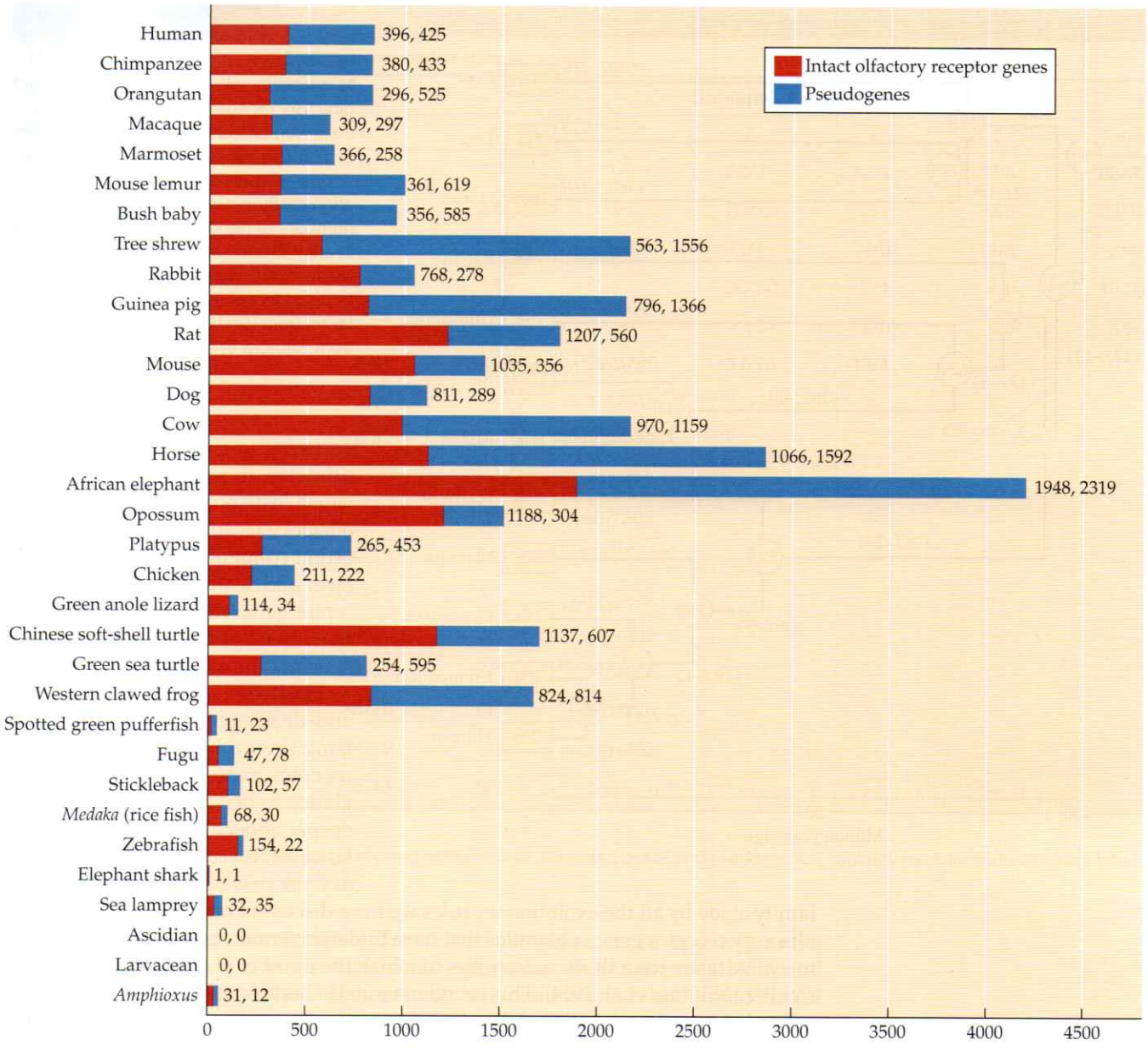

Figure 7.31 Numbers of intact olfactory receptor genes (red) and pseudogenes (blue) in chordates (vertebrates, cephalochordates, and urochordates). Truncated olfactory receptor genes, which are presumably nonfunctional, were included within the count for pseudogenes. The numbers next to the bars represent intact genes (left) and pseudogenes (right). (Modified from Niimura 2012.)

recently. Despite the fact that these two species have similar numbers of functional olfactory receptor genes and a similar fraction of pseudogenes, about 25% of the olfactory receptor genes are species-specific. As seen in **Figure 7.32**, it is estimated that since chimpanzee-human divergence, chimpanzees have gained 8 new species-specific olfactory receptor genes, while humans have gained 18. The rate of gene loss is faster, with chimpanzees and humans losing, respectively, 20% and 19% of the olfactory receptor repertoire of their common ancestor. If we choose as point of reference the most recent common ancestor of all placental mammals, then the largest gain of olfactory receptors occurred in the lineage leading to elephant, resulting in a doubling of the olfactory receptor repertoire. The most impressive loss of olfactory receptors

