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The need for speed

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A new microarray-based technique quickly and inexpensively maps quantitative trait loci.

In laboratory economics, fast and cheap beat long and expensive. Mapping quantitative trait loci (QTLs) traditionally requires a large population with many genetic crossovers and a detailed genetic map containing many markers. Now Lai *et al*. report a rapid high-resolution technique to map QTLs using microarrays in a recent article in *Nature Methods*.

Unlike mice, which live for approximately two years, *Drosophila* live for about 40 days and are therefore preferred models for longevity studies because researchers can examine multiple generations more quickly. The authors previously mapped QTLs affecting longevity in *Drosophila* bred from two inbred strains, Oregon and 2b. However, without more markers and *Drosophila* lines, they could not finely map QTL localization. In the current study, they aimed to use microarrays to increase genetic resolution without expanding the mapping population or the density of genetic markers.

The authors generated 21,207 F_2 *Drosophila* by reciprocally crossing Oregon and 2b *Drosophila* and then crossing their progeny. Most QTLs affecting longevity are sex-specific. The authors collected over 500 male and female F_2 *Drosophila* at 2-3 days of age. Later, when only 10% of the F_2 population was still alive, the authors collected 342 males and females. They differentially labeled pooled DNA from each sex-specific cohort and hybridized young and old F_2 DNA to microarrays.

To localize QTLs, the authors defined candidate single-feature polymorphisms (probes that indicate differential expression) in the parental strains. They hybridized DNA from Oregon and 2b *Drosophila* that had been differentially labeled with biotin and fluorescein, respectively, to one microarray. In standard QTL mapping, researchers look for an additive effect, in which the phenotype measured in the F_2 generation is equal to the mean of the parental strains. From the initial set of differentially expressed SFPs, the authors selected probes that showed expression in the F_2 generation equal to the mean of the parental strains. Among this group, 2326 probes showed different expression levels in young and old *Drosophila*.

The 2326 SFPs mapped to 18 QTLs. Six of the QTLs were within and three QTLs were near previously reported QTLs affecting lifespan. The authors found 11, 7 and 2 QTLs affecting lifespan in males, females and both males and females, respectively, consistent with sex-specific genetic contibutions to longevity. The 8 SFPs in females and 13 SFPs in males that defined one of the shared QTLs localized to the predicted transcript *CG15285*. The

authors sequenced this transcript and identified a 117-bp deletion in 2b *Drosophila* that associated with increased lifespan.

The QTL intervals were smaller in this microarray study than in most initial genome scans, suggesting that microarray-based QTL mapping offers greater genetic resolution at an earlier stage in the mapping process. The authors propose increasing resolution further with tiling arrays or whole-genome SNP arrays and suggest that similar methodology should allow fast QTL mapping in other inbred model organisms as well as outbred populations, like humans.

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1. Lai, C. Q. *et al.* Speed-mapping quantitative trait loci using microarrays. *Nature Methods* **4**, 839–841 (2007). | Article | PubMed | ChemPort |