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NEWS AND VIEWS

PERSPECTIVE

The genomic and physiological basis of life history variation in a butterfly metapopulation

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Unravelling the mechanisms underlying variation in life history traits is of fundamental importance for our understanding of adaptation by natural selection. While progress has been made in mapping fitness-related phenotypes to genotypes, mainly in a handful of model organisms, functional genomic studies of life history adaptations are still in their infancy. In particular, despite a few notable exceptions, the genomic basis of life history variation in natural populations remains poorly understood. This is especially true for the genetic underpinnings of life history phenotypes subject to diversifying selection driven by ecological dynamics in patchy environments—as opposed to adaptations involving strong directional selection owing to major environmental changes, such as latitudinal gradients, extreme climatic events or transitions from salt to freshwater. In this issue of *Molecular Ecology*, Wheat *et al.* (2011) now make a significant leap forward by applying the tools of functional genomics to dispersal-related life history variation in a butterfly metapopulation. Using a combination of microarrays, quantitative PCR and physiological measurements, the authors uncover several metabolic and endocrine factors that likely contribute to the observed life history phenotypes. By identifying molecular candidate mechanisms of fitness variation maintained by dispersal dynamics in a heterogeneous environment, they also begin to address fascinating interactions between the levels of physiology, ecology and evolution.

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Variation in fitness drives adaptation by natural selection, and life history traits, such as age-specific patterns of growth, maturation, reproduction and survival, are the most important whole-organism traits shaping fitness. Despite the importance of these traits for adaptation, however, still relatively little is known about the proximate underpinnings of life history variation. Integrating knowledge of mechanisms into life history evolution is therefore fundamentally important if we are to gain a complete understanding of the evolutionary process (Flatt & Heyland 2011). Genomic tools such as microarrays and next-generation sequencing hold particularly great promise for uncovering the functional architecture underlying adaptations in life history and other fitness-related traits (Van Straalen & Roelofs 2006; Roff 2007). While the most impressive progress in this area has come so far from genomic studies of laboratory populations in model organisms such as *Drosophila*, *Caenorhabditis elegans* or *Arabidopsis* (Van Straalen & Roelofs 2006), the last few years have witnessed a small but growing number of applications to natural populations of both model and nonmodel organisms (Stapley *et al.* 2010). Recent examples include genome-wide analyses of adaptations to latitudinal climate gradients in *D. melanogaster* (Kolaczkowski *et al.* 2011), serpentine soils in *A. lyrata* (Turner *et al.* 2010) or salt versus freshwater in stickleback fish (Hohenlohe *et al.* 2010). These and other studies are now beginning to reveal some of the genomic signatures underlying ecologically relevant adaptations. In this issue of *Molecular Ecology*, Wheat *et al.* (2011) advance this exciting field further by analysing the genomic basis of dispersal-associated life history variants maintained by extinction–colonization dynamics in the well-studied metapopulation of the Glanville fritillary butterfly (*Melitaea cinxia*) in the Åland Islands of Finland (Fig. 1). The authors' genomic analysis of a case of spatially diversifying (disruptive) selection driven by ecological dynamics in a patchy landscape is particularly important given that most studies of adaptation and 'adaptation genomics' deal with cases of rather strong directional selection imposed by major environmental changes.

The large metapopulation of the Glanville fritillary studied by Wheat *et al.* (2011) consists of an extensive patchwork of thousands of small meadows and is characterized by frequent stochastic local extinction and colonization events. Previous work has shown that this dynamic turnover is influenced by several dispersal and life history traits, in particular a difference in the propensity to disperse in comparisons between 'old-population' individuals and 'new-population' individuals that descended from females that colonized a new distant patch (e.g. Hanski *et al.* 2002, 2004; Saastamoinen 2007; Saastamoinen *et al.* 2009). Interestingly, many of these differences—including effects on population growth rate—are associated with a nonsynonymous SNP at the *phosphoglucose isomerase* (*Pgi*) locus (e.g. Haag *et al.* 2005; Hanski & Saccheri 2006; Orsini

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Fig. 1 Habitat patch appropriate for Glanville fritillary butterflies in the Åland islands, Finland. Host plants (*Plantago lanceolata*, *Veronica spicata*) for this butterfly grow in the thin soil bordering granite outcrops but are absent in longer grass, pastures and forest. Inset: Glanville fritillary butterfly (*Melitaea cinxia*). Photo credit: Jim Marden.

et al. 2009; Saastamoinen *et al*. 2009), but whether other loci and mechanisms contribute to this life history differentiation remains unclear. The main goal of the new study by Wheat *et al*. (2011), the product of an international collaboration between Hanski's group at the University of Helsinki and Marden's laboratory at Penn State University, was therefore to investigate the genetic basis of how metapopulation dynamics select for life history variation and to identify novel genetic and physiological candidate mechanisms involved in such selection beyond *Pgi*. Based on a *de novo* transcriptome assembly generated with 454 GS20 sequencing (Vera *et al*. 2008), the authors designed 45K-feature Agilent oligonucleotide microarrays and compared gene expression patterns of common-garden reared adult females from 12 old populations with those of nine new populations. In addition, they also used qPCR, physiological measurements and genotyping to further characterize their old- and new-population samples.

