Dispatches

Evolution: How Fruit Flies Adapt to Seasonal Stresses

Fruit flies inhabit a wide range of latitudes, requiring adaptation to the varying local climates. A recent study reports evidence that the ability of North American flies to endure the winter involves adaptive polymorphism of the *couch potato* gene.

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In autumn, the days shorten and temperatures fall with the leaves. Some people respond dramatically to these seasonal changes, for example by exhibiting changes in temperament and mood, whereas others barely seem to notice. Such natural variation in response to seasonality is common to myriad species. Populations of the diminutive fruit fly, *Drosophila melanogaster*, exhibit seasonal adaptations which depend on the local climate. In temperate climates, adult fruit flies overwinter by selectively suspending their egg production via a process called ovarian diapause (Figure 1) [1]. Diapause involves the arrest of ovarian development and is indicated by the absence of vitellogenin in the eggs [1,2]. Flies are induced to enter diapause by external seasonal cues: shortening days and cooling temperatures [1]. Flies living in climates with little seasonality exhibit a greatly reduced ability to enter diapause. Genetic analysis of natural variation in *D. melanogaster* diapause has begun to provide a glimpse of the mechanisms modulating this fascinating ecologically relevant phenotype [3–5]. Now Schmidt *et al.* [6] have identified a non-synonymous — amino-acid changing — polymorphism in the *couch potato* (*cpo*) gene [7] that contributes to adaptive variation in diapause.

The genetic makeup of the fly affects its ability to undergo diapause. Three genes have been implicated as contributors to natural variation in *D. melanogaster* diapause: *timeless* (*tim*), which encodes a light-responsive component of the fly's circadian clock machinery [4,5]; *Dp110*, which encodes a phosphatidylinositol 3-kinase (PI 3-kinase) on the insulin signalling pathway [3]; and, from the new work of Schmidt *et al.* [6], *cpo*, which encodes an RNA-binding protein.

Flies with the less light-sensitive form of the Timeless protein enter diapause in response to shortening days, and are less responsive to increasing day lengths, prolonging their diapause later into the spring [5]. The involvement of *tim* in diapause suggests that the circadian clock may function in photoperiodic responses to seasonal change. Expression of the *Dp110* encoded PI 3-kinase is inversely correlated with the propensity to diapause [3]. Interestingly, insulin signalling also plays a role in the diapause of the mosquito [8], and in a developmental arrest (dauer formation) of the nematode worm *Caenorhabditis elegans* [9].

Genetic variation associated with reproductive diapause in *D. melanogaster* affects numerous other life-history traits, including rates of senescence, lifespan, fecundity, developmental time, lipid content and stress resistance [10–14]. Schmidt *et al.* [6] show that genetic variation in the *cpo* gene contributes to natural variation in diapause found in a North American cline. Together, these studies allow us to begin to connect genetic contributions to natural variation in diapause with its adaptive significance.

North American *D. melanogaster* populations exhibit clinal variation in diapause. In Florida, only 30% of flies diapause, compared with 90% in New England [10]. Genetic analyses localized this variation to chromosome 3 [10]. Two hundred and fifty recombinant inbred lines, with 15 single nucleotide polymorphism (SNP) molecular markers on chromosome 3, were constructed from the high and low diapause lines [6]. Diapause was measured in these recombinant inbred lines and a single quantitative trait locus (QTL) between cytological regions 90D1 and 92E8 was found [6]. Fine scale mapping using additional SNP markers localized the natural variation in diapause to exon 5 of the *cpo* gene [6].

