In contrast to *LFY* and *AP1,* the *Arabidopsis TERMINAL FLOWER1 (TFL1)* gene inhibits the floral meristem identity (Ma, 1998; Zhao et al., 2001a). Mutations in *TFL1* cause the production of flowers at the apex of shoots or in place of inflorescences, indicating that the inflorescence meristem has been converted to floral meristem. This arrangement is similar to that of the *Antirrhinum centroradialis (cen)* mutant, which produces a terminal flower at the inflorescence apex. *LFY* and *AP1* are ectopically expressed in the *tfl1* mutant apex, suggesting that *TFL1* exerts its effect by preventing *LFY* and *AP1* expression at the center of the inflorescence meristem. This negative interaction is mutual because *LFY* and *AP1* overexpression also represses *TFL1* expression (Liljegren et al., 1999; Ratcliffe et al., 1999; Zhao et al., 2001a). *CEN,* the *Antirrhinum* homologues of *TFL1,* also antagonize *FLO,* but *CEN* expression is later than and depends on *FLO* expression (Zhao et al., 2001a).

The C function genes, *AG* and *PLENA,* play crucial roles in controlling floral meristem determinacy (Ma, 1998). In both *ag* and *plena* mutants, flowers are indeterminate and produce many more floral organs than the normal flower (Mizukami and Ma, 1997; Zhao et al., 2001a). In addition, *ag* mutant flowers can revert to inflorescence-like structures under short-day and other conditions that do not favor flowering in *Arabidopsis.* Furthermore, ectopic expression of *AG* at the inflorescence apex can also lead to the formation of flowers and termination of the inflorescence. *LFY* and *AP1* are required for activation of *AG,* suggesting that at least part of *LFY* and *AP1* function in controlling floral meristem identity is mediated through *AG.* This conclusion is further supported by the observation that ectopic *AG* expression promotes flower formation, partially rescuing the floral meristem defects of *lfy* and *ap1* mutants.

Recently, new insights into the mechanism controlling floral meristem determinancy have been obtained from analyses of the *LFY, AG,* and *WUSCHEL (WUS)* genes (Lenhard et al., 2001; Lohmann et al., 2001). *WUS* encodes a homeodomain protein and is critical for maintaining the stem cell pool in both inflorescence and floral meristems (Mayer et al., 1998; Brand et al., 2000; Schoof et al., 2000). It turns out that WUS is required for activation of *AG* expression by LFY. This makes sense because *AG* expression begins when the floral meristem is still active. AG then negatively regulates *WUS* expression to terminate the floral meristem activity, thereby causing determinacy of the floral meristem. In the inflorescence meristem, the absence of LFY and AP1 means that *AG* is not expressed there and *WUS* is not turned down, allowing indeterminacy. The *SEP* genes are also redundantly required for floral meristem determinacy (Pelaz et al., 2000); therefore, it is possible that one or more SEP proteins also interact with AG to down-regulate *WUS* during later stages of floral meristem.

Genetic and molecular studies in the model plants *Arabidopsis* and *Antirrhinum* have identified many floral homeotic genes and provided much insight into how they control development. Molecular cloning has revealed that, unlike homeotic genes in animals, most floral homeotic genes are members of the MADS-box gene family, with additional ones being plant-specific transcription factors. Other molecular studies have also provided considerable evidence that these genes are generally conserved in derived eudicots, the closest relatives of the model plants (Ma and dePamphilis, 2000). At the same time, functional conservation in basal eudicots and basal angiosperms is still uncertain (Kramer and Irish, 1999; Ambrose et al., 2000; Ma and dePamphilis, 2000). Additional genes will probably be identified with the completion of *Arabidopsis* genomic sequencing and the availability of numerous reverse genetic tools. A major challenge is to determine whether floral genes identified in model species are conserved in all angiosperms, including the basal angiosperms.

