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Evolutionary and Ecological Genomics of Non-Model Plants

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Abstract

Dissecting evolutionary dynamics of ecologically important traits is a long-term challenge for biologists. Attempts to understand natural variation and molecular mechanisms have motivated a move from laboratory model systems to non-model systems in diverse natural environments. Next generation sequencing methods, along with an expansion of genomic resources and tools, have fostered new links between diverse disciplines, including molecular biology, evolution, and ecology, and genomics. Great progress has been made in a few non-model wild plants, such as *Arabidopsis* relatives, monkey flowers, and wild sunflowers. Until recently, the lack of comprehensive genomic information has limited evolutionary and ecological studies to larger QTL regions rather than single gene resolution, and has hindered recognition of general patterns of natural variation and local adaptation. Further efforts in accumulating genomic data and developing bioinformatic and biostatistical tools are now poised to move this field forward. Integrative national and international collaborations and research communities are needed to facilitate development in the field of evolutionary and ecological genomics.

Keywords

Candidate genes; ecological genomics; fitness; natural selection; population genomics; QTL

Questions about evolutionary and ecological genomics

Understanding the genetic basis and evolutionary dynamics of natural genetic variation includes several key questions: which genes control ecologically important traits (Mitchell-Olds, 2001)? What evolutionary factors maintain variation within and between populations (Mitchell-Olds et al., 2007)? How does genetic variation at adaptively important genes differ from genome-wide patterns at neutrally evolving loci? What are the fitness consequences of segregating polymorphisms in natural environments (Korves et al., 2007; Ellegren & Sheldon, 2008; Ungerer et al., 2008)? To address these questions, we need to integrate multiple disciplines, including genetics, genomics, ecology and evolution. For example, population genomics, quantitative genetics, comparative genomics, and proteomics have been applied in attempts to find genes relevant to ecological adaptation. Likewise, molecular population genetics and population genomics have contributed to understanding patterns of variation at functionally important polymorphisms, and ecological genomics is critical for understanding fitness differences of segregating polymorphisms in natural environments.

Advances in sequencing technologies and rapid development of genomic tools have helped our understanding in ecology and evolution, not only for model organisms, but also for non-model species (Lee & Mitchell-Olds, 2006; Ellegren & Sheldon, 2008; Ungerer et al., 2008).

Here, we focus on recent progress and future perspectives in evolutionary and ecological genomics for non-model plants. For related work on the model plant *Arabidopsis thaliana*, see Mitchell-Olds & Schmitt (Mitchell-Olds & Schmitt).

Why Non-Model Plants?

Systems for linking ecology and evolution with the molecular mechanisms influencing adaptation to natural environments require the availability of genomic information, as well as diverse ecologically important traits (Feder & Mitchell-Olds, 2003; Ouborg & Vriezen, 2007; Ungerer et al., 2008). So far, only a few plant species meet both requirements. The traditional model plant species, such as *Arabidopsis thaliana*, has many resources in functional genomics, but its ecological context is often unclear in human-disturbed environments (McKay & Stinchcombe, 2009; Schranz et al., 2009). Many *Arabidopsis* accessions are available in stock centers, but limited information regarding habitats hinders attempts to combine ecology and evolution (McKay & Stinchcombe, 2009) and further dissection of the genetic basis of local adaptation. Thus, many key questions in ecology and evolution cannot be addressed solely using model systems (Lee & Mitchell-Olds, 2006). However, recent progress in *Arabidopsis* has moved from lab to the field to uncover the genetic basis of adaptation, and has helped explore the natural variation found within model plants (Korves et al., 2007; Wilczek et al., 2009). In most model species, the lack of ecological background limits our ability to understand plant variation and natural selection in an ecological context or the dynamics of interaction between genetics and environment (McKay & Stinchcombe, 2009). In order to develop a broader picture of natural variation and adaptation, a transition from *Arabidopsis* to non-model plants will be useful (Ehrenreich & Purugganan, 2006). However, although many non-model plants inhabit diverse habitats and display a wide spectrum of phenotypes, most non-model species lack genome resources. Thus efforts have focused on *Arabidopsis* relatives, monkey flower (*Mimulus*) and sunflowers (*Helianthus*), which have substantial genomic information, habitat diversity, phenotypic variation, and large research communities (see below for detailed information). Encouragingly, during the past several years, the gap between model and non-model organisms has narrowed, primarily due to the declining costs for genome sequencing and genotyping.

