ANIMAL BODY PLANS: HOMEOBOX GENES

How a single fertilized cell develops into a complex organism like a fly, a mouse, or a human being has long been one of biology's greatest mysteries. Von Baer in the early 19th century observed that all vertebrates, from salamanders to humans, look very similar in the early stages of their embryonic development. At about the same time, French zoologist Geoffroy Saint-Hilaire declared that all animals have the same body plan.. Because the main nerve cord is in the front part of insects and in the back part of vertebrates, Saint-Hilaire hypothesized that vertebrates are essentially upside-down invertebrates!

Now the molecular revolution that revealed the double helix has taken on the conundrum of animal development as well. Molecular biologists have discovered remarkable genetic connections between very diverse animal species. Certain genes called homeotic genes (homeo=alike) are amazingly similar in structure and function in all animals; they serve as molecular architects and direct the building of bodies according to definite detailed plans.

Like so many breakthroughs in genetics, this one came from the humble fruit fly, Drosophila melanogaster, a laboratory favorite because it reproduces rapidly, has only 4 chromosomes, and readily exhibits mutations induced by inbreeding and x-rays. Fruit flies are highly specialized insects with 2 wings and 3 body segments. Their ancestors had 4 wings and many body segments. The fruit fly embryo starts out with a series of 16 equal-sized segments. Various segments merge to make the 3 segments we recognize as the head, thorax, and abdomen.

In the 1940s, American biologist Edward B. Lewis began studying the homeotic genes that affect segmentation in Drosophila. He found that mutations in a cluster of genes, called the bithorax complex, caused duplication of a body segment with an extra pair of wings. These mutations were weird and hard to explain because hundreds of different genes participate in the formation of a body segment and wings. Yet here were single mutations creating new body parts and eliminating others. These genes were acting as master switches, turning on and off arrays of other genes involved in body shape, and controlling the number, pattern, position, and fusion of segments and appendages.

Choose a color for (a) and color the "lab" gene on the Drosophila chromosome, HOM C. Color the corresponding part on the embryo (a) and on the adult (a) with the same color. Proceed in this way; choose color (b) and color the "pb" gene next. Color the part of the embryo (b) and adult (b) controlled by the "pb" gene. Notice that the genes are lined up on one chromosome in the same head-to-tail order as the body parts that the genes control. Choose a light color for (f).

In the late 1970s, German biologists Christiane Nüsslein-Volhard and Eric F. Wieschaus sequenced the homeotic genes controlling the development of the fruit fly's body. They observed that in each of these genes a particular DNA segment 180 bases long was virtually identical. This DNA sequence, called the homeobox, translates into a protein sequence 60 amino acids in length. This protein sequence binds to DNA and switches on and off the process of transcription, the expression of genes into proteins. By controlling the transcription in all cells, homeobox (Hox) genes act as master switches determining cell fates, growth, and development.

For their work on the homeobox genes, Lewis, Nüsslein-Volhard, and Wieschaus received the 1995 Nobel Prize for physiology or medicine.

Using the same colors and method, color the mouse homeobox genes (Hox A, B, C, D) lined up on four chromosomes and the matching body parts on the mouse embryo.

Hox genes evidently duplicated twice during the evolution of invertebrates into vertebrates, just as there were multiple duplications of the globin gene. Instead of one cluster of about 10 genes on 1 chromosome like the fruit fly, the mouse has 4 clusters of about 10 genes each, on 4 different chromosomes. Hox genes in mice and humans are very similar in number and chromosomal arrangement. It is remarkable that only about 40 genes out of a total of about 100,000 control most of the development, architecture, and appearance of the body plan of complex mammalian species.

As different as the adult fly and mouse appear, their homeotic genes had a common evolutionary origin, shown by the marked similarity in homeobox sequences. Fly and mouse had a common ancestor half a billion years ago, but the homeobox sequence has hardly changed during that long time period. The same Hox genes that determine the belly side of invertebrates establish the back side of vertebrates. Saint-Hilaire's "ridiculous" idea that vertebrates have the body plan of upside-down insects has also proved to be true.

Hox genes provide spectacular insight into the evolution of the eye. Different kinds of eyes in a variety of animals, for instance, octopuses, flies, and humans, posed a puzzle for evolutionary biologists. Ernst Mayr concluded that eyes may have evolved independently 40 different times. In 1994, however, Swiss biologist Walter Gehring and his team found that the Hox gene responsible for induction of the Drosophilia eye is virtually identical to the one that induces the mouse eye. This Hox gene switches on eye formation in the myriad of creatures that see. Hence, it appears that all eyes, no matter how differently constructed they appear now, had a common evolutionary origin.

Hox genes are the molecular architects for animal body plans that von Baer studied more than a century ago and provide the intrinsic unity of design that Saint-Hilaire supposed.

