WEB WATCH

EVOLUTION

More variation than meets the eye

Genetic variation is so pervasive that it would seem impossible to ignore. Yet ignore it we invariably do, because much of it is hidden in our genomes and surfaces only under certain genetic or environmental conditions. The precise molecular basis of such 'cryptic' variation has not been investigated, but Ian Dworkin and co-workers have now pinpointed the underlying nucleotides in one *Drosophila* gene — the *Epidermal growth factor receptor* (*Egfr*) — by exploiting the characteristic ease with which the phenotype of the fly eye can be perturbed.

Flies that have a dominant gain-of-function allele of *Egfr*, called *Ellipse*[1] (*Egfr*^{E1}), have a rough eye surface that is caused by the presence of too many photoreceptors, which reflects the normal role of *Egfr* in recruiting cells to the photoreceptor fate. The *Egfr*^{E1} phenotype is reasonably stable within a line; however, when *Egfr*^{E1} was crossed into 210 wild-type strains, the eye roughness of the progeny varied widely in severity from severely blistered to almost normal — an effect that had a strong genetic component.

Could this effect be the result of cryptic variation in the wild-type *Egfr* gene, which interacts with *Egfr*^{E1} to modify its phenotype but is otherwise invisible? This theory is supported by the strong and independent association between half a dozen of the 267 bi-allelic SNPs along the *Egfr* gene and the ability to modulate the rough-eye phenotype.

So, the authors showed that a certain *Egfr* nucleotide variant might be associated with the ability to modify the *Egfr*^{E1} eye, but they had yet to confirm a causal link between the two. To do this, they turned to the progeny of 1,000 crosses between the *Egfr*^{E1} allele and a large outbred population; indeed, four of the candidate SNPs identified in the first study were associated with the more extreme rough-eye modifications in this cross.

Although even this result does not constitute formal proof of causality, it is as close as we can get — short of putting the nucleotide variants back in the fly. Such an experiment will no doubt follow, along with others that aim to match the genetic structure observed here with that of hidden variation at other loci, or indeed at *Egfr* in other tissues in which it acts.

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References and links

ORIGINAL RESEARCH PAPER Dworkin, I. *et al.* Evidence that *Egfr* contributes to cryptic genetic variation for photoreceptor determination in natural populations of *Drosophila melanogaster*. *Curr. Biol.* **13**, 1888–1893 (2003)

WEB SITE

Greg Gibson's laboratory: http://statgen.ncsu.edu/ggibson

URLs

Egfr:
http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=37455