Cautiously Optimistic about MAB for Complex Traits

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The majority of research on marker-locus trait (MLT) associations (i.e., connecting genotype to phenotype) is conducted with the intention to carry out marker assisted breeding (MAB) irrespective of trait complexity. At this stage, although the situation is likely to change in the future, it is fair to say that MAS (marker assisted selection, as it is generally called in the literature) has promised a lot since its beginnings about 30 years ago but has delivered little to date. Publications under the subject matter 'marker-aided selection,' 'marker assisted selection' or similar connotations have continued to be on the increase from just over 50 per year in the mid-90s to approximately 300 per year towards the end of 2010. Within the same time period, citations on MAS rose from 300 to over 4500 per year. Simply put, the practical realities of MAB have not caught up with theoretical expectations.

The principles behind MAB include, 1) exploiting the linkage disequilibrium between DNA markers and genes or quantitative trait loci (QTL), and 2) selecting (directly) on markers to (indirectly) increase the frequencies of genes or QTL alleles of interest. These benefits suggest that MAB will have significant advantages over conventional breeding schemes such as, 1) convenience (particularly when phenotypes are difficult to measure), 2) speed (where phenotyping is time-consuming as in the case of progeny testing), 3) improved efficiency, because the heritability at marker locus is 1,and 4) a probable decrease in expense(the cost of genotyping versus phenotyping coupled with the culling of inferior seedlings at juvenile stage resulting in reduction in the cost of raising and maintaining a large number of seedlings in the field).

Other advantages of MAB include parental verification of seedlings, genetic identity establishment, parental selection to develop progenies with a higher proportion of traits of interest, and prediction of genetic potential of advanced selections. Potential applications of MAB include, 1) population screening (such as F2, F3, pseudo-testcrosses, recombinant inbred lines and doubled haploids) to identify genes of interest, 2) backcross breeding to select for the target gene and the recipient genome, 3) recurrent selection including several generations of selection based on markers followed by random mating, and 4) index selection combining both molecular and phenotypic scores.

There is no doubt MAB has been very successful in population screening and backcross breeding with simply inherited traits controlled by major genes. Many success stories exist including many disease resistances. 'Patwin,' for example, was the first variety developed by MAB that was released by UC Davis in 2005. This Hard White Spring wheat variety contains the introgressed stripe rust resistance gene Yr17 and the leaf rust resistance gene Lr37. Many private breeders routinely use MAB to develop simply inherited traits with the results often unpublished. However, the situation is different with polygenic traits presumed to have many QTL alleles conferring minor effects.

Many reasons abound for the difficulty in deploying MAB for complex traits in breeding programs. These include, 1) under-and/or over-estimation of QTL number and the magnitude of the effect size due to small population size and/or low marker density, 2) genetic background effect, 3) trait complexity and inaccurate phenotyping,

and4) significant epistatic as well as QTL x environment interactions [1]. However, one landmark paper on MAB for a polygenic trait includes QTL pyramiding in rice which was published in 2005 by Ashikari et al.[2]. A combination of genetic loci favoring greater seed production and shorter plants (both attributes of yield) significantly improved the yield of a strain of rice. I am convinced this result was possible because the authors were better able to phenotype yield components rather than yield itself thus enabling identification of moderate to large effect QTL for the two components including sd1, for short stature, which reduced plant height by 20%, and Gn1, for grain number, which increased seed production by 45%. Pyramiding these two loci in 'Habataki' rice reduced plant height by 18% and increased grain number by 26%. Although the effects are decreased when combined, the overall yield was still higher than in the wild type rice.

I believe the future is promising for MAB for oligogenetic and polygenic traits. With the reduced cost of sequencing and genotyping and the availability of high density genetic maps based on single nucleotide polymorphisms (SNPs) it may be possible to narrow the QTL confidence interval and/or identify QTL with moderate or large effects. However, this must be facilitated by precision phenotyping (phenomics) and determination of what constitutes trait components for complex traits, where possible. Moreover, SNPs are poised to improve QTL resolution through accurate verification and assignment of pedigree information. Further, deployment of robust marker locus trait associations in breeding programs may be facilitated by bridging the disconnect between genomics discovery and breeding applications. Often, genomics researchers have a simplistic view of breeding operations while on the other hand, breeders are skeptical of genomics technology and what it can offer. They are wary of introducing another layer of complexity in the breeding operations.

In the future, MLT tags may focus on multiple traits to capture pleiotropic or linked QTL effects for multi-trait selection common in conventional breeding. An index can be developed that combines phenotypic scores, marker data and economic weight to predict gain from selection. The next wave of development will include harnessing all the variation contributed by each QTL locus across the genome for a trait. It will be interesting to examine if QTL effects across the genome will be additive or a combination of additive and non-additive effects. This will improve the predictive value of genetic tests for each trait, particularly, where additive effects are more common.

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