Developmental biology

A new homeotic gene

from Peter Lawrence

To all old-fashioned biologists, and to most modern ones, it is obvious that animals are not ill-assorted bags of fibroblasts, neurons and other specialised cells — yet we do not have much idea why they are not. One of the biggest challenges in embryology is to understand how cell types arise together in specific patterns. Homoeotic genes offer a route to attack this problem because a change in the DNA sequence of one gene can comprehensively transform a single cell, and all its descendants, into parts of another organ (for example, a piece of the leg of a fly into a piece of an antenna). Homoeotic genes are often in the news these days and there have been two recent advances that have brought them into the molecular era. First, the DNA for the best known homoeotic locus (the bithorax complex) has been purified and analysis has begun[1]. Second, it is now possible to hybridize molecular probes to sections of *Drosophila* and to find out when, and in which cells, homoeotic genes are being transcribed[2,3].

The difficulty with homoeotic genes, at least for the biologist looking for general principles, is that they have only been found in insects. There is good news therefore in the paper by Dr. Iva Greenwald and her colleagues which has just appeared in *Cell*[4] for it reports the discovery of a homoeotic gene (unmnemonically called *lin-12*) in the nematode, *C. elegans*. Mutations in this gene are of two types; recessive loss-of-function mutations *(lin-12(o))* and dominant gain-of-function mutations *(lin-12(d))* that transform developing cells in related but opposite directions. For example, in the gonad there are a pair of cells whose ancestry does not wholly predict their fate — in a wild type one cannot, by following the steps of cell lineage in an individual, predict which of the pair will become a type *A* cell and which will become a type *B* cell — but there is always one of each in each worm. In *lin-12(o)* they both become *A*, while in *lin-12(d)* they both become *B*. The same principle applies to several other pairs of cells elsewhere in the body. The cells affected by mutations in *lin-12* are usually those whose fate is not completely defined by their ancestry and whose development appears to depend on particular cell interactions (because laser ablation of one such cell, or its neighbours, has effects in addition to the elimination of the ablated cell and its descendants).

The opposing properties of the loss-of-function and gain-of-function mutations suggest that, in the wild type, the amount of gene product is directly engaged in determining the fate of certain cells so that type *A* cells need less product than type *B* cells. Understanding the wild type role of a gene is more difficult than describing the phenotypes of mutants but Greenwald and colleagues have tried to build a case that the wild type role of the *lin-12* gene is to act as a "binary switch to control decisions between alternative cell fates". Apart from the suggestive phenotypes of the mutations themselves, the authors have used a temperature sensitive form of *lin-12(d)* to define the time when changes of level in gene product can change the cell fate. They find that this time occurs at about the latest stage in development that cell fate can be altered by killing nearby cells. These observations suggest, but do not establish, that the extra gene product directly affects the cells at the time that their fates are being determined.

lin-12 is clearly a homoeotic gene in the loose sense (even in *Drosophila*, homoetoic genes are defined loosely) and there are some interesting unanswered questions. In the wild type, does the gene act only in some cells and not at all in others, or are we seeing in the mutants some threshold effects in the least canalized steps of the cell lineage? If the action of the gene is restricted to a certain set of cells, what other properties define that set? Most important: is the wild-type role of the gene to control the activity of other genes directly or does it just provide a product necessary for the nuts and bolts of cellular diversification? In other words is *lin-12* a gene whose only role is to direct cells along particular developmental pathways (like the elements of the bithorax complex, or the *transformer* genes of the nematode or the fly) or does it have a general function in cell physiology which is critical only to those cells altered by *lin-12(o)?* Whatever the answers to these questions I am sure we will learn more from *lin-12* in the future. □

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1. Bender, W., Akam, M., Karch, F., Beachy, P., Peifer, M., Spierer, P., Lewis, E.B. and Hogness, D.S. *Science* **221**, 23 (1983).
2. Hafen, E., Levine, M., Garber, R.L., & Gehring, W.J. *EMBO J.* **2**, 617 (1983).
3. Akam, M. *EMBO J.* (in the press).
4. Greenwald, I.S., Sternberg, P.W. & Horvitz, H.R. *Cell* **34**, 435 (1983).

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Some studies pursued by the writer have led him to believe that in the atom groupings which modern chemistry reveals to us the several atoms occupy distinct portions of space and do not lose their individuality. The object of the present paper is to show how far this conclusion is in harmony with the symmetrical forms of crystals.

If we are to suppose that crystals are built up of minute masses of different elements symmetrically disposed, it is natural to inquire what very symmetrical arrangements of points or particles in space are possible. It would appear that there are but *five* (Fig.2-6).

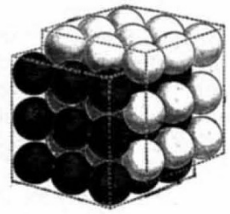


Fig. 2.

Plan *a*.

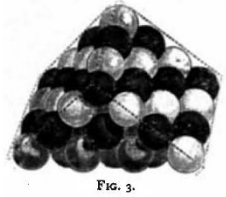
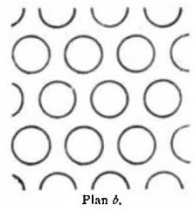


Fig. 3.



Plan *b*.

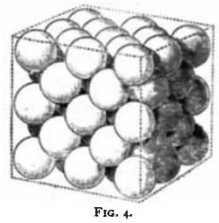
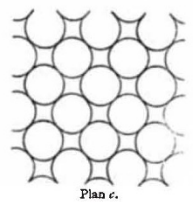


Fig. 4.



Plan *c*.

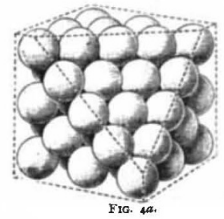
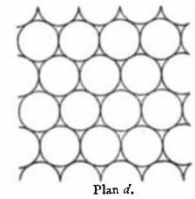
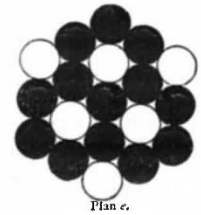


Fig. 4*a*.



Plan *d*.

Fig. 5.



Plan *e*.

Fig. 5*a*.

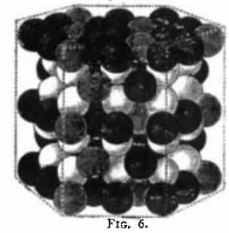
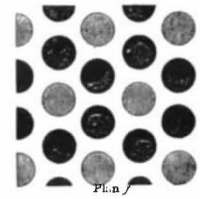


Fig. 6.



Plan *f*

From *Nature* **29**, 186 (1883).

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