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Use of Quantitative Trait Loci (QTL) mapping in breeding

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ABSTRACT: In breeding programs, because of the time, resources, large quantities of grain required to perform several quality traits analyses, full-scale milling and baking tests are only performed on advanced breeding lines to predict varietal performance. The first published large scale QTL mapping experiments (in yeast and mouse) involved small experimental populations and mostly described the results of genetic mapping. These were soon followed by more focused studies on specific complex traits and aimed at a better understanding of the molecular networks underlying the trait QTLs and experimental validation of inferred candidate genes. QTLs have been identified for quantitative traits as reported in the literature. The number of QTLs detected in a given study depends on different factors, including type and size of mapping population used, trait investigated, the number of environments used for phenotyping, and genome coverage. The QTLs reported in the literature include two groups of genes. The first group constitutes a small proportion of the published literature and includes major genes of very large effects on highly heritable traits, with each explaining a large portion of the total trait variation in a mapping population. The two general goals of QTL mapping in plants are to (a) increase our biological knowledge of the inheritance and genetic architecture of quantitative traits, both within a species and across related species, and (b) identify markers that can be used as indirect selection tools in breeding.

***Keywords*:** QTL mapping, molecular markers, Genetic variation

INTRODUCTION

In breeding programs, because of the time, resources, large quantities of grain required to perform several quality traits analyses, full-scale milling and baking tests are only performed on advanced breeding lines to predict varietal performance. Plant breeding is a three step process, wherein populations or germplasm collections with useful genetic variation are created or assembled, individuals with superior phenotypes are identified, and improved cultivars are developed from selected individuals (Moose and Mumm, 2008). To address this challenge, several research groups have used wheat germplasm covering different market classes to identify quantitative trait loci (QTL) and genes influencing specific end-use quality traits (Campbell . 2001; McCartney . 2006; Elangovan . 2008; Mann . 2009). Phenotypes of the majority of traits in nature and agriculture are continuous variables. This continuous distribution has been attributed to the collective action of many genes -termed quantitative trait loci (QTLs) (Geldermann 1975) interacting with environment (Johanssen 1909). Therefore quantitative traits are those controlled by naturally occurring allelic variation at several genes, which are influenced variably by environmental conditions. The wheat grain quality traits are considered to be inherited as quantitative traits as it is known to be controlled by a group of genes and being very affected by environmental variations (Kuspira and Unran 1957, Diehl . 1978, Nachit . 1995a, Porceddu . 1990). The quality cannot be expressed in terms of a single property, but depend on several milling, chemical, baking, processing, and physical dough characteristics; each one of them is important in the

production of each end-product. Positioning QTLs on genetic maps is a powerful technique to portion quantitative traits on Mendelian genes, especially that more genetic maps are available now (Paterson . 1991). Several QTLs associated with important traits have been identified in many crops including QTLs related to yield, Heading date, pollen sterility, and root morphology in rice (Ray . 1996; Doi . 1998; Lin . 1996; Moncada . 2001); QTLs associated with agronomic performance, grain and malt quality, and disease characters in barley (Backes . 1995; Tinker . 1996; Mather . 1997; Zhu . 1999; Igartua . 2000); QTls for amylose content, disease resistance, and grain-yield in wheat (Araki . 1999; Waldron . 1999; Kato . 2000).

The theory of QTL mapping

Seed size in bean (a complex trait) was associated with seed coat color (a simple, monogenic trait). This concept was further elaborated by Thoday (1961), who suggested that if the segregation of simply inherited monogenes could be used to detect linked QTLs, then it should eventually be possible to map and characterize all QTLs involved in complex traits. Before the advent of modern QTL mapping, traits showing quantitative variation were studied by statistical analysis of appropriate experimental populations based on the means, variances and covariances of relatives, with no actual knowledge of the number and location of the genes that underlie them (Kearsey and Farquhar, 1998). These studies focused on phenotypic distributions of populations and correlations in phenotypes among related individuals or lines. New interest in QTL mapping in crops was generated when studies on fruit traits of tomato (Paterson . 1988) and the morphological and agronomic characters of maize (Stuber . 1992) successfully demonstrated that some molecular markers explained a substantial proportion of the phenotypic variance of quantitative traits.