Analysis of Non-Model Plants

Methods for finding the ecologically-important causal loci have been discussed in several recent reviews (Mitchell-Olds & Schmitt, 2006; Stinchcombe & Hoekstra, 2007). With the surge of genomic data and lowered cost of genotyping, some of these methods can be applied to non-model plants. Population genomics, QTL mapping, transcription profiling, proteomics, and other techniques will contribute to identification of causal genes in non-model plants (Mitchell-Olds & Schmitt, 2006; Shiu & Borevitz, 2006; Hall, 2007; Karr, 2007; Stinchcombe & Hoekstra, 2007). Recent statistical advances enable genome-wide scans of DNA polymorphism to infer adaptive divergence, as well as association mapping in ecological and evolutionary studies in non-model plants (Yu et al., 2006; Li et al., 2009). Furthermore, expression studies, such as microarray technology and transcriptome profiling using high throughput sequencing, will also play important roles in finding candidate genes involved in the ecological adaptation of wild plants (Mitchell-Olds et al., 2008; Nevo, 2009).

As illustrated in Figure 1, finding causal genes influencing ecologically important traits leads to a new set of exciting questions in ecology and evolution (Mitchell-Olds et al., 2007; Stinchcombe & Hoekstra, 2007). These include: What evolutionary forces influence patterns of genetic variation in nature? Does population history and demography confound interpretation of this variation? Do adaptive polymorphisms arise from new mutations or

from standing genetic variation? How often are there fitness differences in different alleles in native populations? Methods for detecting signatures of selection include polymorphism spectrum-based methods, haplotype-based approaches, etc. (Mitchell-Olds et al., 2007). Natural selection acting to maintain variation at ecologically important loci has been indicated by patterns of nucleotide polymorphism in many loci (Olsen et al., 2002; Olsen et al., 2004; Wright & Gaut, 2005; Toomajian et al., 2006; Voight et al., 2006). Epistatic selection (the fitness effects of alleles at one locus depend on alleles at other loci) and heterogeneous selection (selection favors different alleles in different habitats) have been theoretically suggested as possible mechanisms for the maintenance of genetic polymorphism, both within and among populations (Mitchell-Olds & Schmitt, 2006; Korves et al., 2007). Epistatic selection and heterogeneous selection contributing to maintaining genetic variation were also suggested in experimental studies (Ellner & Nelson G. Hairston, 1994; Weinig et al., 2003; Kroymann & Mitchell-Olds, 2005; Mitchell-Olds et al., 2007). Segregating polymorphisms arising from recent mutation (hard sweep) or standing genetic variation (soft sweep) have been tested by extended haplotype homozygosity (Mitchell-Olds et al., 2007; Barrett & Schluter, 2008). Demographic factors have been considered when interpreting sequence variation to infer selection (Mitchell-Olds & Schmitt, 2006; Mitchell-Olds et al., 2007; Song et al., 2009).

Beyond exploring the significance of natural variation, the integration of molecular genetics and ecology will facilitate understanding of fitness variation in the wild. However experimental studies on the effect of natural selection on candidate genes underlying complex traits has been relatively slow (Korves et al., 2007), partly because measuring fitness in natural environments requires tremendous field effort. So far, few studies have examined the mechanisms of natural selection that affect candidate polymorphisms under natural conditions in plants (Watt, 1977; Eanes, 1999; Tian et al., 2003). However, hybrid segregates, recombinant inbred lines (RIL), and near isogenic lines (NILs) have been used to identify quantitative trait loci contributing to variation in specific traits, as well as the fitness consequences of segregating polymorphisms (Bradshaw et al., 1995; Mitchell-Olds, 1996; Schmitt, 1999; Burke & Rieseberg, 2003; Korves et al., 2007; Lowry et al., 2009).

