Journal club

BUILDING ON THE SHOULDERS OF GIANTS

Major breakthroughs in science often originate from fundamental biological discoveries or significant technological or methodological advances. For those of us working with model organisms, methods that allow and facilitate the manipulation of genomes transform the field by enabling the creation of animals, tissues or cells of specific genotypes, thus allowing a myriad of questions in cell and developmental biology, neurobiology and physiology to be addressed. The ΦC31-mediated transgenesis method introduced to *Drosophila melanogaster* by the Calos laboratory is one of these transformative techniques.

> “The ΦC31-mediated transgenesis method … will have a long-lasting impact on science…”

ΦC31-mediated transgenesis allows the introduction of a sequence of interest at a selected site in the genome. In its simplest version, a plasmid that contains the sequence of interest, the attachment-B site (attB) from *Streptomyces lividans* and a selection marker is co-injected with the ΦC31 site-specific integrase into embryos that contain the ΦC31 bacteriophage attachment-P site (attP). Recombination between the attB and attP sequences, which is mediated by ΦC31, promotes integration of the sequence of interest at the attP sites.

This method supplements previous random integration approaches to transgenesis by allowing the integration of plasmids at predetermined attP sites. The selection of these sites, and thus of the genetic insertion point, reduces the problem of position effects — the effects on the expression of a gene when its chromosomal location is changed. Furthermore, ΦC31-mediated transgenesis is approximately five times more efficient at generating transgenic animals than earlier methods — an obvious advantage in the rapidly moving field of genetic research.

The ΦC31-mediated transgenesis method is a technical advance that will have a long-lasting impact on science, not only because it is remarkably simple and efficient but, importantly, because it provides endless versatility. For example, because attP sites can be targeted to specific regions or genes by homologous recombination, researchers can direct plasmid integration to predetermined attP sites of their choice. So, although the individual components of this system are minute, taken together, they leave researchers building on the shoulders of giants.

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