DAVID B. WAKE

Homology and Homoplasy

The word *homology* is used in diverse ways, always with an implication of similarity. The concept of homology is ancient, though Owen (1843) is credited with developing a precise definition of a homologue: "the same organ in different animals under every variety of form and func-

tion" (p. 379). The word "same" meant something very different to Owen than to evolutionary biologists today, which is why homology has remained a topic of discussion for over 150 years. Owen, an outstanding anatomist and powerfully influential member of the British scientific establishment who became Director of the British Museum, Natural History), resisted Darwinism and evolution in general to his death (Rupke, 1994). Evolutionists seized Owen's term and made it their own, going so far as to give their homology a central place in evolutionary thinking. Their adaption of the form led to problems, some of which persist today.

Owen envisioned a Platonic archetype, at first in the form of a Platonic idea inherent in what he termed the *organizing principle*. In his later work, the archetype itself became the idea (Rupke, 1994; Panchen, 1994). Owen's explanation of homology is key to understanding how we have reached the present state of argument on the subject. Two structures in different organisms, such as the seventh cervical vertebra of a mouse and of a monkey, are *special homologues* as two versions of the same structure. They are also each and collectively *general homologues* of a vertebra in the archetype that includes vertebrae but not necessarily the seventh cervical vertebra. The seventh cervical vertebra was to Owen the *serial homologue* of the first thoracic vertebra, the eighth caudal, and so on in the same organism.

Owen also developed criteria for recognizing homologues. The critical criteria were relative position (e.g., the last vertebra pierced by a spinal nerve) and connections (e.g., lying between the sixth cervical and first thoracic vertebrae). He defined an *analogue* as a part or organ in one animal that has the same function as another part or organ in a different animal (Owen, 1843). Some organs could be both homologues and analogues. The flippers of whales and lateral fins of sharks, for example, are homologues because they are both paired appendages; these structures are also analogues because they are used for swimming though they are not used in the same way and they do not contain the same parts. The flipper of a whale more closely resembles a limb of a land mammal than the fin of a shark.

While Owen was explicitly nonevolutionary in his approach, other early nineteenth century biologists were more ambiguous in their views on evolution. The word "affinity" was widely used with respect to homologues. Toward the end of the nineteenth century, in the wake of developing Darwinism, biologists accepted the reality of homology but were uneasy with Owen's interpretation and sought an alternative explanation—evolution. Lankester (1870) attempted to sort out problems associated with homology. He used "homogeny" as a replacement name for homology, arguing that an evolutionary rather than a Platonic philosophical framework required a more technical term. Homogenous organs in two species are present in their most recent common ancestor; all other resemblances are "homoplastic." Thus, serial homologues within an organism are homoplastic; and while the whale flipper and the shark lateral fin are homologues (i.e., homogenous) as paired appendages, they are homoplastic as swimming organs. Analogous organs that are not homologues—such as the whale flipper and a crustacean swimmeret—are also homoplastic. Lankester's concept of homoplasy survives, but his definition of homogeny was rarely used and has effectively disappeared. Perhaps had it survived with its original meaning, we could have avoided years of disputatious argument (reviewed by authors in Hall, 1994).

Lankester was not alone in recognizing the evolutionary foundation of what earlier scientists had tried to capture in their use of the term homology. In the same year the German anatomist Carl Gegenbaur embraced evolution as the explanation for homology (Gegenbaur, 1870). Of course, Owen would have none of it! Confusion and debate ensued.

Van Valen (1982) defined homology as correspondence resulting from continuity of information. In the spirit of this view, Wake (1999) argued forcefully that the homology debate is the result of biologists attempting to save an ancient, vague concept. Homology is not evidence for evolution, as has often been claimed. Rather, once evolution is understood to have occurred, homology is the "anticipated and expected consequence" (Wake, 1999, p. 27) of common ancestry. There is no reason to seek a naturalistic explanation for instances of homology; biologists should instead turn their attention to questions that can be resolved. Wake emphasized the opportunities inherent in homoplasy for understanding similarity.