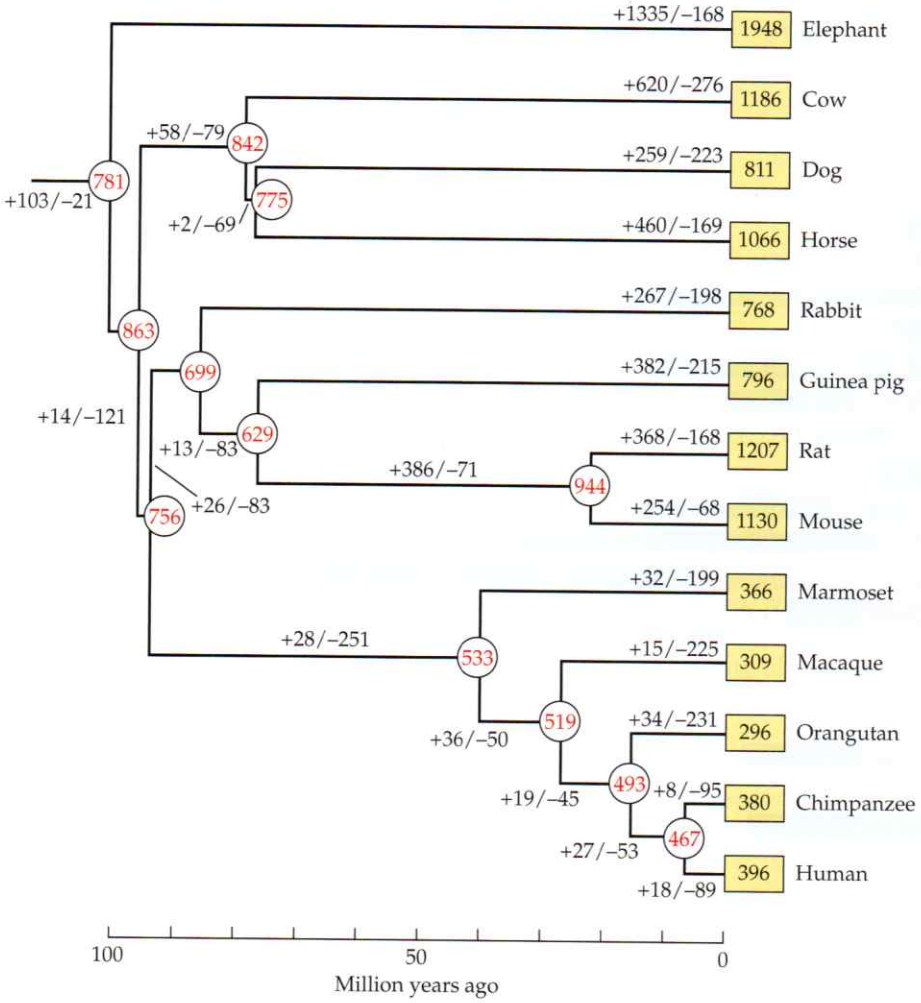

Figure 7.32 Changes in the number of olfactory receptor sequences during the evolution of placental mammals. Numbers in yellow boxes indicate intact olfactory receptor genes in extant species. Numbers in red represent functional olfactory receptor genes in ancestral nodes estimated by the tree reconciliation method (Chapter 11). Estimated numbers of gene gains and gene losses in each branch are shown as + and −, respectively. Speculative divergence times at the nodes of the tree were taken from www.timetree.org. (Modified from Niimura et al. 2014.)

occurred in the lineage leading to primates, in particular orangutans, which lost approximately 70% of the olfactory receptors found in the placental common ancestor. The mean birth and death rates of olfactory receptor genes during placental evolution are 6.2×10^{-3} and 5.9×10^{-3} per gene per million years, respectively.

The extreme rapidity of the birth-and-death gene process characterizing the evolution of the olfactory receptor gene family looks at first glance to be an exceptional case. A deeper understanding of the process, however, reveals that the evolutionary processes affecting this gene family abide by all the evolutionary rules we have discussed previously. For example, olfactory receptor gene subfamiles that have undergone many gene duplications tend to evolve faster than those subfamilies in which the number of duplications has been smaller (Niimura et al. 2014). This is understandable because gene duplication creates redundancy and a relaxation of functional constraint.

The vertebrate olfactory receptor multigene family originated most probably more than 550 million years ago in chordates. Phylum Chordata consists of three subphyla: vertebrates, urochordates (e.g., tunicates), and cephalochordates (e.g., lancelets). Among the three subphyla, cephalochordates are the most basal clade. The amphioxus, a member of Cephalochordata, lacks any distinctive olfactory apparatus. Nevertheless, more than 30 vertebrate-type olfactory receptor genes were identified within its genome. Amphioxus olfactory receptor genes are highly divergent from the vertebrate counterparts, but they are clearly olfactory receptor genes rather than G-coupled proteins unrelated to olfaction. No olfactory receptor-like genes were found in any of the two sequenced urochordate genomes. The absence of vertebrate-type olfactory receptor genes from urochordate genomes suggests that all olfactory receptor genes were lost in this lineage.

Phylogenetic analysis has shown that vertebrate olfactory receptor genes can be classified into at least seven subfamilies (α, β, γ, δ, ε, ζ, and η), each of which originated from one or a few ancestral genes in the most recent common ancestor of vertebrates (Nei et al. 2008). The taxonomic distribution of these subfamilies suggests that they can be further divided into three functional categories (**Table 7.4**). One category contains α and γ, which are present in tetrapods but absent in fish (with the exception

Table 7.4

Relative abundance of olfactory receptor sequences[a]

Organism	Subfamily[a]						
	α	β	γ	δ	ε	ζ	η
Zebrafish	—	4/3	1/0	62/7	12/1	37/4	38/7
Medaka	—	3/0	0/1	33/15	3/1	9/3	20/10
Stickleback	—	1/0	0/3	71/45	4/0	18/5	8/4
Fugu	—	1/0	—	30/50	2/1	4/6	10/21
Spotted green pufferfish	—	—	—	4/14	2/0	2/0	3/9
Western clawed frog	8/4	14/8	752/780	27/16	13/4	—	10/2
Green anole lizard	1/0	—	111/34	—	—	—	—
Chicken	9/4	—	202/218	—	—	—	—
Platypus	31/39	—	234/414	—	—	—	—
Opossum	216/37	5/4	967/263	—	—	—	—
Cow	140/132	2/0	828/1,027	—	—	—	—
Dog	159/55	1/1	651/233	—	—	—	—
Mouse	110/50	3/0	922/306	—	—	—	—
Rat	132/31	2/1	1,073/528	—	—	—	—
Macaque	36/76	0/1	273/220	—	—	—	—
Chimpanzee	64/39	0/1	316/393	—	—	—	—
Human	58/43	0/1	329/371	—	—	—	—

Source: Data from Niimura (2012).

