, which were suggested to be associated with genomic imprinting [10]. Whereas in some studies, the minimal parent-of-origin effects on allele-specific expression were also detected [19]-[21].

A recent study gives a mechanism that allelic diversity is sensitive to dosage-sensitive factors [22]. Besides genetic factors, epigenetic factor was also suggested to play a potential role in allelic expression in hybrids [17] [18]. Recently, small RNA levels were measured in inbreds and hybrids. The differential expression patterns of small RNAs have been linked to heterosis [23] [24]. Importantly, several genes including circadian clock gene *CCA1* and flowering gene *SINGLE FLOWER TRUSS* have been found to play an important role in heterosis [25].

The expression of proteins in inbreds and hybrids has been measured in various studies, some of which indicated a strong correlation between heterosis and protein patterns [26] [27]. Proteomic analysis in maize and rice showed that more frequency of non-additive protein expressional variation than non-additive gene expressional variation in hybrids [27] [28]. Recently, the expression level of protein was compared using heterotic and non-heterotic maize hybrids. Interestingly, the differential expressions of proteins detected in heterotic hybrids were mainly involved in stress response, protein and carbon metabolism. In addition, the degree of heterosis was suggested to be linked to the frequency of protein isoforms and modifications [28].

Although the different modes of gene action as well as protein expression patterns were observed in hybrids and they supported the genetic models of dominance and over-dominance, the molecular basis of heterosis is still largely unknown.

4. Epigenetics Analysis of Heterosis

Combination of diverged maternal and paternal genomes in the same nucleus may lead to genomic instability, epigenetic and gene expression changes, which ultimately caused the changes of phenotype in hybrid. In the past few years, various studies have been carried out to find the role of epigenetics in heterosis.

Genome-wide methylation, sRNAs expression, gene expression and physiological index have been analyzed comprehensively in both hybrid and its parents. The variations of DNA methylation and sRNAs were observed between parents and their progeny. A recent study by Shen *et al*. (2012) found that hybrids had increased cytosine methylation compared with the parents [24]. Contrast to the higher methylation levels, more down-regulated genes were existed in the hybrids than the parental lines. The down-regulated genes including the circadian clock genes *CCA*1, *LHY*, have been shown to be involved in heterosis previously. In consistent with the study by Shen *et al*. (2012), Greaves *et al*. (2012) also found altered methylomes between hybrid and its parents in *Arabiodposis* [23]. In both studies changes occur most frequently at loci where parental methylation levels are markedly different.

A recent study by Chodavarapu *et al*. (2012) found that regions of altered methylation are often correlated with changes in sRNA levels [18]. Using *Arabidposis*, Greaves *et al*. (2012) and Shen *et al*. (2012) also found a close relationship between DNA methylation and sRNA [23] [24]. Interestingly, research by Shen *et al*. (2012) found that the growth vigor was compromised in the F1 hybrids of hen1 (RNA methyltransferase, *HUA ENHANCER*1) mutants, which further supported the notion that sRNAs play a role in heterosis, perhaps by guiding methylation of DNA via the RNA-directed DNA methylation pathway [24].

Differential expression patterns of small RNAs were observed in rice, wheat and tomato hybrids recently [17]. For example, in rice hybrids sRNAs showed more down-regulated than up-regulated. Previously, various studies have proved that sRNAs play an important role in gene regulation and genome integrity maintaining [29] [30]. It is possible that, the changes in sRNAs profiling could result in the expression patterns of gene that they control in hybrids, which might be related with the phenotype of the hybrids.

5. Energy Model Proposed for Heterosis

A recent energy model was proposed by Goff (2011) to explain differences in growth and yield between inbreds and hybrids [31]. According to this model, allele-specific gene expression is linked to protein folding and stability, and helps conserve energy and allows faster cell division. It is possible that allelic choice available in hybrids but not inbreds provides the opportunity for hybrids to express the favorable allele and use energy efficiency to accelerate crop improvement.