Homology

Study of homology is in essence the study of evolution, and it can be pursued at many levels of biological organization and with respect to virtually all organismal traits. The central questions include: Is an organ, part, or trait in different organisms the same organ, part, or trait? How have these apparently homologous organs come to differ? Related questions focus on homoplasy: How have independently derived organs

come to resemble each other? Do the organs have a common developmental basis? Or, is the similarity related to the ultimate function, such as swimming, flying, or lekking, rather than to detailed form? To make any progress in answering these questions, scientists need a phylogenetic hypothesis, the more robust the better. Although much progress has been made in defining terms and in developing general explanations for the phenomena, there remain many issues related to the nature of the questions being asked and the criteria for assessing sameness.

There are two general categories of approaches to studying homology. The first is a *taxic approach* (Rieppel, 1994), which involves generating phylogenetic hypotheses from character data. This approach asks: Are two features in two different taxa the same thing? All statements that two features represent the same character are hypotheses that are rejected or tentatively accepted depending on some criteria of tree topology and reliability. There is a large, technical literature dealing with taxic homology, with most researchers operating within the cladistic framework of Hennig (1966), who devised a technical terminology including apomorphy, synapomorphy, symplesiomorphy, and so on. Taxic homology uses criteria to establish hypotheses of homology, but only a phylogenetic analysis that rejects the hypothesis of common ancestry serves as a test.

With the advent of molecular systematics and ever-growing molecular databases, a commonly encountered question is: What is to be compared? On the one hand, there are long sequences of base pairs. On the other is the issue of alignment, which determines what the unit characters will be. A growing technical literature deals with this topic (e.g., Giribet, 2001). Alignment of multiple sequences often involves introducing gaps to make unequal lengths of sequence equal, whereas optimization alignment creates a unique set of homology hypotheses for each tree topology in an analysis (e.g., Wheeler, 2001).

The second general category of approaches to homology is *transformational homology,* which deals with the evolution of homologues, tracing the changes and perhaps the causes of the changes that have occurred. Transformational homology asks questions such as these: Are whale flippers homologues of ungulate forelimbs and how have they been derived? How have limbs been derived from pectoral fins of ancestral forms that have persisted relatively unchanged in sharks? Often transformational homology tries to infer from diverse criteria whether

two features are homologues. Such inferences usually are treated not as testable hypotheses but as conclusions.

Regardless of the approach used, criteria are required to identify homologues. Owen had relatively few criteria; but by the time of Remane (1952), the list had grown. The goal (an ancient one, predating even Owen's work) is to establish "correspondence" among the parts or phenomena being compared, and all agree that relative position (in the case of structure) is important. Remane added a second criterion, special quality; because of its imprecision, this criterion has led to much confusion. For example, common development is a special quality, but it could be extended to any special nature that two features in different organisms share. Remane also used intermediate forms as a criterion. For example, the three inner ear ossicles of mammals are said to have homologues in outgroups because of the evidence of intermediacy in fossil taxa.

Patterson (1988) proposed three "criteria" (from our perspective, one criterion and two tests): similarity, conjunction, and congruence. *Similarity* is the starting reason for even thinking two things might be homologues. *Conjunction* refers to the presence of two features thought to be homologues in the same organism, and is thus a test of homology. Conjunction rejects a homology hypothesis (the characters were incorrectly delineated). *Congruence* is the failure of a phylogenetic hypothesis to reject the homology hypothesis. Patterson's focus was taxic homology and so he was trying to determine which homology hypotheses should be viewed as sufficiently robust to be considered characters for phylogenetic analyses.

A persistent problem in questions relating to homology and homoplasy involves hierarchy (Lauder, 1994). Whale flippers and shark lateral fins are homologues at the level of paired vertebrate appendages, but whale flippers and porpoise flippers are homologues at the level of mammalian anterior limbs in which the phalanges are enclosed in a pad-like structure used for aquatic locomotion.

Homology relates to something biological that is inherited and shared by two or more taxa, whether with absolute fidelity or not. Keeping the level of analysis clearly in mind is important. Thus guanine in a particular position in a particular polypeptide in two organisms is homologous if it occurred in their most recent common ancestor even if a mutation in one molecule has led to a silent codon. Lekking behavior might be ho-

mologous in all grouse, if it can be inferred that their common ancestor lekked, assuming that we have defined lekking at an appropriate level—grouse and their immediate relatives—and with appropriate delimitations (e.g., males gathering in a particular area and displaying solely to attract mates). So delimited, lekking might also be studied in drosophilid flies, in which the character is homoplastic relative to grouse.