[a] Functional olfactory receptor genes and presumed nonfunctional (truncated genes and pseudogenes) olfactory receptor sequences are listed to the left and right of the slashes, respectively.

of a single intact γ gene in zebrafish). The second category consists of δ, ε, ζ, and η genes, which are found in teleost fishes and amphibians, whereas reptiles, birds, and mammals completely lack them. Interestingly, amphibians retain both categories of genes. This observation suggests that the primary function of α and γ receptors is to detect airborne odorants, while the primary function of δ, ε, ζ, and η receptors is to detect water-soluble odorants. The third category consists of the genes for β olfactory receptors, which are present in both aquatic and terrestrial vertebrates. It has been speculated that β olfactory receptors may detect odorants, such as alcohol, that are both water-soluble and airborne (Niimura 2009), although at present experimental evidence for this hypothesis is lacking.

Water-soluble odorants disperse more slowly than airborne odorants. Nevertheless, smell is an important source of information also for aquatic animals. Fish, for instance, use olfactory information for finding food, avoiding predators, and identifying potential mates and as identifiers of geographical locations. For example, the salmon's remarkable homing ability relies on olfaction and odorant memory. Most fish have four nostrils through which water flows in one direction carrying odorants. This one-way flow allows fish to constantly access new odor information. Fish detect mainly four groups of water-soluble molecules as odorants: amino acids, gonadal steroids, bile acids, and prostaglandins. These are nonvolatile chemicals, and thus humans cannot smell them. As shown in Table 7.4, teleost fishes (zebrafish, medaka, stickleback, fugu, and spotted green pufferfish) generally have much smaller numbers of olfactory receptor genes than mammals, but a much larger representation of gene subfamilies.

In nonamphibian tetrapods, an enormous expansion in the number of α and γ genes occurred. As shown in Figure 7.31, primates tend to have smaller numbers of olfactory receptor genes than other mammals, possibly because primates rely on vision more heavily than on olfaction in sensing the world around them. Indeed, the relative sizes of the olfactory bulb in the brain and olfactory epithelium in the nasal cavity are smaller in primates than in most other mammals. On the basis of their nostril morphology, the order Primates is classified into two suborders, Strepsirrhini and Haplorhini. Strepsirrhines and haplorhines are characterized, respectively, by the presence or absence of the rhinarium, the moist and hairless surface at the tip of the nose, so familiar to us on cats and dogs, that is used to detect the direction of odorants. Haplorhines also have a smaller olfactory epithelium than strepsirrhines. Moreover, most strepsirrhines are nocturnal while most haplorhines are diurnal, and color vision is well developed in haplorhines. Therefore, the reliance on olfaction is decreased in haplorhines compared with that in strepsirrhines. Consistent with these observations, the number of putatively functional olfactory receptor genes is smaller in haplorhines than in strepsirrhines.

Old World monkeys generally have a smaller number of functional olfactory receptor genes than rodents and a higher proportion of pseudogenes. For example, mice have approximately 600 more functional genes than humans and a much lower proportion of pseudogenes (~24% compared with 52% in the human genome). Why do rodents and Old World monkeys differ so conspicuously in the number of functional genes and proportion of pseudogenes? A popular explanation is that Old World monkeys are equipped with trichromatic color vision (see below) and, therefore, olfaction is no longer of vital importance. Thus, it was originally thought that olfactory receptor genes were lost concomitantly with the acquisition of trichromatic vision. The "vision priority hypothesis" (Gilad et al. 2004) states that the evolution of color vision in primates may have decreased primate reliance on olfaction, which resulted in the relaxation of selective constraint and the consequent accumulation of pseudogenes. A phylogenetic analysis by Niimura (2012) indicated that there was no sudden loss of olfactory receptor genes coincident with the emergence of trichromacy. Neither was the accumulation of pseudogenes sudden. Rather, olfactory receptor genes were lost gradually in all primate lineages, not only in those that possess trichromatic vision. In humans, the process of pseudogenization in olfactory receptor genes seems to be ongoing, as many loci seem to be polymorphic and segregate a functional allele and a pseudogene, whereas their corresponding homologous loci in chimpanzees have only functional alleles, thus indicating that the pseudogene is a derived character state in humans (Menashe et al. 2003).

The vision priority hypothesis was based on the assumption that the number of functional olfactory receptor genes is correlated to olfactory versatility. In this view, a decrease in the number of functional olfactory receptor genes would cause a decrease in smell ability. This assumption is most probably flawed. For example, dogs, which are famous for their keen olfactory sense, nevertheless possess an unremarkable number of olfactory receptor genes. While the number of olfactory receptor genes in a species may indeed be positively correlated with the number of odorants among which it can discriminate, the sensitivity to a specific odorant may be determined by levels of expression of particular olfactory receptor genes.