Emerging Plant Systems and Progress in Ecological and Evolutionary Genomics

As described above, advances in sequencing technology are accelerating the study of the molecular ecology and evolution in some emerging wild plant systems, including the monkey flower complex (*Mimulus*), wild sunflowers (*Helianthus*), and wild relatives of *Arabidopsis thaliana* (e.g., *Boechera*, *Arabidopsis lyrata*, *Capsella*, *Thellungiella*). Here, we summarize recent studies of several non-model plants in ecology and evolution, integrating genetic and genomic approaches. Studies on these plant systems exemplify practical approaches for transitioning from model plants to non-model plants, in order to uncover the genetic basis of natural variation and ecological adaptation.

Arabidopsis wild relatives

Ecological genetic studies of wild relatives of *Arabidopsis* illustrate the transition from model to non-model plants in ecology and evolution (Mitchell-Olds, 2001). The genus *Boechera* is closely related to *Arabidopsis*, providing access to information and techniques from this model plant species. *B. stricta* is an inbreeding-tolerant sexual diploid, which is very important for development of near-isogenic lines for QTL cloning. This species is widely distributed in the western United States, especially in the Rocky Mountains, which provides largely undisturbed research sites and environmental heterogeneity across a 2,000 m elevation gradient (Figure 2). Further, *Boechera* populations have been shown to be

locally adapted to some of the ecological differences across these diverse habitats (Mitchell-Olds, 2001; Knight et al., 2006; Song et al., 2006).

Mitchell-Olds and colleagues used *Boechera stricta* to test evolutionary hypotheses, with glucosinolates providing a functional link between genotype and phenotype. They began with insect resistance, an ecologically important quantitative trait which is controlled in part by complex variation in the glucosinolate pathway. Based on this biochemical information, they found evidence for a physiological polymorphism within and among diverse populations, which predicts quantitative levels of insect damage. Genetic dissection identified a major QTL controlling one aspect of glucosinolate polymorphism (Schrantz et al., 2009). In addition, they used molecular population genetics to infer demographic and geographical histories (Song et al., 2006; Song et al., 2009, Figure 4), which is critical for interpreting sequence variation of ecologically important genes (Mitchell-Olds et al., 2007). To directly test fitness of the causal locus, F₆ Near Isogenic Lines (NIL) were planted in the parental sites (Colorado and Montana) and fitness were measured in the natural environments (Mitchell-Olds et al., 2010, unpublished data).

The availability of whole genome sequences for *Arabidopsis lyrata* (an outcrossing perennial) provides exceptional opportunities for evolutionary and ecological genomic studies of this close wild relative of *Arabidopsis*. The distribution of *Arabidopsis lyrata* is disjunct and geographically structured with diverse phenotypes and potential adaptive traits in the natural populations. Savolainen and colleagues use *Arabidopsis lyrata* as the study system, applying reciprocal transplant experiments, QTL mapping, candidate gene methods, and molecular population genetics to detect local adaptation and genetic basis of adaptive variation in natural populations, especially flowering time variation (Sandring et al., 2007; Kuittinen et al., 2008; Leinonen et al., 2009). Flowering time in *Arabidopsis lyrata* varies with latitude in response to day length and vernalization (Riihimäki & Savolainen, 2004). Kuittinen et al., (2008) using candidate gene methods demonstrated that the *FRI* gene plays important roles in controlling flowering time variation, and that balancing selection might be a major driving force in maintaining flowering time variation in nature. Local adaptation in diverse environments was also investigated by reciprocal transplantation. The demonstration of adaptive population differentiation is a prelude to mapping QTLs and subsequently measuring fitness in natural populations (Leinonen et al., 2009).

Mimulus (Monkey Flower)

The genus *Mimulus* is another emerging plant system for analyses of the genetic and genomic basis of adaptation and speciation (Bradshaw & Schemske, 2003; Wu et al., 2008). This group contains a wide spectrum of phenotypic variation, such as life history, developmental and physiological traits, with a rich diversity in habitat distribution within and between species. Populations in this group span a wide range of elevation with diverse habitats, such as grasslands, desert streams, coastal cliffs and sand dunes. In addition, some species grow in toxic copper mine tailings and coastal regions with high salt concentrations, which allows the exploration of mechanisms underlying copper and salt tolerance. Recent extensive focus on *Mimulus* has led to great progress in the development of genomic resources and bioinformatics tools during the past several years (Wu et al., 2008). Thus, the availability of the wide spectrum in traits, diverse environments, and genome resources will allow researchers to explore how genomic complexity and diversity evolve in the natural populations.