Although the term *functional homology* is misused when it is intended to denote mere similarity of function for traits, particular functions may be homologous as characters if shared among taxa due to common ancestry. In Figure 1, gene function "role 2" is homologous for taxa 1 and 2, but not taxa 1 and 5 (Mindell and Meyer, 2001). Potential confusion regarding the level at which homology is implied by authors can be avoided by stating explicitly whether the homology is genic, structural, functional, or behavioral. Further hierarchical subdivision might be needed within any one of these major levels.

Although these considerations would seem to make the study of homology clear, problems arise from every direction! Many different

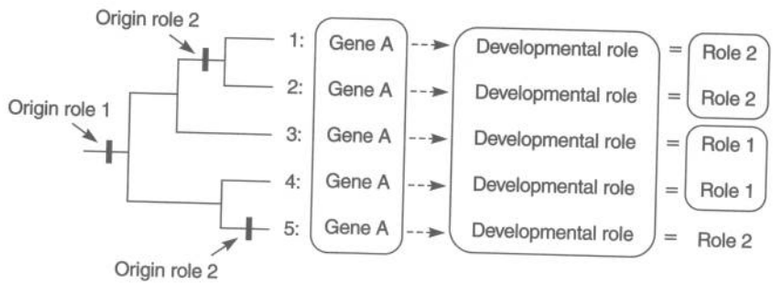

FIGURE 1. Application of common ancestry as the criterion for homology in a hypothetical case of dissociation between a regulatory gene and its role in development. Homologous characters and states are enclosed in boxes. Regulatory gene A first plays a developmental role (role 1) in the common ancestor for taxa 1 to 5. Dissociation events occur such that role 2 is substituted for role 1 in the most recent common ancestor for taxa 1 and 2 and in taxon 5. The following homology relationships can be described. Both gene A and developmental role are homologous in all five taxa. However, the state of the character developmental role changes such that character state 1 (role 1) is homologous in taxa 3 and 4 and character state 2 (role 2) is homologous in taxa 1 and 2. Character state 2 (role 2) in taxon 5 is not homologous to that in taxa 1 and 2, as character state 2 is not shared owing to inheritance of character state 2 (role 2) from the most recent common ancestor of taxa 1 and 2. After Mindell and Meyer, 2001, with permission of the publisher).

reasons are adduced for wanting to "know" homologies and to differentiate them from homoplasies. For example, in studies of molecular evolution the apparent similarity of macromolecules has led to many explanations, including homology.

Several terms are in common use to explain molecular similarity (Fitch, 2000; Mindell and Meyer, 2001). Two similar macromolecules (e.g., hemoglobins differing only in a few amino acids) might arise simply as a result of sister taxa evolving independently; this is *orthology* (lineage splitting, perhaps just species formation, or even cladogenesis if other than immediate sister taxa are involved), or the independent evolution of both taxa from an inferred ancestor. *Paralogy* is the result of gene duplication, which produces two versions of the original macromolecule. These versions can exist in the same taxon, thus violating the conjunction test and disclosing a problem—in this instance, a levels problem. Just as cervical and thoracic vertebrae are homologues at the more general level "vertebra," so also α and β hemoglobin in whales are homologous at the level "hemoglobin," but not at the lower levels of α and β (which are inferred on phylogenetic grounds to have evolved by gene duplication in a remote ancestor). Iterated parts in an organism, or serial homologues, are essentially paralogues, but at the level of organs.

Homology as a general issue in modern biology can be viewed from three perspectives (Butler and Saidel, 2000; Wagner, 1989): historical, biological, and generative.