What happens to the olfactory apparatus of terrestrial mammals that become secondarily aquatic? Can the ability to sense water-soluble odorants be reacquired after it has been lost? Can olfactory receptors suitable for smelling airborne odorants evolve into receptors for water-soluble ones? The answers seem to be negative. For example, dolphins and other toothed whales, which secondarily adapted to the marine habitat, have completely lost the olfactory apparatus. A toothed whale has no olfactory bulbs, and its nose (blowhole) is located at the top of its head where its sole function is breathing. Apparently the olfactory system that had been used in the terrestrial ancestors neither works in water nor can evolve into one that does. Indeed, the number of intact olfactory receptor sequences in the dolphin genome is extremely small, and almost all of them are pseudogenes. As it takes time to accumulate disruptive mutations in a

coding region of a gene after the gene is no longer subject to functional constraint, even intact-looking genes in the dolphin genome are likely to be nonfunctional.

What determines the size and the makeup of the olfactory receptor gene repertoire in a species? They are determined by the mutational process of gene birth and death as well as by historical contingency. Whether a new gene is retained and whether a functional gene is allowed to die seem to reflect selective constraints determined by the reliance of the organism on olfaction. At present, we have no strong evidence for positive selection, nor can we rule out positive selection. We cannot tell whether the numbers and types of olfactory receptor genes in vertebrates are affected more by selection or by chance. Similarly, we are clueless about the factors determining the numbers of pseudogenes. A case in point is the extraordinary repertoire of olfactory receptors found in African elephants. Are the olfactory capabilities of African elephants really exceptional? As yet, no systematic studies assessing olfactory capabilities in African elephants have been published. However, anecdotal evidence indicates that African elephants do indeed have an extraordinarily keen sense of smell. For example, Bates et al. (2007) reported that African elephants can distinguish between two ethnic groups—one with a tradition of elephant hunting and another with no history of direct threat to elephants—by using a mixture of olfactory and visual cues. Additionally, African elephants are said to be able to recognize up to 30 individual family members from olfactory cues in mixtures of urine and earth (Bates et al. 2008).

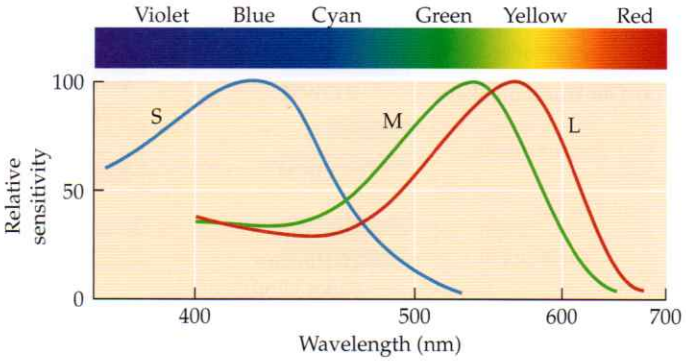

Figure 7.33 Sensitivity spectra for the three photoreceptors in humans. S, short wavelength; M, medium wavelength; L, long wavelength. (Modified from Bowmaker and Dartnall 1980.)

PRIMATE OPSINS Color vision in primates is mediated in the eye by up to three types of photoreceptor cells (cones), which transduce photic energy into electrical potentials. Each type of color-sensitive cone expresses one type of color-sensitive pigment (photopigment). Each photopigment consists of two components: a transmembrane protein called opsin, and either of two lipid derivatives of vitamin A, 11-*cis*-retinal or 11-*cis*-3,4-dehydroretinal. Variation in spectral sensitivity, i.e., color specificity, is determined by the sensitivity maximum of the opsins (**Figure 7.33**). In humans, there are three opsins, S, M, and L, which are maximally sensitive at approximately 430, 530, and 560 nanometers (nm), respectively. S, M, and L opsins are sometimes referred to as "blue," "green," and "red" opsins, respectively, although this nomenclature is somewhat confusing because the sensitivity maxima of the receptors do not coincide with the wavelengths ordinarily recognized as corresponding to these color names.

Each color stimulates one or more kinds of cones. Red light, for example, stimulates L cones much more strongly than M cones, and S cones hardly at all. Blue light, on the other hand, stimulates S cones, but L and M cones more weakly. The brain combines the information from each type of receptor to give rise to different perceptions of different wavelengths of light.

The S opsin is encoded by an autosomal gene, while the L and M opsins are encoded by X-linked genes. In humans, the 364-amino-acid sequences of the L and M opsins are 96% identical, but they share only 43% amino acid identity with the S opsin, which is shorter. The *S* gene and the ancestor of the *L* and *M* genes diverged about 500 million years ago (Yokoyama and Yokoyama 1989). In contrast, the close linkage and high sequence similarity between the *L* and *M* genes, as well as their restricted taxonomic distribution, point to a relatively recent duplication event (~25–35 million years ago). Three amino acid replacements account for the differences in spectral tuning between the red and the green opsins (**Figure 7.34**).

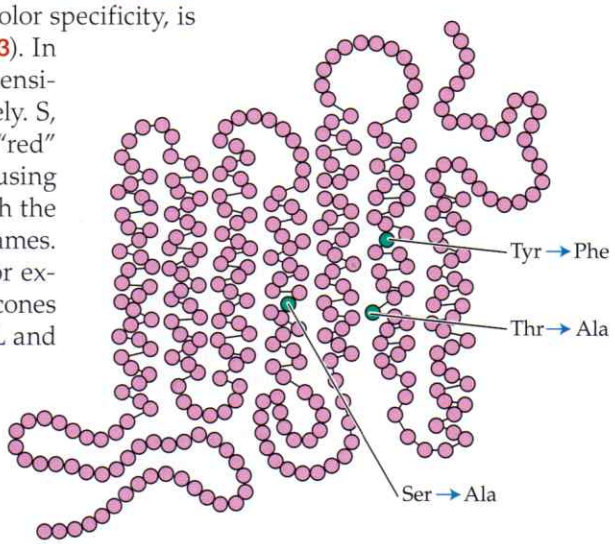

Figure 7.34 Three amino acid replacements in the red opsin protein account for the spectral tuning of the green opsin. At position 180, swapping serine for alanine produces a 6 nm shift of the absorption spectrum; tyrosine to phenylalanine at position 277 provides a 9 nm shift; and changing a threonine to an alanine at position 285 confers another 15 nm shift in maximum absorption. Together, these three changes produce the 30 nm gap between the maximum absorptions of the red and green opsins. (From Grens 2014.)