QTLs have been identified for quantitative traits

QTLs have been identified for quantitative traits as reported in the literature. The number of QTLs detected in a given study depends on different factors, including type and size of mapping population used, trait investigated, the number of environments used for phenotyping, and genome coverage. The QTLs reported in the literature include two groups of genes. The first group constitutes a small proportion of the published literature and includes major genes of very large effects on highly heritable traits, with each explaining a large portion of the total trait variation in a mapping population. Most QTLs reported in the literature fall in another group that are regulated by many genes, each explaining small portion of the total trait variation. For example, Laurie . (2004) reported about 50 QTLs that explained approximately 50% of the genetic variance for oil concentration in the maize kernel. Buckler . (2009) evaluated nearly a million maize plants in eight environments and found no evidence for any single large effect QTL for flowering time. The authors identified numerous QTLs of small additive effects that are shared among families. However, the genetic variation of most quantitative traits likely involves a small number of major genes or QTLs, a larger number of loci with moderate effects, and a very large number of loci with minor effects (Robertson, 1967; Kearsey and Farquhar, 1998).

The first published large scale QTL mapping experiments

The first published large scale QTL mapping experiments (in yeast and mouse) involved small experimental populations and mostly described the results of genetic mapping (Brem ., 2002; Schadt ., 2003). These were soon followed by more focused studies on specific complex traits and aimed at a better understanding of the molecular networks underlying the trait QTLs and experimental validation of inferred candidate genes (Mehrabian ., 2005; Yang ., 2009).

Recently the QTL approach

Recently the QTL approach has been extended to genome-wide association studies in humans, mostly addressing complex diseaserelated traits (e.g. Emilsson ., 2008, for the recent review see Cookson ., 2009), and to traits in Drosophila such as aggressive behaviour (Edwards ., 2009).

The goals of QTL mapping in plants

The two general goals of QTL mapping in plants are to (a) increase our biological knowledge of the inheritance and genetic architecture of quantitative traits, both within a species and across related species, and (b) identify markers that can be used as indirect selection tools in breeding (Bernardo, 2008).

Expression QTLs

Expression QTLs are those genetic regions identified by applying QTL analysis methods to data on the abundance of transcripts of particular genes in samples taken from different individuals (genotypes) in a segregating population, or populations with other genetic structures. Transcript abundance is used as a measure of the level of that gene's expression in each individual and can be analysed as a trait (an 'eTrait') just like other phenotypes (pTraits) such as plant height or yield. Expression is normally measured for many thousands of genes simultaneously and hence there are thousands of eTraits recorded. As with pQTL analyses, eQTL analysis requires genetic markers which can be genotyped in all individuals in the population and used to form a framework genetic map of the whole genome. These markers and their map locations may have been developed in the population before the eQTL study or may be developed de novo entirely or in part from the expression data itself. A high quality genetic linkage map is a critical component of such experiments, because the map resolution, marker density and polymorphism will condition the quality of pQTL and eQTL analyses, and how we interpret the impact of allelic variation on physiological processes through transcriptional and other molecular networks (Sieberts and Schadt, 2007).

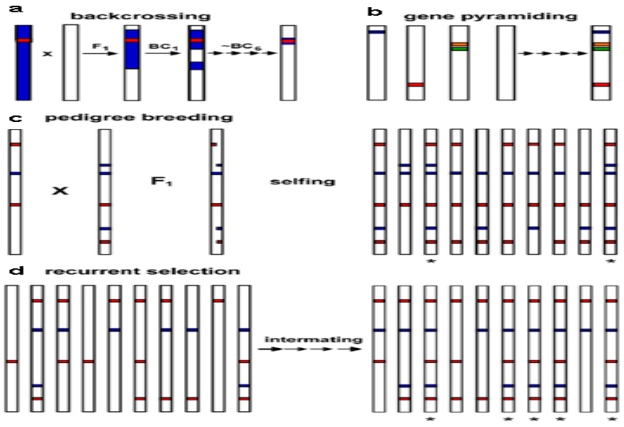

Figure 1. Common plant breeding and selection schemes. Each vertical bar is a graphical representation of a chromosome of an individual within a breeding population, with colored segments indicating genes and/or QTLs that influence traits under selection. Genes associated with different traits are shown in different colors (e.g. red, blue). ''X'' indicates a cross between parents, and arrows depict successive crosses of the same type. Asterisk below an individual signifies a desirable genotype. (a) In backcrossing scheme, a donor line (blue bar) is crossed to an elite line for transferring a specific gene of interest (red). Selected progenies were repeatedly backcrossed to the elite parent with each backcross cycle involving selection of individuals with the gene of interest and of the highest proportion of elite parent outside the target genome. (b) In gene pyramiding, genes or QTLs associated with different beneficial traits (blue, red, orange, green) are combined into the same genotype via crossing and selection. (c) In pedigree breeding, two individuals with desirable and complementary phenotypes are crossed; F1 progeny are self-pollinated to fix new, improved genotype combinations. (d) In recurrent selection, a population of individuals (10 in this example) segregate for two traits (red, blue), each of which is influenced by two major favorable QTLs. Intermating among individuals and selection for desirable phenotypes/genotypes increases the frequencies of favorable alleles at each locus. For this example, no individual in the initial population had all of the favorable alleles, but after recurrent selection half of the population possesses the desired genotype (Moose and Mumm, 2008)