1. *Historical homology* is the domain of phylogenetic systematics. Following the revolutionary work of Hennig (1966), a consensus developed to base phylogenetic hypotheses on shared derived states of characters, termed *synapomorphies.* When the characters are directly observable in living and fossil taxa, procedures exist for segregating synapomorphies from *symplesiomorphies,* which are shared ancestral states of characters. Criteria for polarization include use of outgroups and sequence of ontogenetic appearance (a highly controversial issue). The criteria are all problematic, and with the advent of large volumes of DNA sequence data, the problems become acute. Thus, *a priori* assessments have largely been abandoned. Historical homology involves the procedure known as *optimization;* once a phylogenetic hypothesis is proposed, states of characters are mapped back onto a tree using explicit criteria (such as maximal parsimony) to give the homology hypothesis for each character.

2. *Biological homology* focuses on the character itself and how it has evolved. Preservation of what might be called "design" has led those in-

terested in biological homology to seek the essence, or cause, for such preservation—the "biological" basis of homology. An example comes from the structure of the wrists and ankles of salamanders (Shubin and Wake, 1996). Variation displayed in a large sample of a newt population discloses a dominant pattern of arrangement of the carpal and tarsal elements, one that is characteristic of the taxon and its close relatives. However, symmetrical variant patterns are found that are recognizable to those who have studied the entire salamander radiation and fossils of outgroups (Shubin et al., 1995). Some of these are atavistic, restoring conditions found in phylogenetically more basal salamander taxa or in remote fossil outgroups. Others are identical to derived patterns that are dominant in species of the same clade, or of related clades, thus revealing the potential to evolve in specific directions. Rather than focusing on the question of biological homology, a potentially productive research program might seek the biological reasons for the conservation of form over many millions of years. Such reasons are likely to lie in the mechanics of morphogenesis.

3. *Generative homology* focuses on the genetic and developmental basis of characters; the approach recalls the archetype. The idea of an animal *zootype,* a genetic groundplan, has been postulated to unite all animal body plans that were founded on a shared pattern of regulatory gene expression (Slack et al., 1993, Schierwater and DeSalle, 2001). The zootype model is essentialistic; it implies that underlying morphology is an even more universal basal set of genetic mechanisms that is highly conserved. The idea that body plan evolution has a fundamental genetic and developmental basis harkens back to earlier ideas of Haeckel and even Owen. In the framework of this general view, the Hox gene cluster is envisioned as the central organizing principle in the evolution of form in complex metazoans (for criticism, see Schierwater and DeSalle, 2001).

The idea that organisms during their development pass through a *phylotypic stage* at which they most closely resemble one another, although they diverge before and very much after this stage, is similar to the zootype concept but at a different organizational level. Reasons for phylotypic stability may derive from the many interactions that take place throughout the embryo at this stage, as well as from the general modularity of development (Raff, 1996). Homology of developmental process (e.g., Gilbert and Bolker, 2001) is another approach that lies within this perspective. Once one accepts that process can be homologized, the possibility of *partial homology,* evident at the level of

macromolecules (Hillis, 1994), must be considered at higher levels of organization as well (Minelli, 1998).

Implicit in studies of biological and generative homology is a quest for a naturalistic or mechanistic explanation for the causes for homology (Laubichler, 2000). However, the ultimate cause for the appearance of sameness is evolution itself. Rather than seeking an elusive and ultimately circular explanation, a more productive approach would explicitly state which explanation is sought. Why has a character or set of characters remained static? Why might a phylotypic stage be a biological reality rather than an idea? How has a given process evolved (such as the Hox gene system in relation to appendages or the brain stem, or the Pax gene system in relation to vision)? To call all of this "homology assessment" is to detract from efforts to understand central biological problems (Wake, 1999).

Homoplasy

Homoplasy travels intellectually with homology and the associations can be confusing. From a phylogenetic perspective, homoplasy is false homology (derived similarity that is not the result of immediate common ancestry), and productive research programs entail study of the reasons for the apparent similarity. Study of homoplasy may elucidate the questions so many biologists have sought to understand in the debate over homologies. Chief among these is the controversy in transformational homology over biological homology (e.g., Wagner, 1989, 1999). Homoplasy has been the subject of much attention recently (e.g., Sanderson and Hufford, 1996; Wake, 1999; Meyer, 1999; Hall, 2002), but its study has been an integral part of evolutionary biology from the beginning.