One classic example of combining evolutionary and ecological genetics to understand plant adaptation is the genetic basis of the interaction between flower color and pollinators (Bradshaw et al., 1995; Bradshaw et al., 1998; Bradshaw & Schemske, 2003). A QTL mapping study using artificial F₂ hybrids between red- vs. pink-flowered *Mimulus* species

found that flower color had marked effects on pollinator visitation (Bradshaw et al., 1998) and that yellow pigment concentration is controlled primarily by a major QTL *YUP* (Bleiweiss, 2001; Beardsley et al., 2003). To examine the potential contribution of the QTL, Schemske & Bradshaw (1999) compared plant pollination by bees vs. hummingbirds in the field using near-isogenic lines (NILs) segregating at the locus. Flower color NILs showed highly significant differences in pollinator visits, suggesting that an adaptive change in pollinator preferences may be initiated by a single major mutation (Bradshaw & Schemske, 2003).

Another recent study in *Mimulus* is the genetic basis of salt tolerance (Lowry et al., 2009). In this study, they conducted QTL mapping, followed by reciprocal transplant experiments using recombinant inbred lines (RILs), to explore the physiological mechanisms driving adaptive divergence between coastal and inland ecotypes of *Mimulus guttatus*. Results showed that though some QTLs had significant fitness effects at the coastal field site, while no effect was detected inland. Another abiotic stress adaption study in *Mimulus* is copper tolerance. QTL analysis and field experiments for the parental plants, as well as F₂ hybrids were conducted to test the association between field fitness and candidate copper tolerance loci. These examples illustrate how researchers can combine genetic, genomics and field experiments to dissect the genetic basis of natural variation and locally adaptation.

Helianthus (Wild Sunflowers)

Wild sunflowers (*Helianthus*, Compositae) provide a useful system for studying adaptation and speciation. Rieseberg and colleagues have employed integrative methods (including QTL analyses, candidate gene studies, field experiments, and comparative genomics) to uncover genetic basis responsible for adaptation to divergent habitat.

Sunflower is also a good system for studying ecology and evolution of homoploid hybrid speciation. The diploid hybrid can adapt to extreme new environments, where new adaptive traits are favored. Further, hybridization can facilitate ecological transitions (Rieseberg et al., 2003). One example is the salt tolerance study in a diploid hybrid (*Helianthus paradoxus*) between two wild annual sunflowers (*Helianthus annuus* and *Helianthus petiolaris*). Lexer et al. (2003a) planted early generation of (BC₂) hybrids in the natural salt marsh habitat. The strength of selection on candidate adaptive traits in the BC₂ was measured. They detected positive directional selection for leaf succulence and Ca uptake, two traits important for plant response to salt stress. QTL analysis was used to dissect the genetic basis of salt tolerance by examining mineral ion uptake, as well as survivorship. A total of 14 QTLs were detected for mineral ion uptake and three for survivorship. Further, several mineral ion QTLs mapped to the same position as the survivorship QTLs (Lexer et al., 2003b).

Crop wild relatives and application to agriculture improvement

Beyond the evolutionary and ecological studies in the non-model plant systems described above, great progress has been made in crops and their close relatives through the investigation of domestication of crop species and the divergence of their wild relatives (e.g., Forster et al., 2000; Liviero et al., 2002; Doebley et al., 2006; Li et al., 2006a, b; Sang & Ge, 2007b, a; Buckler et al., 2009; HÜBner et al., 2009; McMullen et al., 2009; Moyle & Rausher, 2009; Nevo, 2009; Zhang et al., 2009).