Quantitative Trait Loci Associated with Micronutrient Concentrations in Two Recombinant Inbred Wheat Lines

The application of molecular markers for quantitative trait locus (QTL) analysis has provided an effective approach to determine these genetic factors. Recombinant inbred lines or doubled haploid populations have been used to identify QTLs associated with micronutrient concentration on almost all the 21 chromosomes of wheat (Distelfeld . 2007; Ozkan . 2007; Shi . 2008; Peleg . 2009; Tiwari . 2009). Furthermore, a codominant molecular marker (Xuhw89) tightly linked to the Gpc-B1 locus (genetic distance, 0.1 cM) of Triticum dicoccoides has been shown to improve Fe, Zn and Mn concentrations by 18%, 12%, and 29%, respectively (Distelfeld . 2006, 2007). The related species of wheat are one of the most important genetic resources for improving micronutrient concentration. Previous studies have indicated that the A- and D-genome donor species of common wheat have high Zn efficiency (Schlegel . 1998; Cakmak . 1999). Furthermore, the grains of synthetic hexaploid wheat (SHW) lines obtained using distant hybridization between Triticum turgidum L. and Aegilop stauschii had higher Fe, Mn and Zn concentrations than cultivated wheat (Calderini and Ortiz-Monasterio 2003). Therefore, the micronutrient concentration of wheat

grains can be improved by hybridization of commercial wheat varieties with wild-type triticeae species having higher micronutrient efficiency (Cakmak . 1999; Chhuneja . 2006; Rawat . 2008; Xu . 2011).

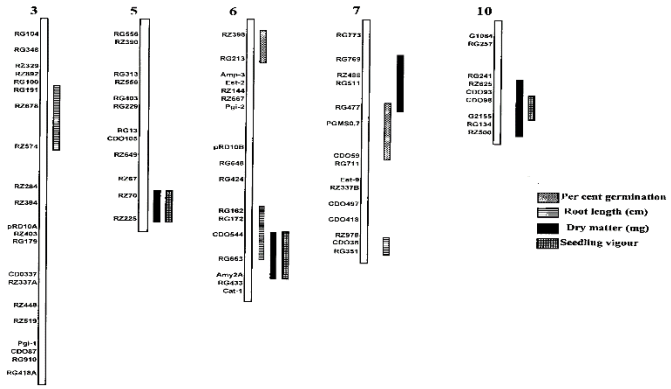

Figure 2. Rice chromosome map showing the position of QTL associated with seedling tolerance to salt stress for various seedling characters at 0.5 per cent NaCl stress

Recombinant inbred lines (RILs)

Recombinant inbred chromosome lines are superior to recombinant inbred lines (RILs) for studying the effect of a specific chromosomal region because they have a more uniform genetic background and knowing the targeted chromosome facilitates molecular marker selection. Recombinant inbred chromosome line populations have been used to construct genetic linkage maps in tetraploid wheat (T. turgidum L.) for chromosome 6A and 6B (Chen ., 1994) and to map grain protein content gene(s) on chromosome 6B (Joppa ., 1997).

Genetic variation

Authors identified numerous QTLs of small additive effects that are shared among families. However, the genetic variation of most quantitative traits likely involves a small number of major genes or QTLs, a larger number of loci with moderate effects, and a very large number of loci with minor effects (Robertson, 1967; Kearsey and Farquhar, 1998). The effects of the major genes can be studied via segregation analysis as well as evolutionary and selection history. The numerous genes with small effects, however, cannot be investigated individually.

The ability to transfer target genomic regions using molecular markers

During the past two decades, the ability to transfer target genomic regions using molecular markers resulted in extensive QTL mapping experiments in most economically important crops, aiming at the development of molecular markers for marker assisted selection (Xu, 1998; Collard . 2005; Semagn . 2006a; Xu, 2010) and QTL cloning (Salvi and Tuberosa, 2005). Results from such studies provide information on (a) the number and chromosomal location of QTLs affecting a trait; (b) the magnitude and direction of effect of each QTL (i.e., whether a phenotypic trait is controlled by many genes or many independent loci of small effect or by a few genes of large effect); (c) the mode of gene action at each QTL (dominant or additive); (d) the parental sources of beneficial QTL alleles, and (e) whether there is interaction between different QTLs (epistasis, i.e., interactions between two QTLs that result in an effect on the trait that would not be predicted from the sum of the individual QTL effects) or between genotypes and environment (Bradshaw, 1996).

