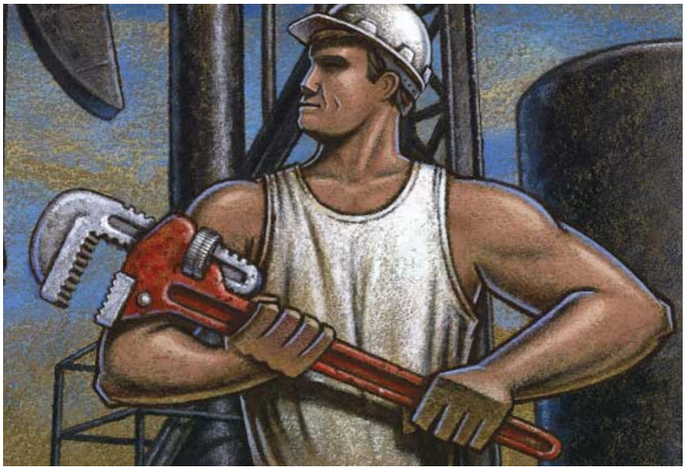
HIGHLIGHTS

TECHNOLOGY

Back to basics



In this day of global analysis and systems biology, who would have believed that such fundamental genetic tools as transposon-mediated deletions would be making the waves. And yet, in the most recent issue of *Nature Genetics*, two groups describe the generation of a new and improved fly transposon tool kit to systematically generate high resolution deletions in the *Drosophila melanogaster* genome. What makes these techniques better is their ease of use, molecular precision and the lack of sequence bias.

Fly reverse genetics has for years relied on disruptions that are induced by *P*-element transposition, although its insertion bias has made genome-wide knockouts impossible to achieve. Thibault *et al.* have modified a moth transposon called *piggyBac* and a *D. melanogaster P*-element to carry splice-traps and transcriptional silencing elements, and used both types of construct to simultaneously disrupt and tag fly genes. Unlike *P*, *piggyBac* does not preferentially insert into 5′ regulatory regions. Rather, *piggyBac* inserts within coding exons more than three times as frequently as *P*, making gene disruption more efficient. Because *piggyBac* insertions do not cluster in hotspots, which are characteristic of *P*, fewer insertions will be required to reach genome saturation. In fact, the authors have already tagged 53% of the genes. Importantly, from the point of view of the fly community, the use of isogenic lines in this work simplifies future phenotypic comparisons.

Parks and Cook *et al.* took advantage of these insertion lines to generate chromosome deletions. In contrast to traditional deletions, most of which are large and have poorly defined break points, the new deletions are small (140 kb on average). And because deletions are obtained through FLP-mediated recombination between FLP-recombination target (FRT) sites that lie in the transposon constructs made by Thibault *et al.*, the break points can be easily and precisely mapped. The specially designed crosses allow the authors to recover deletions in four generations, and the high density of the original transposon insertions, combined with the predictabilty of deletion end points, make it possible to design deletions that target as little as a single gene.

The FRT-based deletion strategy has already yielded 56% genome coverage. And Parks and Cook *et al.* announce that the Bloomington *Drosophila* Stock Center and DrosDel Consortium will generate further deletions using this and related strategies, providing a resolution that is unprecedented in metazoa.

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References and links

ORIGINAL RESEARCH PAPERS Thibault, S. T. *et al.* A complementary transposon tool kit for *Drosophila melanogaster* using *P* and *piggyBac*. *Nature Genet.* **36**, 283–287 (2004) | Parks A. L. & Cook, K. R. *et al.* Systematic generation of high-resolution deletion coverage of the *Drosophila melanogaster* genome. *Nature Genet.* **36**, 288–292 (2004)

FURTHER READING Adams, M. D. & Sekelsky, J. J. From sequence to phenotype: reverse genetics in *Drosophila melanogaster*. *Nature Rev. Genet.* **3**, 189–198 (2002)

WEB SITES

Bloomington *Drosophila* stock Center: http://fly.bio.indiana.edu

DrosDel Consortium: http://www.drosdel.org.uk