

García-Bellido A, Ripoll P & Morata G. Developmental compartmentalisation of the wing disk of *Drosophila*. *Nature* 245:251-3, 1973.

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The offspring (clones) of single proliferating cells genetically labelled appear as compact spots occupying any region of the adult wing of *Drosophila*. However, these clones stop along constant or invariant lines of the final organ. These mosaic borders delimit closed "compartments." Compartments arise during development along with cell information by successive, binary, topographical partition of groups of cells with characteristic morphological fates. Fourteen such compartments have been identified in the wing. Some of these compartments are the realm of known expression of homoeotic genes. [The *SC*<sup>1</sup>® indicates that this paper has been cited in over 310 publications.]

## Compartments Are Supracellular Units of Development

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June 12, 1989

The possibility of genetically labelling individual cells during development has largely enriched our understanding of morphogenetic processes. Since Curt Stern discovered mitotic recombination in *Drosophila*, in 1936, development can be described in terms of cell lineages or clones. Clonal analysis reveals quantitative parameters (e.g., number of founder cells, mitotic waves and rates, and so on) and qualitative parameters (e.g., topographical and histotypical restrictions) of cell proliferation during development. The finding of constant lines of restriction, in the final pattern, to the growth of cells, suggested genetic decisions implemented in cell lineages. The verification of the invariance of such restrictions needed the confrontation of populations of cells growing at different speeds. This could be possible

using mutations that change cell proliferation rate in a cell autonomous way. The Minute (*M*) type of mutations were such candidates because their heterozygotes have two to three days longer developmental times. I could not believe, at the time, that this delay could be a cell autonomous property and asked my collaborators in Madrid, G. Morata and P. Ripoll, to test it. They demonstrated that I was wrong, which caused me not to coauthor that paper.<sup>1</sup> The overgrown *M*<sup>+</sup>/*M*<sup>+</sup> clones in an *M*/*M*<sup>+</sup> background readily confirmed the known restriction lines and revealed new ones that delineated closed topographical units, which we named "developmental compartments."

The analysis was first carried out in the dorsal mesothoracic (wing segment) anlage. The study of *M*<sup>+</sup> clones initiated at different times during development uncovered that compartmental segregations (1) affected groups of cells, i.e., the compartments were multicellular in origin (later designated polyclones<sup>2</sup>), (2) appeared through binary partitions of cell populations into complementary compartments, along with cell proliferation in the anlage, and (3) developed in an iterative fashion, subdividing it into 2<sup>n</sup> compartments. We found 14 such compartments in the final population of 50,000 wing cells. This work was presented *in extenso* in a subsequent paper.<sup>3</sup>

These rules were found later to apply to other appendages and segments in *Drosophila*, through the contribution of our own laboratory (Morata) and others (E. Steiner, P.A. Lawrence, and G. Struhl). (Ripoll later focussed his attention on aspects of *Drosophila* somatic cell genetics.) Topological clonal restrictions or associated features of compartments also have been found in other animals (including vertebrates) and plants. But the most relevant feature of compartments in *Drosophila* is that they correspond to the realm of expression of genes, in particular homoeotic genes. Mutations in these genes transform whole compartments from one to another.<sup>4</sup> This relates compartments, as supracellular units of development, to the action of control genes. The notion of systemic morphogenetic operations—opposite to histotypic differentiation—has since opened a new avenue in the understanding of genetic development.<sup>5</sup>

1. Morata G & Ripoll P. Minutes: mutants of *Drosophila* autonomously affecting cell division rate. *Develop. Biol.* 42:211-21, 1975. (Cited 175 times.)
2. Crick F H C & Lawrence P A. Compartments and polyclones in insect development. *Science* 189:340-7, 1975. (Cited 205 times.)
3. García-Bellido A, Ripoll P & Morata G. Developmental compartmentalization in the dorsal mesothoracic disc of *Drosophila*. *Develop. Biol.* 48:132-47, 1976. (Cited 180 times.)
4. García-Bellido A. Homoeotic and atavic mutations in insects. *Amer. Zool.* 17:613-29, 1977. (Cited 135 times.)
5. ———. Cell lineages and genes. *Phil. Trans. Roy. Soc. London B* 312:101-28, 1985. (Cited 5 times.)