– adapted from *The Human Evolution Coloring Book*, 2d ed., by Adrienne L. Zihlman.
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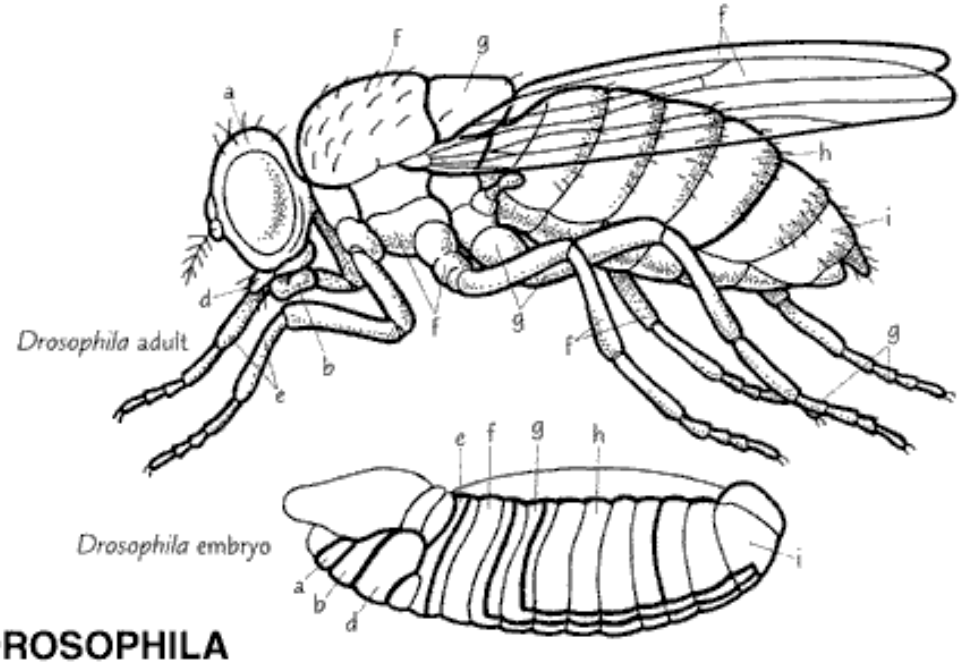
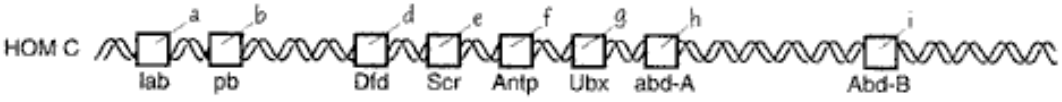
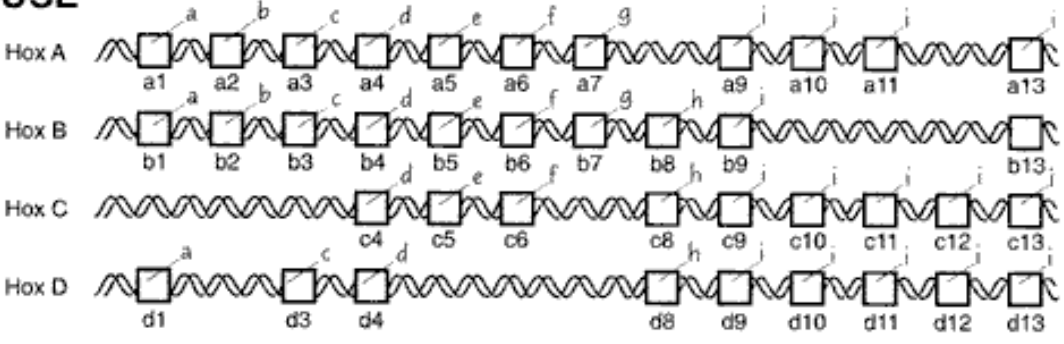
HOMEOBOX GENES

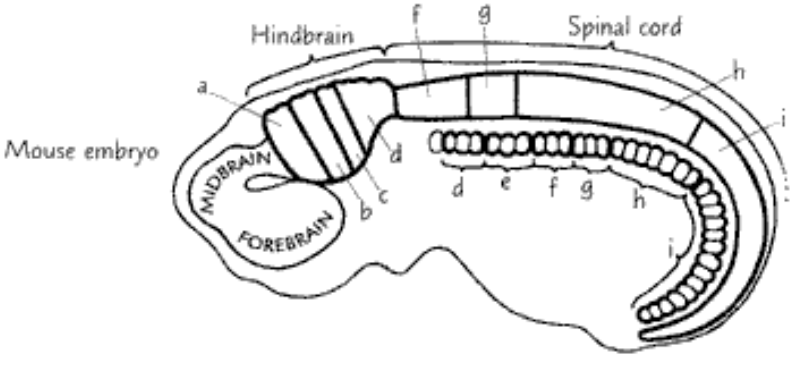


DROSOPHILA



MOUSE





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