For example, Grillo et al. (2009) applied QTL analysis to investigate the genetic architecture for the adaptive origin of *Oryza nivara*, the wild progenitor of cultivated rice. The adaptive origin of this annual wild rice from a perennial ancestor was associated with an ecological shift from persistently wet to seasonally dry habitats. This study developed the system of

wild relatives of rice for understanding the genetic basis of adaptation and speciation (Grillo et al., 2009). In addition, wild tomatoes also emerge as promising systems for studying ecological genetics and genomics, due to the availability of markers, genomic information, and well-developed molecular genetic tools (Moyle, 2008). Another example of ecological adaptation in the crop relatives is the fitness investigation of wild barley in natural environments (Verhoeven et al., 2004). This study used direct tests of fitness by planting F_3 progeny of two ecologically diverged genotypes (a coastal Mediterranean population and an inland steppe population) in the native environments of the parents. None of the QTLs showed changes in rank fitness in the different environments, which indicates local adaptation without genetic trade-offs across environments (Verhoeven et al., 2004).

Perspective

The aforementioned progress represents the beginning of the transition from model to non-model plants in dissecting natural variation and ecological adaptation. The following topics should be further considered in the field of evolutionary and ecological genomics:

The lack of sufficient genomic resources is still a critical limitation for non-model systems. Though great progress has been made in finding ecologically relevant QTL in non-model plants, in most cases, the resolution has not yet reached the gene level. Moreover, the subsequent testing of natural selection based on the variation of causal mutations further lags behind. Reciprocal transplantation of RILs and NILs to test QTLs in parental environments has been studied in some non-model plants, such as *Arabidopsis* wild relatives, *Mimulus*, and wild sunflowers. The fitness of segregating polymorphisms has been tested for chromosomal regions harboring QTL, where ecological consequences may be influenced by multiple linked loci. Thus, analysis at single gene resolution is the future research goal. This can be achieved by having more genomic resources that allow the development of dense markers within QTL regions. Applications of next-generation sequencing may substantially accelerate the progress (Huang et al., 2009). To date, the *Mimulus* complex, sunflowers, *Boechera* species and other *Arabidopsis* relatives, and the wild relatives of crops (such as rice, tomato, barley, etc.) are on track for whole genome sequencing or resequencing.

Tools for bioinformatics and biostatistics are important in the genomics era for studies of ecology and evolution. For example, bioinformatics skills make it possible to process large sequence and expression data sets. New statistical methods also will be needed to interpret the large quantity of high-throughput data in the context of ecology and evolution.

The information on genetic mechanism can be extended across taxa providing hypotheses on responses of other organisms. But the genetic complexity and environmental dependency have been illustrated in some studies (Weinig et al., 2002). However, the species or population specific interaction opened a broad field for studying diverse systems to understand natural variation and genotype-by-environment interactions in nature. Studies focusing on *Arabidopsis* relatives and a few other plants described above are unfortunately insufficient to draw a general picture of natural variation and evolutionary forces maintaining the variation. Nevertheless, these examples provide a good starting point for transitioning from model plants to non-model plants, and from lab-based studies to field experiments. Future efforts will require a broader diversity of study systems for conducting evolutionary studies in an ecological context.

The common characteristic for these relatively well developed plant systems involves interdisciplinary approaches, combining genetics, genomics, physiology, and bioinformatics to address evolutionary questions in an ecological context, both within species and between species. This requires broader collaborations. Most of the systems described above have already built up large research communities and shared resources, such as:

- *Boechera*: <http://ephedra.hip.uni-heidelberg.de/boechera/>; <http://boechera.com/>;
- *Mimulus* <http://www.mimulusevolution.org/>;
- Sunflowers: <http://cgpdb.ucdavis.edu/>.

In summary, the diversity of natural systems provides opportunities to address fundamental ecological and evolutionary questions that cannot be satisfactorily answered by the use of model plants alone. Rapid advances in genomics, bioinformatics and biostatistics have begun to foster new links between molecular biology, evolution, ecology, and functional genomics. These efforts, including technology and system development, will ultimately greatly improve our understanding of complex biological processes within the natural world.

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Fig. 1.
Interdisciplinary approaches to evolutionary and ecological genomic studies. Approaches are shown linking variation in phenotypes to variation on genotypes, followed by testing natural selection and fitness in natural environments.

Fig. 2.
Boechera stricta habitats and research site. **A**, Low elevation, wet meadow habitat. **B**, High elevation, dry mountain habitat. **C**, Field experimental site in Colorado. **D**, Near Isogenic Lines (NILs) were planted in the parental environment to measure fitness and test local adaptation.