Remarkably, Wheat *et al*. (2011) found that the gene expression profiles and the physiology of individuals from new populations represent a nonrandom draw from the set of individuals present in old (source) populations, both in terms of reproductive physiology and in terms of flight metabolism. Females from new populations exhibited overall higher expression of abdominal genes involved in egg provisioning and fecundity, including upregulation of amino acid transporters and storage molecules known as *larval serum proteins* (*LSPs*) and important for egg provisioning; lipid transporters such as *lipophorins* and *perilipin* involved in nutrient mobilization and transfer for egg production; the egg yolk precursor *vitellogenin* (*Vg*); and the fecundity regulator *angiotensin-converting enzyme* (*Ace*). New-population females also had a higher titre of juvenile hormone, a major gonadotropin in insects, and a larger number of mature, chorionated eggs than old-population females. New-population females therefore reach reproductive maturity faster and seem to fuel egg production by accelerating the release of proteins from fat body tissue. In terms of flight physiology, new-population females had a higher peak metabolic rate during flight and increased expression of proteasome and unfolded protein response (chaperone) genes in the thorax, with the expression levels of these genes being positively associated with metabolic rate. New-population females also exhibited downregulation in the thorax of two protease inhibitors (*serpins*) and upregulation of NADH-ubiquinone reductase (NADH dehydrogenase). Thus, these females have thoracic gene expression patterns that are suggestive of increased protein turnover and replacement of molecular damage, perhaps reflecting the high energetic demands of increased flight activity required for dispersal and colonization.

Gene expression differences also varied between alleles at two metabolic loci, *Pgi* and *succinate dehydrogenase d* (*Sdhd*), which differ in their frequency between old and new populations. A previously identified *Pgi* allele (*Pgi f* = *Pgi_111_AC*), which is more common in new populations and known to have higher fecundity, peak metabolic rate and dispersal ability, was associated with increased expression of abdominal chorion genes involved in oogenesis and oxidoreductase and ribosomal complex genes in the thorax. A newly discovered *Sdhd* allele (*Sdhd D*), which reaches a higher frequency in new populations and shows improved flight endurance metabolism, was also associated with higher expression of chorion genes, as well as with increased expression of genes involved in carbohydrate metabolism. Although the alleles at these loci assorted independently, the highest flight performance was found in butterflies possessing both alleles, suggesting that *Pgi* and *Sdhd* interact epistatically and are components of the same functional network.

Among the many facets of the study of Wheat *et al*. (2011), three strike us as particularly interesting. The first is that several of the results support the idea that the endocrine system might play a key role in explaining some of the life history differences between old and new populations. Several of the discovered genetic and physiological factors appear to be part of a larger endocrine–metabolic network, variation in which drives the observed life history differentiation between old and new populations. For example, the authors found that new-population butterflies have higher titres of JH, a major pleiotropic insect hormone with pervasive effects on life history traits (Flatt *et al*. 2005). As JH is known to regulate LSP expression, Vg pro-

tein synthesis and fecundity in lepidopterans and other insects (e.g. Jowett & Postlethwait 1981; Ramaswamy *et al.* 1997; Gkouvitsas & Kourti 2009), the increased JH titre might be causally involved in a number of the observed physiological changes. Similarly, ecdysteroid hormones, which often interact with JH, have been found to regulate LSPs, Vg and Ace in *Drosophila* and other insects (e.g. Jowett & Postlethwait 1981; Ramaswamy *et al.* 1997; Siviter *et al.* 2002), and it is thus possible that these steroid hormones also influence some of the physiological variables investigated by Wheat *et al.* (2011).

Another noteworthy aspect of the current study relates to life history trade-offs. Because new-population females have enhanced reproductive and flight performance, they must turn a substantial fraction of their larval-derived protein resources into *both* eggs *and* flight muscle—so where is the 'catch-22', the trade-off? Two previous studies might hold a possible answer. When measured in large outdoor field cages that permit mobility, the more dispersive new-population females had reduced maximal lifespan, suggesting that increased flight metabolism and reproductive performance might trade-off with longevity (Hanski *et al.* 2006). Perhaps consistent with this notion, Saastamoinen *et al.* (2009) found that the more active *Pgi f* (*Pgi_111_AC*) genotype had *extended* lifespan when measured in a *flight-restricted* laboratory setting, indicating that increased flight metabolism might exact a survival cost. Moreover, when analysing females that did or did not reproduce separately, *Pgi f* only extended lifespan in nonreproducing females, supporting the idea that the enhanced reproductive output of this genotype might reduce lifespan. To confirm or refute the existence of a survival cost of flight and/or reproduction in these butterflies, it might thus be informative to experimentally manipulate both flight ability and reproduction and test how this affects survival. If the existence of a survival cost were to be confirmed, it would be tempting to speculate that JH might also play a functional role in it: JH is thought to promote reproduction at the expense of lifespan in several insects including butterflies (Herman & Tatar 2001; Flatt *et al.* 2005).

Finally, the study by Wheat *et al.* (2011) begins to reveal some fascinating and intricate connections between life history physiology, ecological dynamics and evolution (cf. Zheng *et al.* 2009). In a previous study, Hanski & Saccheri (2006) found that the effects of *Pgi* alleles on population growth depend significantly on patch size, and Wheat *et al.* (2011) now find a similar interaction for *Sdh*d alleles. Remarkably, their new analysis of the effects of both *Pgi* and *Sdh*d alleles and patch size accounts for over 60% of the observed variation in annual population growth. This stunning result not only suggests that the *Pgi* and *Sdh*d alleles are selected by metapopulation dynamics but in fact also suggests that these alleles are actively driving ecological dynamics. One possible model to explain this pattern would be that the highly dispersive life history variant does better in small (new) patches where mates are relatively scarce because it matures faster and has higher fecundity, but performs worse in larger (old) patches with ample mating opportunities because of its shorter residence time and lifespan (Hanski & Saccheri 2006). While the details of this heuristic model await future verification, the study by Wheat *et al.* (2011) makes it clear that the Glanville fritillary is not only a superb model for genomic study of life history adaptation in the wild but also for investigating the coupling of ecological and evolutionary dynamics.

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P.K. and T.F. are interested in the evolution and physiological mechanisms of life history traits and aging, using Drosophila as a model system.

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