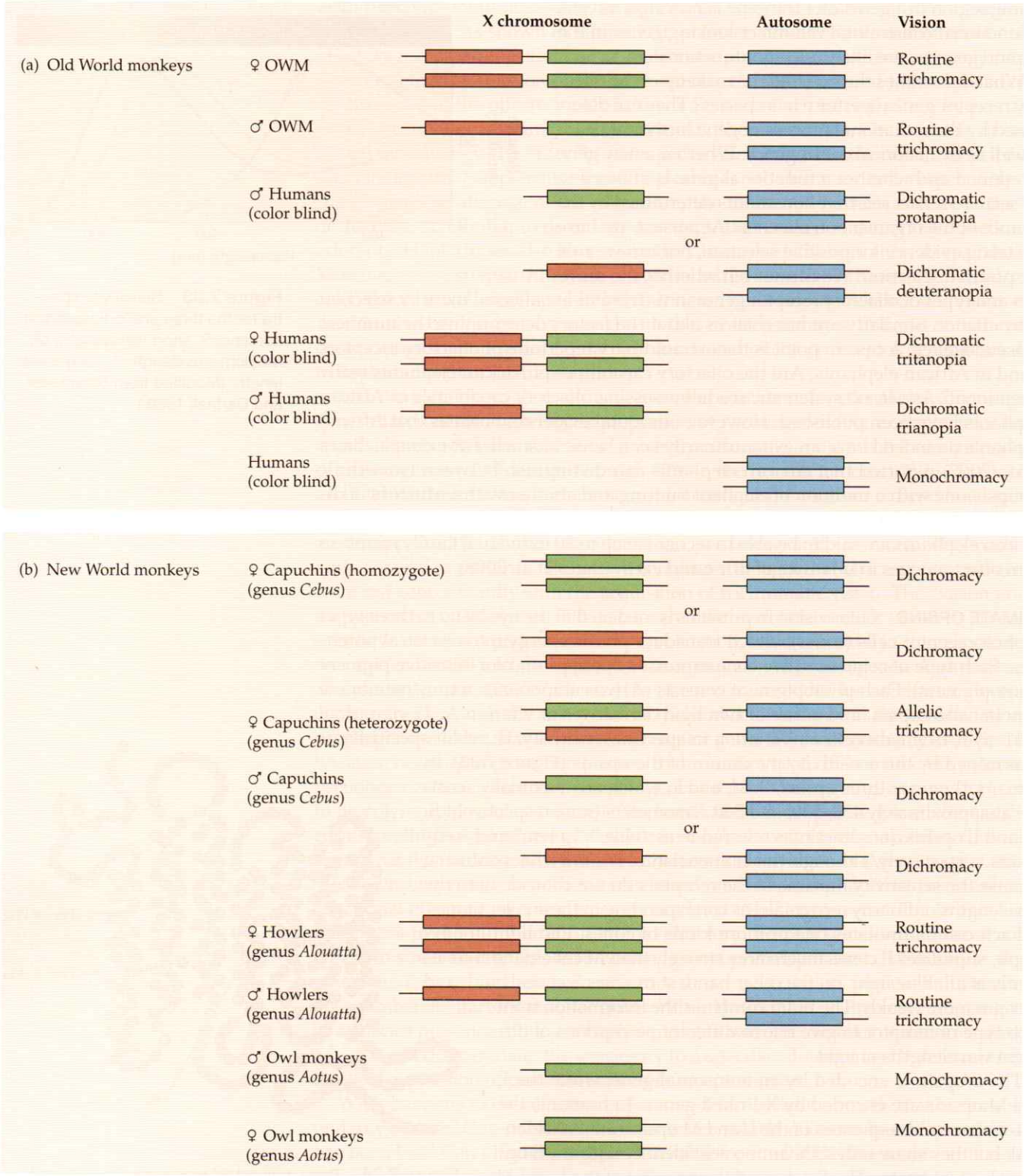

Figure 7.35 Molecular basis of trichromatic, dichromatic, and monochromatic vision in males and females of humans and some Old World monkeys, New World monkeys, and strepsirrhines. Note the distinction between routine and allelic trichromacy. L, M, and S opsins are depicted as red, green, and bue boxes, respectively.

All Old World monkeys (including humans) possess trichromatic vision that is achieved through three distinct opsins encoded by three separate loci. This type of trichromacy is called **routine trichromacy** because all individuals, regardless of sex, can achieve it (Figure 7.35). Genetic defects in any one of the opsin genes can lead to dichromacy (which in humans is referred to as color blindness). There are three types of dichromacy: protanopia due to L photopigment deficiency, deuteranopia due to M photopigment deficiency, and the extremely rare tritanopia due to S photopigment deficiency. Because of X linkage, protanopia and deuteranopia are considerably more common in males than in females. Monochromacy can occur if both L and M photopigments are faulty.

Most prosimians (Strepsirrhini) and New World monkeys (Platyrrhini) carry only one X-linked pigment gene and are therefore dichromatic. The ancestral X-linked opsin is thought to resemble the M opsin, and indeed most prosimians and New World monkeys are protanopic. However, because shifts in the maximal sensitivity of opsins can be achieved quite easily by nonsynonymous substitutions in as few as 3–5 codons, in a few diurnal taxa of prosimians, *L* alleles have been produced. In some lineages (e.g., woolly lemurs), the *L* allele became fixed in the population at the expense of the *M* allele. In consequence, these taxa are deuteranopic. In other cases (e.g., sifakas and capuchins), a polymorphic state consisting of two or more alleles is maintained in the population. As an example, in white-faced capuchin monkeys (*Cebus capucinus*), there exist two alleles at the X-linked opsin locus, the maximal-sensitivity peaks of which are similar to those of human L and M opsins, respectively.

