

Indeed, the Homeobox has been called the 'Rosetta Stone' of Developmental Biology

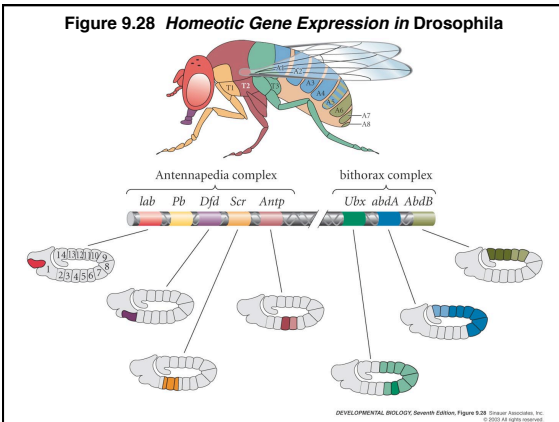
"Indeed, the Homeobox has been called the 'Rosetta Stone' of Developmental Biology"

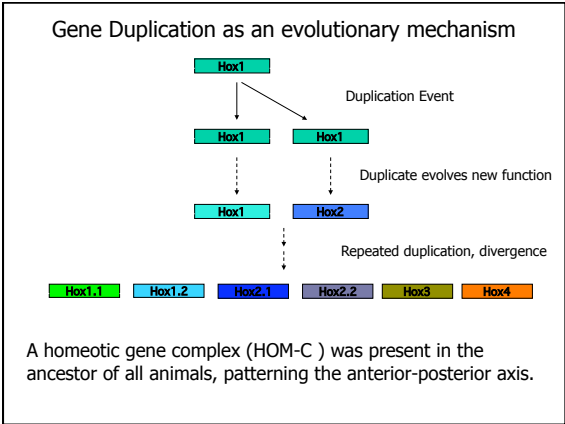
The Rosetta Stone - discovered in 1799 by the French under Napoleon, surrendered to the British. Now resides in London in the British Museum.

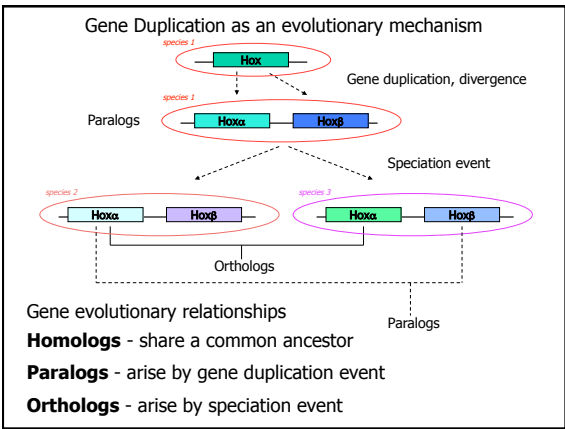
Contains a proclamation in Greek and Egyptian (hieroglyphics and demotic) from the Ptolemaic era (196 BC).