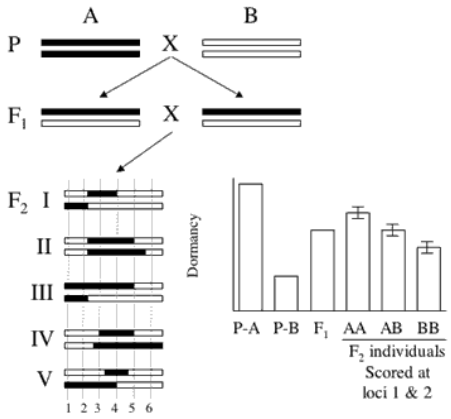

Figure 3. Two parental (P) inbred lines, A & B, which differ for a trait of interest (e.g. dormancy) are crossed to produce heterozygote F1 progeny which have an intermediate degree of dormancy. Only one chromosome pair is depicted for simplicity. The F1 progeny are crossed to produce a large segregating F2 population (usually 100-500 individuals are analyzed, here only five individuals, I-V, are depicted). Because of recombination during F1 meiosis, the F2 individuals have varying genetic combinations of the original inbred lines (depicted by shading of chromosomes) and have continuous variation, from high to low, in degree of dormancy. In order to estimate whether segments of the chromosome are homozygous for one of the parental-lines or heterozygote, the F2 individuals are scored for marker loci (1-6) along the chromosome. For example, loci 1 & 2 are identified as homozygous for A-line alleles in individual III, as heterozygous in individuals I & V and as homozygous for B-line alleles in individuals II & IV. The F2 individuals are also scored for their dormancy. After scoring many F2 individuals a correlation between the genotypes at locus 1 & 2 and phenotype is determined and therefore this segment likely contains at least one gene affecting dormancy (bar graph). The analysis is repeated for each chromosomal segment to identify which ones are likely to contain genes affecting dormancy

Progresses and future prospects

Since the early 1990s, numerous studies have identified molecular markers linked to QTLs involved in the inheritance of ergonomically important traits in a wide range of crop species. Following the discovery of promising QTLs and identification of molecular markers, MAS has been used to transfer single genes or QTL in various species. However, published results in QTL introgressions through MAS are variable, ranging from successful experiments to those with limited success and even a failure (see Semagn . 2006b for review). The rate of success starts to decrease when five or more target QTLs for complex traits are introgressed in to a given germplasm (Lawson . 1997; Shen . 2001; Bouchez . 2002; Ribaut . 2002a; Lecomte . 2004; Thabuis . 2004). Several factors may contribute for such failure or unexpected results in MAS: (i) errors in QTL mapping (the putative QTL may be a false positive or the QTL effect might have been over estimated); (ii) the repeatability of the QTL across different genetic background and/or environments might have not be confirmed (e.g., Melchinger . 1998; Schon . 2004); (iii) there may be QTL by environment and QTL by QTL interactions (e.g., Ribaut . 2002a, Ribaut . 2002b); (iv) pleiotrophic effects (Tuberosa . 2002); and (v) the chromosomal segments associated with QTL hold not just one but several genes, and recombination between those genes would then modify the effect of the introgressed segments (e.g., Eshed and Zamir, 1995; Monna . 2002). For example, Kroymann and Mitchell-Olds (2005) find mapped phenotypic effects segregating within a onecentimorgan chromosome interval in Arabidopsis thaliana for which lines with mapped recombination breakpoints were available, and examined the sequence signature of historical polymorphism. The authors found that the 1 cM chromosome interval contained two growth rate QTLs within 210 kilobases (kb). Both QTLs showed epistasis (i.e., their phenotypic effects depended on the genetic background). This amount of complexity in such a small area suggests a highly polygenic architecture of quantitative variation, much more than previously documented (Koornneef . 2004).

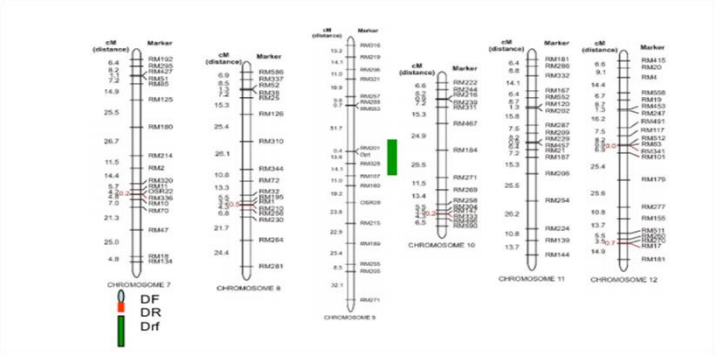

Figure 4. Molecular linkage map on 12 chromosomes in BC2F2 population of OM1490/WAB880-1-38-18-20-P1-HB.

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