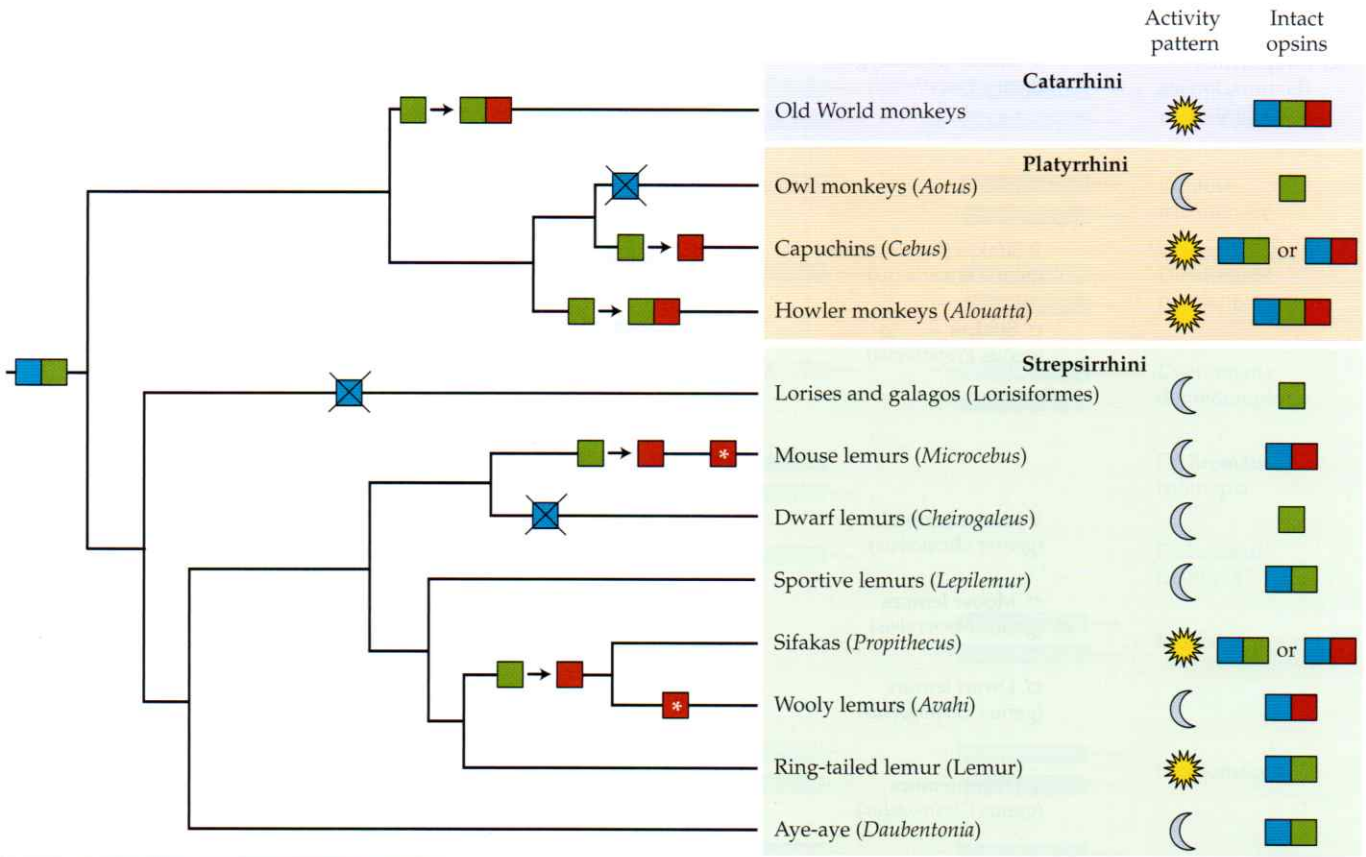

Figure 7.36 The birth-and-death process of primate color vision genes in relation to activity patterns (diurnal or nocturnal). Phylogenetic relationships are based on *SINE* presence/absence as well as on mitochondrial DNA sequences (Roos 2003; Roos et al. 2004). S, M, and L opsins are depicted as blue, green, and red boxes, respectively. Asterisks indicate fixations of the *L* alleles. In *Cebus* and *Propithecus*, an X-linked balanced polymorphism for M and L opsin alleles is maintained, such that heterozygous females may achieve allelic trichromacy. Note the absence of either routine or allelic trichromacy in nocturnal animals. (Data from Perry et al. 2007.)

For this reason, while males and homozygous females are dichromatic, heterozygous females are trichromatic (Figure 7.35). This type of trichromacy is called **allelic trichromacy**.

The long-term maintenance of a high level of polymorphism at the X-linked opsin locus most probably requires some strong form of balancing selection, for example, overdominance or frequency-dependent selection. One possible selective advantage of trichromatic vision is thought to be the ability to detect ripe fruits against a background of dense green foliage.

Interestingly, the evolution of opsin genes in primates can be characterized as a birth-and-death process. As seen in Figure 7.36, trichromacy arose twice through independent gene duplications, once in the lineage leading to Catarrhini, the other in the lineage leading to howler monkeys (genus *Alouatta*). Similarly, independent gene deaths of the S opsin in some nocturnal lineages gave rise to independent instances of monochromacy.

