

Consequences of molecular evolution, part 1**Reading: Chp 19, pp 683-690****Learning Goals**

- Explain why many of the genes used by embryos early in development are highly conserved, while later developing structures are often defined by more dramatic molecular changes, or by different molecules altogether.
- Explain what is meant by deep homology, and be able to propose series of experiments that would provide evidence for deep homology
- Interpret experiments that have demonstrated how changes in populations have arisen at the molecular level
- Design a series of experiments that would help to demonstrate that a structure in two different organisms is homologous (descended from a common ancestor).

Whole classes are devoted to the topic of evolutionary developmental biology, so I cannot hope to impart these complex ideas to you in only a few class periods. For this class, we will focus on some principles that underlie mechanisms of evolutionary change, and the demonstration of “deep homology”, using examples of molecules we have already discussed that are required for development.

Unity of type

Charles Darwin argued in 1859 that there were two principles that governed formation of all creatures on the planet: “unity of type” and the “conditions of existence.” He theorized that the many variations we see in organisms (like the flipper of a seal compared to the arm of a human) had not arisen independently to allow animals to adapt to their surrounds, but rather were similar because they were all based on a structure from a common ancestor: the now well-known idea of descent with modification. The conditions of existence were the selective environmental pressures that different organisms were faced with that could potentially result in such changes. We can now support Darwin’s ideas about unity of type with evidence of changes that occur at the DNA level: the molecular underpinnings of evolution.

Important principles of development and molecular change***Modularity***

Changes can occur in important genes without completely halting development because embryos develop in a modular way. Although some sequences of development are dependent on each other (gastrulation and neurulation, for example), the development of later units such as the eye, the kidney and the limbs, are separate from each other. One can disrupt formation of the eye without affecting the limbs; thus mutations can occur that lead to changes in one structure without killing the animal. Needless to say, fewer changes can be made to genes required for very early events in embryonic development, since those kinds of changes are more likely to result in a dead embryo. Importantly, not only are the anatomical units of a body modular as they develop, but regions of DNA are also modular. Thus, the enhancer or silencer elements of genes can be changed without changing the function of the gene. Instead, one might change where the gene is expressed, or to what level it is expressed. This has been elegantly demonstrated with the stickleback fish, which will be discussed in class.

Duplication and divergence

Many genes exist in several copies within an organism—for example, there are many different kinds of muscle related transcription factors, each expressed during a different time of muscle development. If one looks at all of these transcription factors, it is clear that they arose through duplication and modification (e.g. mutations) of a single common ancestral gene.

Deep homology

When organisms in widely divergent classes (ie, protostomes and deuterostomes) have a whole series of genes that are conserved AND used in a similar way (homologous pathways made of homologous parts), this is termed deep homology. Such findings suggest that that portion of development really only occurs in one way, with small modifications. Two examples of deep homology follow.

Inductive centers: the organizer

Many (not all) organisms require an early set of signaling events to determine the site of gastrulation. In these organisms, the site of gastrulation is determined by the presence of beta-catenin. Expression of beta catenin results in transcription of signaling molecules that have inductive effects on the tissues around them.

Determination of neuronal vs. epidermal fate

The molecules released by the organizer have a similar role and origin across species. Although not all organisms make their nervous system on the dorsal side, all organisms with a central nervous system (even if they don't have an actual neural tube) express BMP homologs in the cells fated to be epidermis, and express BMP inhibitors in the cells fated to be neural. These BMP inhibitors are again all homologous—chordin in vertebrates, and its homolog Sog in *Drosophila*.

Modularity: conservation of eye development

Until recently, eyes were thought to be an example of convergent evolution: an organ that had evolved independently many times, because if you look at eyes from different species (for example, a mollusk, an insect and a vertebrate, the differences are striking. However, all eyes use the photopigment rhodopsin to absorb light and transduce an electrical signal that results in sight. There are now a number of experiments that demonstrate a single origin of the eye from which the different structures have diverged. The most dramatic piece of evidence has been the discovery that the gene *pax-6* is conserved across enormously divergent phyla, and in all cases, is both necessary and sufficient for all organisms to develop an eye. When organisms have a loss of function mutation in *pax-6*, the phenotypes are similar: in humans, mouse, and *Drosophila*, heterozygotes have small eyes, homozygotes have no eyes. Pax-6 is a transcription factor with two domains seen in many transcription factors: a paired domain and a homeodomain. These regions are particularly well-conserved across different species, even at the DNA level. At the amino acid level, the Pax-6 proteins in humans and mouse are 100% identical.

One indication of the importance of this gene for eye development is that it can induce ectopic eyes wherever it is expressed. When the *Drosophila* homolog of *pax-6* was ectopically expressed in the imaginal discs (clusters of cells that make the sensory systems), fully formed eyes developed in ectopic locations (leg, wing, antennae, depending on where *pax-6* was induced) (G, 23.1b). But the most impressive evidence for deep homology among different *pax-6* genes is that one can substitute the sequence of one species' gene with the sequence of another species' gene, and have everything work normally. When the mouse *pax-6* cDNA was expressed in *Drosophila*, it also induced ectopic eyes (further demonstrating the conservation of function of the two genes). These ectopic eyes actually function, transducing an electrical signal even though they are not correctly hooked up to the brain! The *Drosophila pax-6* gene can also be used to rescue *pax-6* mutants in mouse, and vice versa. The *pax-6* gene alone is estimated to trigger a cascade of transcription of approximately 2500 genes that are involved in eye development.