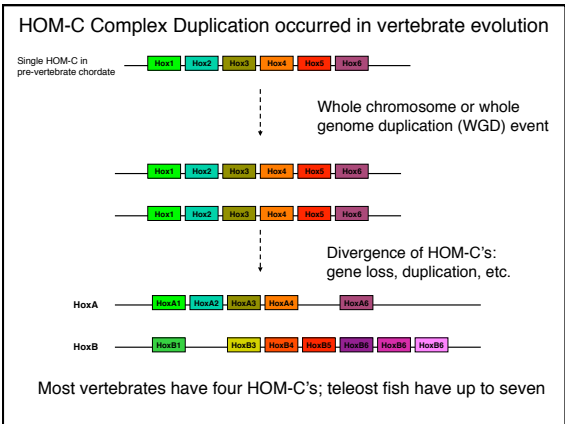


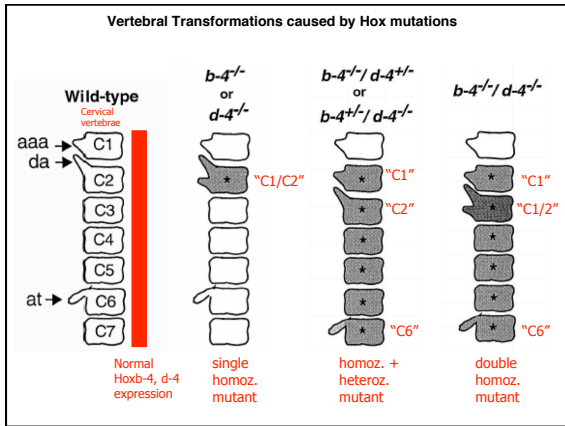
Figure 9.28 Homeotic Gene Expression in Drosophila

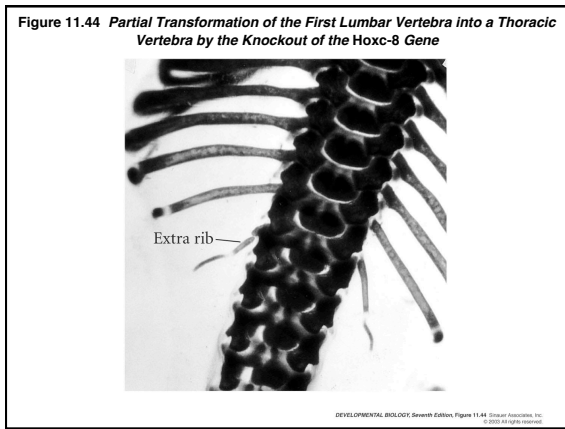


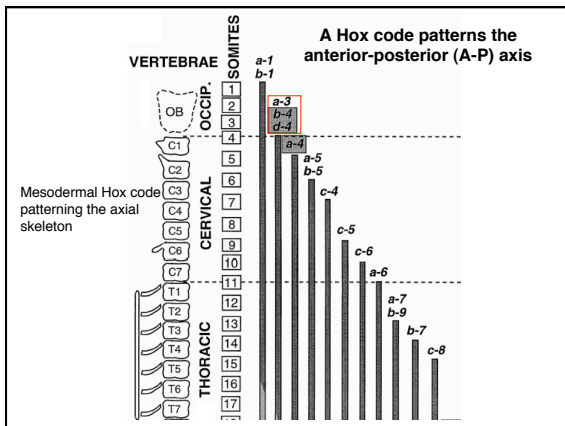


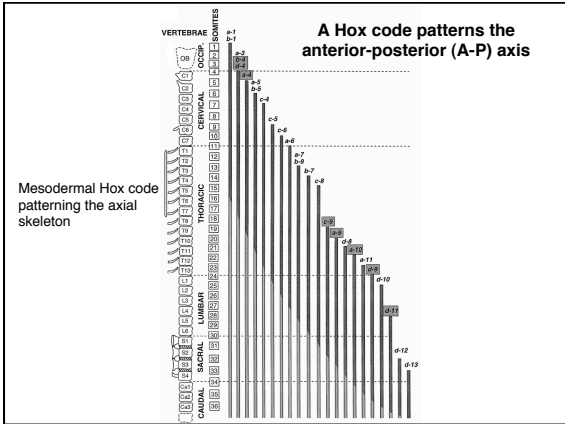












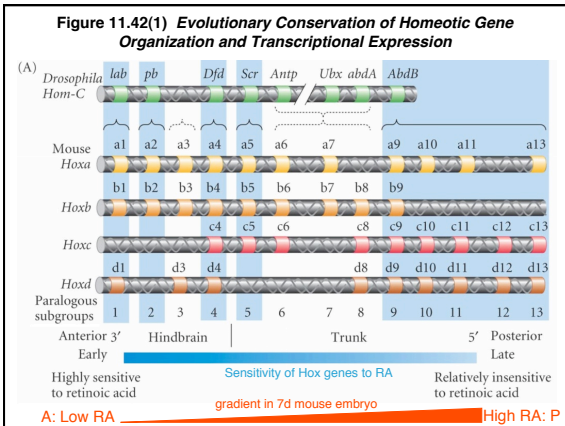
Hox genes activated in part by endogenous retinoic acid (RA)