BIRTH-AND-DEATH EVOLUTION WITH STRONG PURIFYING SELECTION IN HISTONE MULTIGENE FAMILIES Histones are small basic nuclear proteins in eukaryotes. They are involved in the packaging of DNA and the regulation of gene expression. There are five major histone classes, which can be classified into two groups according to their functional and structural features: core histones (H2A, H2B, H3, H4) and linker histones (H1). Histone genes are extremely conserved in evolution, although *H1* genes evolve faster, on average, than the genes encoding core histones.

How can we distinguish between concerted evolution and birth-and-death evolution when the genes are under extreme functional constraints? A number of groups studied the evolution of several histone gene families (Piontkivska et al. 2002; Rooney et al. 2002; Eirín-López et al. 2004). They rea-

soned that if concerted evolution is the main driving force in the evolution of histone multigene families, then the number of synonymous substitutions per synonymous site and the number of nonsynonymous substitutions per nonsynonymous site must both be close to zero because gene conversion affects both synonymous and nonsynonymous sites in the same manner. In contrast, if protein similarity is caused by strong purifying selection but every member gene in the family evolves independently, then the number of synonymous substitutions per synonymous site is expected to be greater than the number of nonsynonymous substitutions per nonsynonymous site because synonymous substitutions will be subject to very weak or no purifying selection.

When this approach was applied to histone *H1*, *H3*, and *H4* genes from diverse groups of organisms, the synonymous substitution rate was higher than the nonsynonymous rate in the vast majority of comparisons. These results, therefore, indicate that the members of the histone gene families are mainly subject to strong purifying selection, rather than evolving in unison by gene conversion.

There were some exceptions to these observations. For example, chicken *H1* genes showed similarly low levels of synonymous and nonsynonymous divergence. There are three possible explanations. First, a very recent series of gene duplications produced the duplicates and, hence, there was simply not enough time to accumulate nucleotide substitutions. Second, there is a high degree of codon bias in the genes, which means that synonymous similarity is maintained either by selection at synonymous sites or by biased mutation patterns resulting in high GC contents at synonymous positions. Finally, the results could be explained by gene conversion.

The death of gene families

If a single gene is left in a family, its loss will result in the extinction of that gene family. The death of gene families is simply the continuation of the loss of genes and does not involve any special evolutionary processes. Naively, we might expect that the complete loss of a biochemical function via loss of the last member of a gene family would be deleterious, and consequently rare. Therefore, the loss of gene families might serve as an indicator of shifts in the physiological constraints of an organism. Genome-wide analyses in animals suggest that gene families producing metabolic enzymes frequently undergo independent extinction in multiple lineages (Hughes and Friedman 2004). This may indicate that shifts in nutrient availability or acquisition are most often responsible for conditions that permit gene family extinction.

Mixed Concerted Evolution and Birth-and-Death Evolution

It should be noted that concerted evolution and birth-and-death evolution are not mutually exclusive processes. Indeed, in a gene family some members may undergo concerted evolution, while others may undergo birth-and-death evolution. One such example is the β-globin family (Figure 7.15), which consists of five functional genes (ε, $^{G}\gamma$, $^{A}\gamma$, δ and β) and one pseudogene (ψβ). Within this family, divergent evolution has created four functionally distinct subfamilies (ε, γ, δ, and β), the genes $^{G}\gamma$ and $^{A}\gamma$ have experienced concerted evolution by gene conversion, and one duplicate has died (ψβ). Another example is the α-globin family, which consists of five functional genes (α_1, α_2, μ, θ, and ζ) and two pseudogenes (ψα and ψζ). The α_1 and α_2 genes are virtually identical within each of the genomes of the great apes studied to date, likely because of gene conversion. However, the other genes differentiated considerably, and two underwent nonfunctionalization.

In general, in a small gene family, there is usually a strong constraint on family size (gene number), so the number of genes in the family cannot fluctuate much. As a consequence, unequal crossover does not play a major role in the evolution of such a gene family, and if there is evidence of concerted evolution, it is likely due to gene conversion. In contrast, in a large gene family, some fluctuations in family size may occur because of unequal crossing over or nonfunctionalization.

Polysomy

Euploidy refers to a chromosome number that is an exact multiple of the haploid chromosome number. Thus, haploids, diploids, triploids, tetraploids, pentaploids, and any other multiple of the haploid state are euploids. **Aneuploidy** refers to the condition in which the number of chromosomes in a cell is not an integer multiple of the typical haploid set for the species. The duplication of a complete chromosome is called **polysomy**; the duplication of a segment of a chromosome is called **partial polysomy**.

Polysomy is almost invariably deleterious or lethal in animals. In mammals, for instance, it is frequently associated with lethality or infertility. In humans, only three trisomies are not lethal at birth—Down syndrome (trisomy 21), Patau syndrome (trisomy 13), and Edwards syndrome (trisomy 18)—but the evolutionary fitness of individuals with these conditions is zero. Autosomal monosomy, i.e., the presence of a single autosome, is invariably lethal. Sex chromosomes, on the other hand, can routinely withstand monosomy. In fact, the presence of a lone X chromosome without a counterpart (X or Y), such as is the karyotype in Turner syndrome, is a nonlethal condition in humans. Severe deleterious manifestations are often associated with partial polysomy, such as partial trisomy and partial tetrasomy (e.g., cat eye syndrome, which involves a small segment of chromosome 22). Therefore, chromosomal duplication or deletion—either complete or partial—is not expected to contribute significantly to animal evolution.