The least controversial kind of homoplasy is *convergence,* when organisms attain "sameness" in different ways or by following different phylogenetic routes. Wings of flies and birds are convergent, as are eyes of squids and sharks. Lekking is convergent in flies and grouse. Fossoriality and associated elongation and attenuation in tropical salamanders has evolved independently in two different segments of a single clade, one by evolving more trunk vertebrae and the other by making each of the vertebrae (the same number as in inferred ancestors) longer (Parra-Olea and Wake, 2001). This kind of evolution can be envisioned as being founded on elaboration of different developmental pathways or more generally by having different generative systems.

More problematic are the other kinds of homoplasy: *reversals* and *parallelisms*. Reversal is a term from taxic homology; the comparable term for transformational homology is atavism. Reversal is the phylogenetic reappearance of the "same" organ. Frogs typically have no maxillary teeth, but most frogs have mandibular teeth. Only one frog, *Gastrotheca guentheri* from Ecuador and Colombia, has maxillary teeth (some others have convergently evolved tooth-like bony fangs on the maxillary bone). *Gastrotheca guentheri* is deeply nested not only within *Gastrotheca* but within the Hylidae, itself a deeply nested clade of anurans. These maxillary teeth are biologically identical to those of the mandible except in position, and probably develop identically as well. It is this kind of phenomenon, sometimes termed *latent homology,* that has led scientists to propose a kind of continuum from homology to this kind of homoplasy. Butler and Saidel (2000) coined the term *syngeny* for this kind of generative homology, and they contrast it with generative homoplasy, which they term *allogeny,* in which different generative pathways lead to the apparently same feature. Hall (2002) does not care for these terms; he goes further to suggest that, while different developmental pathways generate convergent characters, parallelism is founded on similar or even identical developmental mechanisms and should be considered a form of homology. Examples include the evolution of elongate fossorial salamanders by the same method of increasing the numbers of trunk vertebrae in separate lineages of tropical and temperate salamanders (Wake, 1991), and the repeated evolution of a sword-like tail in a clade of xiphophorine fishes (Meyer, 1999). Atavistic traits might be either.

A theme in comparative developmental work is the possibility of what might be termed *deep homology.* For example, there are many similarities in the development of appendages of arthropods and vertebrates (e.g., Shubin et al., 1997), which may be an example of *generative homoplasy.* As outgrowths controlled by the same genes, the structures are the result of syngeny; from a historical perspective, the organs are clearly convergent and result from homoplasy. The gene *Pax6* is involved in the production of eyes in very diverse taxa, some derived from taxa that may have been eyeless. What is troubling about the designation of organs produced by the same genes as sharing generative homology is the reductionist perspective. Perhaps we should view visual organs as the level of focus. This perspective would interpret *Pax6* genes as the most immediately useful tools that organisms deploy in order to evolve eyes. There is no reason to believe that homologues share some kind of essence just because they use some of the same genetic tools in their development.

Many questions about homology can be resolved by making certain that one has selected the correct hierarchical level for analyzing the characters in question, and by making certain that one is proceeding within the correct phylogenetic framework. Technical debates over definitions of homology doubtless will continue; but if we understand that homology is a necessary component of any theory of evolution, rather than something to be understood on its own, evolutionary biology as a discipline will be well served.

JAN SAPP

Inheritance: Extragenomic

Extragenomic mechanisms of inheritance, from those based on self-perpetuating states of gene regulation to those based on pre-existing cell structure, are sometimes lumped together and discussed under the rubric of *epigenetic inheritance.* This term distinguishes them from the more well known inheritance based on nucleic acids, which is a genetic system (Jablonka and Lamb, 1994). However, because the term epigenetic is an antonym of preformation and the phenomenon of structural inheritance is an argument precisely for preformation, this entry refers to structural inheritance as such and distinguishes it from both epigenetic inheritance and nucleic acid inheritance. The recognition of a plurality of mechanisms of hereditary reproduction and transformation calls for a broader, more inclusive definition of heredity that includes horizontal gene transfer—the inheritance of acquired genes and genomes. Each of these different mechanisms of hereditary change counters classical neo-Darwinian tenets.