Many HOM-C genes have RA receptor-binding enhancers

Early embryo has A-P gradient of RA (lo - anterior, hi - posterior)

Hensen's node also has RA (varying conc. over time)

Hox genes vary in sensitivity to RA
(generally low sensitivity in posterior, high sensitivity in anterior)

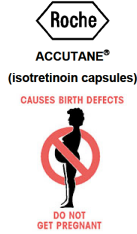


Hox genes activated in part by endogenous retinoic acid (RA)

Exogenous RA is a powerful teratogen in humans

After exposure to RA, in 59 pregnancies:
12 spontaneous abortions (20%)
21 infants with major malformations (36%)

Lammers et al., 1985



CONTRAINDICATIONS AND WARNINGS
Accutane must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking Accutane in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.
Birth defects which have been documented following Accutane exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.
Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, microplasia, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphism; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve defects); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

Hox genes activated in part by endogenous retinoic acid (RA)

Exogenous RA is a powerful teratogen experimentally, in mice

Exposure to additional RA typically causes structures to be transformed to more anterior

Transformations consistent with shifts in Hox gene expression - 'anterior' Hox genes expressed further posterior

Some exposure causes complete loss of many posterior structures

Figure 11.45(1) The Effect of Retinoic Acid on Mouse Embryos

Retinoic Acid is a powerful teratogen.

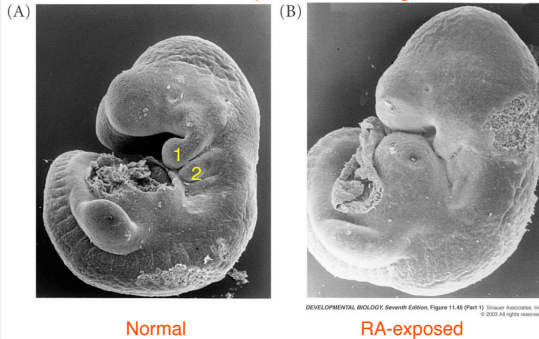
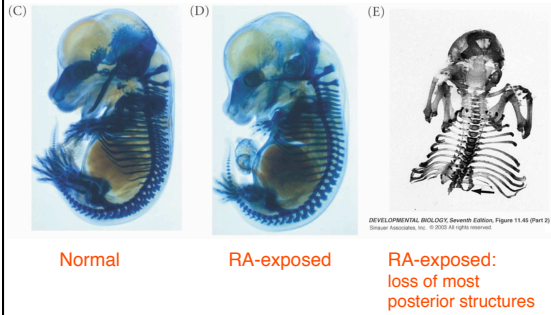


Figure 11.45(2) The Effect of Retinoic Acid on Mouse Embryos

High RA (exogenous) turns on "anterior" HOM-C genes



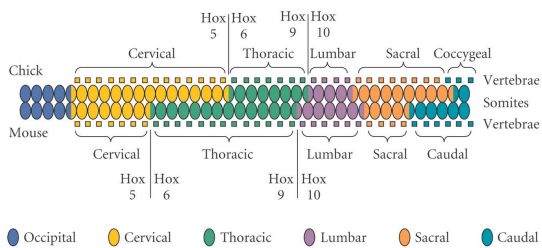
The Hox gene 'code' may explain evolutionary changes

Boundaries between Hox gene expression define body regions (seen clearly in axial skeleton).

Regions of Hox gene expression in mammals vs. birds are consistent with differences in numbers of vertebral types.

For example, the boundary between cervical and thoracic vertebrae is marked by the Hox group 5 and 6 boundary.

Figure 11.46 Mouse and Chick Vertebral Pattern along the Anterior-Posterior Axis



Hox gene expression correlates with vertebral type

DEVELOPMENTAL BIOLOGY, Seventh Edition, Figure 11.46 Sinauer Associates, Inc. © 2003. All rights reserved.