Heterosis is a common phenomenon in maize, rice and other species [6]. It is likely that a common biological mechanism underlying heterosis is existed in a wide variety of different species. Dominance and overdominance models have been proposed to explain single trait heterosis [32]. At gene expression level, both additive and non-additive mode of differential gene actions have been shown to be involved in the manifestation of heterosis [11] [14]-[16]. Genes influencing heterosis could be affected by genomic dosage [22]. Recently, mounting evidences of the epigenetic machinery was provided to explain heterosis [18] [23] [24] [33] [34]. Quantitative trait locus (QTL) mapping studies indicated many QTLs associated with specific heterosis traits [35]-[37]. Circadian clocks affected many traits in hybrids [6]. Energy-use efficiency likely plays an important role in heterosis [31]. Taken together, it is likely that the combination of many mechanisms across many genes accounts for the complex heterosis traits (**Figure 1**).

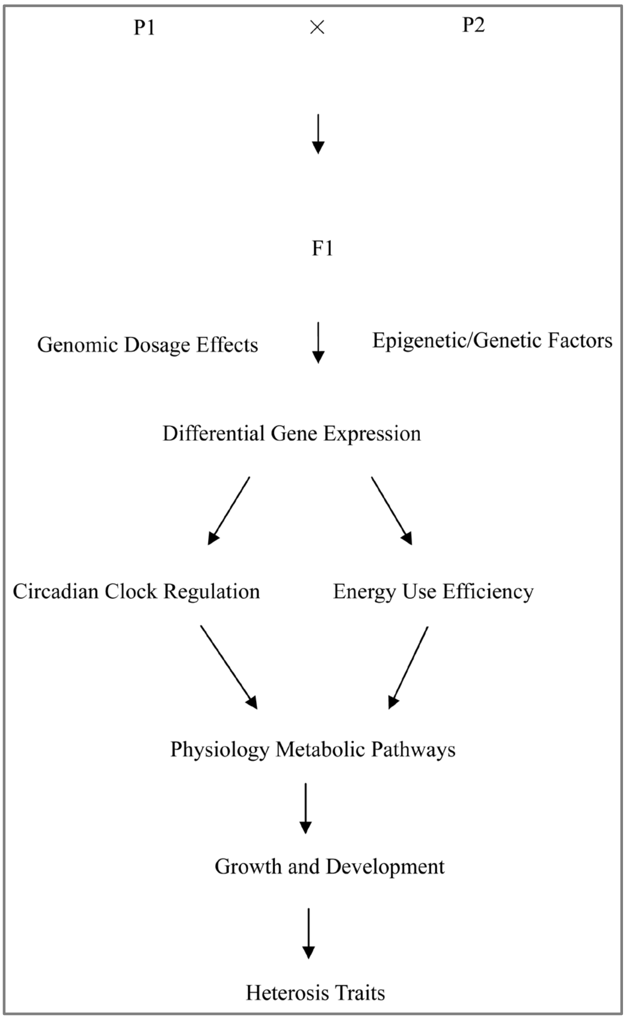

Figure 1. Possible mechanisms underlying heterosis. In the hybrids (F1), differential gene expression was induced when parent 1 (P1) and parent 2 (P2) genomes was mixed, mainly caused by epigenetic and genetic factors, and could be affected by genomic dosage. These expression changes may affect some major regulatory pathways including circadian clock pathway and energy regulatory pathway. A number of downstream physiology metabolic pathways could be affected, which ultimately affect various aspects of growth and development.

To date, there are still many things that are not clear but with promising for future breakthrough in uncovering the heterosis. First, what is the relationship between genome combination and gene activity at a single gene level? It is known that the differential expression of a large number of genes is emerged when two different genomes come together in a hybrid. Do all these changed transcriptome in hybrid have biological functions? What proportion of the altered hybrid transcriptome could have a major influence on heterosis besides the circadian clock genes? What factors affect on the variable profile of these key genes, mechanisms? Second, how to choose the best combinations of parents for producing "super hybrids" to meet the growing demand in food and biofuels? As we known, the degree of heterosis is proportional to the genetic differences in two parental strains. However, many interspecific hybrids especially distant hybrids cannot survive, which cause hybrid incompatibility. A better understanding of the mechanism for hybrid vigor will help us effectively select the best combinations of parents for the predicting breeding goal, such as the increased production of seeds, fruits and metabolites.

Acknowledgements

This work was supported by National Natural Science Foundation of China (31201593).

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