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Epistasis and genotype-environment interaction for quantitative trait loci affecting flowering time in *Arabidopsis thaliana*

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Abstract

A major goal of evolutionary biology is to understand the genetic architecture of the complex quantitative traits that may lead to adaptations in natural populations. Of particular relevance is the evaluation of the frequency and magnitude of epistasis (gene–gene and gene–environment interaction) as it plays a controversial role in models of adaptation within and among populations. Here, we explore the genetic basis of flowering time in *Arabidopsis thaliana* using a series of quantitative trait loci (QTL) mapping experiments with two recombinant inbred line (RIL) mapping populations [Columbia (Col) x Landsberg *erecta* (L*er*), L*er* x Cape Verde Islands (Cvi)]. We focus on the response of RILs to a series of environmental conditions including drought stress, leaf damage, and apical damage. These data were explicitly evaluated for the presence of epistasis using Bayesian based multiple-QTL genome scans. Overall, we mapped fourteen QTL affecting flowering time. We detected two significant QTL–QTL interactions and several QTL–environment interactions for flowering time in the L*er* x Cvi population. QTL–environment interactions were due to environmentally induced changes in the magnitude of QTL effects and their interactions across environments – we did not detect antagonistic pleiotropy. We found no evidence for QTL interactions in the L*er* x Col population. We evaluate these results in the context of several other studies of flowering time in *Arabidopsis thaliana* and adaptive evolution in natural populations.

Introduction

A central goal of evolutionary biology is to elucidate processes that constrain or facilitate adaptive phenotypic change. Evolutionary biologists have traditionally used either single locus population genetic or quantitative genetic theory to understand the importance of selection, genetic architecture, mutation, recombination, and drift on phenotypic evolution (Lynch & Walsh, 1998). While great theoretical progress has been made in this regard (Barton & Turelli, 1989), many empirical questions remain concerning the details underlying the genetics of adaptation (Barton & Turelli, 1989; Orr & Coyne, 1992; Orr, 1998). In particular, accurate reconstructions or predictions of adaptive evolution based on theory will ultimately require a more detailed understanding of both the function and genetic basis of variation in traits within nature (Mitchell-Olds & Rutledge, 1989). Consequently, a current empirical challenge is to elucidate the genetic architecture, including the number, magnitude of effect, and mode of gene action of the loci controlling ecologically important traits.

Epistasis or gene interaction is of particular interest as it plays a controversial role in the theory

of adaptive evolution within and among populations (Wade, 2000). Epistasis occurs when differences in the phenotypic values of an allele at one locus are dependent on differences in specific alleles at other loci (gene–gene interaction) or across environmental heterogeneity (gene–environment interaction). These differences manifest as changes in the magnitude or order of allelic values contingent on the genetic or environmental background. Epistasis is thought to be important in several areas of evolutionary biology including speciation, developmental canalization, phenotypic plasticity, inbreeding depression, the evolution of sex, genome evolution, the maintenance of genetic diversity, and adaptive evolution via Wright's shifting balance theory (Fenster et al., 1998; Wolf et al., 2000; Wade et al., 2001). Given the broad interest in the role of epistasis in the evolutionary process (Wolf et al., 2000) its evaluation is a critical aspect of modern quantitative genetics (Lynch & Walsh, 1998; Zeng et al., 1999).

Gene interactions are commonly detected in molecular genetic studies that utilize loss-of-function mutants to resolve molecular pathways. Much less is known about interactions among naturally occurring alleles and how these interactions contribute to the partitioning of overall phenotypic variation. Historically, epistasis has been studied in a quantitative genetics framework using inbred line crosses aimed at detecting departures from the predictions of strictly linear additive models. Unfortunately, these tools are of limited value as they are restricted to the evaluation of composite directional non-additive effects summed across entire genomes (Lynch & Walsh, 1998). More recently, quantitative trait locus (QTL) mapping methods have been utilized to explore QTL–QTL and QTL–environment interactions in experimental populations (Mackay, 1995; Routman & Cheverud, 1997; Gurganus et al., 1998; Lynch & Walsh, 1998; Vieira et al., 2000).

In its simplest form, QTL mapping is a search for statistical associations, due to linkage disequilibrium, between quantitative phenotypic variation and genetic marker alleles segregating in an experimental population. Although this technique is not new, recent advances in genetic markers, high-throughput genotyping, and statistical techniques have greatly improved the power and resolution of the approach. Most QTL mapping efforts have sought phenotypic associations using single QTL models and have explicitly ignored interactions. Several QTL studies have progressed to the secondary testing of interactions between QTL after first locating them through their strictly additive effects. Although this method has revealed numerous QTL–QTL interactions, it is clearly limited in scope and will necessarily fail to detect interacting pairs of loci that lack strictly additive effects (Wade, 1992; Cheverud, 2000; Sen & Churchill, 2001). Finally, the accuracy with which the 'real' genomic positions of QTL can be located depends critically on the development of an accurate description of the genetic model (Zeng et al., 1999). QTL models failing to incorporate complex interactions when they occur can produce spurious or inappropriate QTL localization and confidence intervals. Here, we explore the genetic architecture of flowering time using multiple-QTL genome scans that incorporate pairwise interactions (Sen & Churchill, 2001).

Timing of reproduction is an important component of life–history variation in many plants and animals. For example, theory and empirical data suggest that the flowering phenology of annual plants can influence a variety of ecological factors including interactions with other species (e.g., competitors, pollinators, natural enemies), the matching of vegetative growth with seasonal pulses in soil nutrients and moisture, and the completion of fruit set by the close of the growing season. These factors can have dramatic impacts on plant fitness.

A. thaliana is a small crucifer with a vegetative growth period that produces a leafy rosette followed by the bolting of an indeterminate reproductive shoot. In nature, *A. thaliana* populations exhibit a winter annual life–history (with an over-wintering rosette stage), a spring annual life–history (with over-wintering seeds) or a mixed strategy (Donohue, 2002). Life-history variation and within-season flowering time are probably both important ecological traits in *Arabidopsis* populations. For instance, several studies have documented natural selection imposed on *A. thaliana* flowering time (or related traits such as bolting time) within a reproductive season due to variation in seedling density (Dorn et al., 2000), shading (Scheiner & Callahan, 1999; Dorn et al., 2000; Callahan & Pigliucci, 2002), timing of germination (Donohue, 2002), and season length or vernalization (Pigliucci & Marlow, 2001). Our focus is on