Further analyses confirmed *cpo*'s involvement in diapause. High diapause lines have 15% less *cpo* transcript than low ones [6]. Mutations in *cpo* were found to result in changes in the percentage of flies entering diapause — for example, a deletion in *cpo* caused a significant increase. Sequencing a 3.5 kilobase stretch of *cpo* in a sample of 35 natural lines

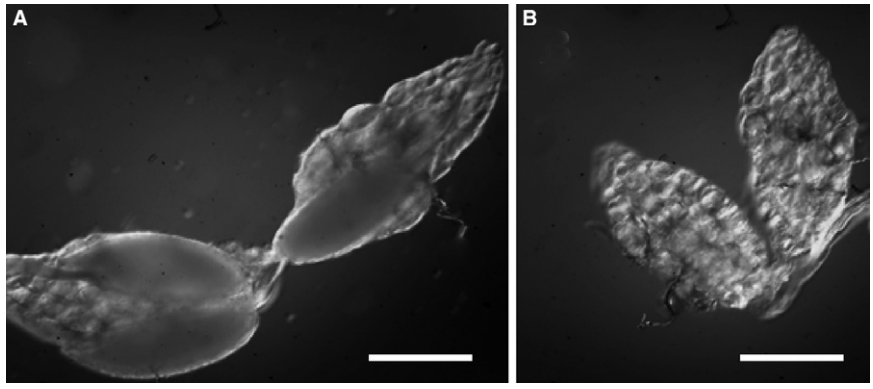

Figure 1. Diapause in *Drosophila melanogaster* is a reproductive arrest.

Dissected ovaries from (A) non-diapausing flies are larger and contain eggs whereas those from (B) diapausing flies are smaller and egg production is halted. Non-diapausing flies were reared at 22°C under 12L:12D light cycle; diapausing flies were reared at 11±1°C under 10L:14D for more than 14 days. Scale bar in (A, B) is 250 μm.

showed that high diapause was associated with amino-acid-changing variation in two sites in the 3′ end of exon 5: one polymorphism changed alanine to valine and the other isoleucine to lysine. The strongest association was found with the latter polymorphism [6]. It is not clear how this amino-acid polymorphism might be related to the differences in *cpo* transcript abundance between the high and low diapausing recombinant inbred lines.

While the above results firmly establish a role for *cpo* in fly diapause, some important questions remain. For example, how does the *cpo* amino acid polymorphism translate to phenotypic variation in diapause? How do *tim*, *Dp110* and *cpo* interact to affect natural variation in diapause and its associated adaptive phenotypes, such as lifespan, fecundity, lipid levels and stress resistance?

The *cpo* gene was first identified through a screen for genes expressed in sensory organ precursor cells during peripheral nervous system development: *cpo* mutant flies exhibit a variety of behavioural phenotypes, including abnormal responses to light [7]. The *cpo* gene is expressed in the peripheral and central nervous systems of embryos, larvae and adults and in the midgut, glia, salivary glands and in the ring gland which is the primary endocrine structure of *Drosophila* [15]. This expression pattern is intriguing as diapause is known to be under neuroendocrine control [2]. Further studies addressing the temporal and spatial patterning of *cpo* required for natural variation in diapause are warranted.

The coordination of metabolism and reproduction with circadian cycles is found among yeast, worms, flies and mammals [16]. Synchronization of reproduction in spring time can occur as a result of mammalian embryonic diapause [17]. In human seasonal obesity, climatic factors alter the coordination of resource use and reproduction [18,19]. Future research on the mechanisms of diapause will not only expand our understanding of the function and evolution of this fascinating overwintering strategy in insects, it will also provide us with candidate genes and pathways modulating the diverse responses of a variety of organisms to seasonal changes.

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Neuronal Homeostasis: Does Form Follow Function or Vice Versa?

Nerve cells adjust their electrical excitability and the overall strength of synaptic connections to maintain their functional identity. A recent study suggests that they may also regulate dendritic branch patterns to compensate for the variability of synaptic contacts and help ensure appropriate connectivity in the brain.

Dirk Bucher

The elaborate morphology of neuronal dendrites and the complex spatial distribution of synapses they receive are cell-type specific and determine how signals are integrated, thereby lending considerable computational power to a single neuron [1]. However, even in the case of individually identified invertebrate neurons, which can unambiguously be compared across individuals, neuron morphology is variable [2,3]. Furthermore, the number and distribution of physical synaptic contact sites throughout the dendrites are variable. Despite this variability, nerve cells have to function in a consistent manner that is appropriate for their role in circuit activity (Figure 1). How does variability arise? During development, the precise branching patterns and the placement of synapses are