

Enhancer trap technique – A novel tool for identification and developmental characterization of *Drosophila* genes

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The classical technique of mutational screen for identification of genes controlling early development has now approached saturation. A new era in genetic identification and developmental characterization of genes in *Drosophila* has commenced with the advent of the enhancer trap technique. This technique involves mobilization of a P *lacZ* vector to diverse chromosomal locations in the fruit fly genome to bring it under the regulation of developmentally expressed genes or their enhancer elements. The technique offers a strikingly elegant method of gaining entry into fruit fly genes.

DURING the development of the higher organisms, an apparently uniform egg cell gives rise to a complex metamerized adult. In the past decade and a half there have been dramatic improvements in our understanding of the principles governing the correct segregation of the developmental potential of cells in a growing embryo in a well-defined spatial and temporal order. Much of our understanding in these areas has emerged from the studies on the fruit fly, *Drosophila*. To understand the logic behind the process of embryonic differentiation and determination, it is necessary to know how many genes are involved in the embryonic pattern formation, whether each of these genes is unique and what types of pattern alterations are caused by mutations in a single gene. The answer to all these diverse questions lies in the identification and subsequent developmental and molecular characterization of the genes which regulate these developmental steps and cell differentiation. In this review, a recently developed technique, popularly referred to as enhancer trap technique, for identification of *Drosophila* genes has been discussed.

One important aim of developmental biology is to elucidate the complex mechanism controlling early embryonic development. The classical mutagenesis approach to study development is to obtain genetic variants that alter or block developmental decisions during embryogenesis. Several classes of genes have been found to operate during development to establish the final body pattern of *Drosophila*¹⁻⁴. Based on their mode of inheritance, two types of genes have been distinguished – the maternal genes and the zygotic genes. The maternal genes act during oogenesis. The products of maternal genes are provided to the embryo by the

germline and the somatic cells of the mother. These maternally derived products function in the syncytium to organize the antero-posterior and the dorso-ventral axis of the embryo⁵. Subsequently, the activities of the zygotic genes ensure the origin of diverse spatial pattern in the developing embryo. The zygotic genes act in a hierarchical fashion to divide the embryo into segments and the latter into smaller groups of cells – the compartments. The category of genes classified as homeotic genes specify the individual segmental identity⁶⁻⁸.

A series of intensive screens for the embryonic lethal mutations leading to pattern defects originally initiated by Nusslein-Volhard and Weischaus¹ have now provided a large list of genes implicated in the genetic control of development in *Drosophila*^{1,9-11}. These screens for mutations inducing embryonic lethality have truly been exhaustive and currently it is believed that the technique has come to saturation. At least the prospects of finding new loci by the use of classical mutagenesis screen has receded to the point of unprofitability. Moreover, screens based on mutant phenotype alone may lead to an underestimation of the number of genes required for pattern formation^{1-3,9,10}. For example, haploinsufficiency loci, duplicated genes¹², mutations with subtle phenotypes, existence of 'shunts' in the development, and mutations causing developmental arrest before differentiation² would have been mostly overlooked in these classical mutagenesis screens. The stage has now been set to search for newer methods of genetic screens for the identification of genes controlling fruit fly development.

One of the possible approaches towards identification of new genes is by virtue of DNA homology. In this reverse genetics approach, for example, the gene *caudal* essential for the normal segmentation process was discovered using the conserved 180 nucleotide sequence as the homeotype^{13,14}. Another method involves a screen for gene expression patterns using panels of monoclonal antibodies raised against specific parts or whole of the organism¹⁵. The antibodies which react with the antigen of the tissue of interest are used to clone the corresponding gene from the cDNA expression library¹⁶. Screens based on homology, however, have their own limitations. These include the nature of the DNA or the protein probes used and the fact that these depend,