Even in plants, in which polyploidy is common and polysomic individuals are produced with great regularity, permanent polysomy is hardly ever tolerated. One of the earliest studies on plant trisomy, and thus far the most thorough, was carried out by Blakeslee and colleagues (e.g., Blakeslee and Avery 1919; Blakeslee et al. 1920). Jimsonweed (*Datura stramonium*) has 12 pairs of chromosomes, and all 12 trisomics have been identified in nature. Each one was distinguishable by specific morphological features, and they all were "of feeble growth."

Polyploidization

Polyploidy entails the addition of one or more complete sets of chromosomes to the original set. An organism whose cells contain two copies of each autosome is a diploid, an organism with four copies is a tetraploid, one with six copies is a hexaploid, and so on. The gametes of diploid organisms are haploid, those of tertraploids are diploid, those of hexaploids are triploid, and so on. Organisms with an odd number of autosomes, such as the triploid domestic banana plant (*Musa acuminata*), can neither undergo meiosis nor reproduce sexually. Since its discovery in the early 1900s, polyploidy has been recognized and an important evolutionary phenomenon, particularly in vascular plants (de Vries 1904; Lutz 1907). Paralogs created en masse after polyploidization are sometimes referred to as either **ohnologs**, an eponym coined in honor of Susumu Ohno by Leveugle et al. (2003), or **homeologs**, a homophone that is sometimes difficult to distinguish aurally from "homologs."

There are two main types of polyploidy. **Autopolyploidy**, or **genome doubling**, entails the multiplication of one basic set of chromosomes. **Allopolyploidy** is the condition arising from the combination of genetically distinct, but similar, chromosome sets. Thus, autopolyploids are derived from within a single species, whereas allopolyploids arise via hybridization between two species.

Hybridization may not always result in polyploidy. **Homoploidy** is a process of hybridization between two species that results in the creation of a distinct new species without a change in ploidy level (Gross 2012). In homoploids, one chromosome in each homeologous pair is derived from one parental species while the other chromosome is from the other parental species. Thus, the result of homoploid hybridization between two diploid species is a diploid. *Senecio squalidus* is a homoploid species that has been studied extensively (e.g., Brennan et al. 2012). The species originated roughly 300 years ago, and both parental species (*S. aethnensis* and *S. chrysanthemifolius*) as

well as hybrids are still present in their native habitat on the slopes of Mount Etna, Sicily (James and Abbott 2005). *Senecio squalidus* was introduced by humans to the British Isles and is currently classified as an invasive species.

AUTOPOLYPLOIDY Autopolyploidy may be common in plants, although its prevalence may be quite underestimated in the taxonomic literature (Soltis et al. 2007). One species that is doubtlessly a true autopolyploid, rather than an allopolyploid derived from two very similar diploids, is the potato, *Solanum tuberosum* (Potato Genome Sequencing Consortium 2011).

The main selective advantage of autopolyploidy in nature may be the fact that populations of autopolyploids can maintain much higher levels of heterozygosity than their diploid progenitors can, because of their polysomic inheritance; that is, the number of allelic combinations at each locus is larger than the three possible combinations in diploids (Muller 1914; Haldane 1930; Moody et al. 1993). Let us consider, for example, an autotetraploid (*aabb*) derived from a heterozygous diploid (*ab*). Assuming simple tetrasomic inheritance, the genotype *aabb* is expected to produce diploid gametes in the ratio 1*aa*:4*ab*:1*bb*. In the progeny, the ratio of the genotypes will be 1*aaaa*:8*aaab*:18*aabb*:8*abbb*:1*bbbb*. That is, heterozygotes (*aaab, aabb, abbb*) are expected to outnumber homozygotes (*aaaa, bbbb*) 17 to 1. In comparison, in diploids the heterozygote-to-homozygote ratio is 1:1. Moreover, autopolyploids can maintain more than two alleles per locus, allowing them to produce a larger variety of allozymes than diploids, which, in principle, may allow them to achieve higher fitness values (Parisod et al. 2010). Finally, by reason of their polysomal inheritance, autopolyploid populations have larger effective population sizes than diploids, suggesting that selective processes are much more effective relative to random genetic drift (Ronfort 1998).

Autotetraploidy is a common mutational occurrence in nature. Indeed, somatic autotetraploidy is found in almost all organisms, including algae, plants, mollusks, insects, and vertebrates (Nagl 1990). However, during evolutionary history autotetraploids seem to have survived only rarely. The reason is that, in many cases, autotetraploidy may be deleterious and will be strongly selected against. Deleterious effects include (1) prolongation of cell division time, (2) increase in the volume of the nucleus, (3) increase in the number of chromosome disjunctions during meiosis, (4) genetic imbalances, and (5) interference with sexual differentiation when the sex of the organisms is determined either by the ratio between the number of sex chromosomes and the number of autosomes (as in *Drosophila*) or by the degree of ploidy (as in Hymenoptera).

ALLOPOLYPLOIDY Allopolyploidy is much more common in nature than autopolyploidy. It is extremely common in plants; about 80% of all land plants may be allopolyploids (**Figure 7.37**). In animals, allopolyploidy is not nearly as prevalent; however, it is by no means nonexistent. Allopolyploidy has been found in both parthenogenetic and sexually reproducing species of insects, fish, reptiles, and amphibians. For example, *Xenopus laevis*, the African clawed frog of laboratory fame, is an allotetraploid. No cases of polyploidy have ever been found in birds. And, although two mammalian species—the red vizcacha rat (*Tympanoctomys barrerae*) and the golden vizcacha rat (*Pipanacoctomys aureus*)—were suspected to be tetraploids, much disagreement exists in the literature about their ploidy status (Gallardo et al. 1999, 2004; Svartman et al. 2005; Suárez-Villota et al. 2012).

In the last 15,000 years, the domestication of plants, but not of animals, frequently involved allopolyploid species. The most famous example is, of course, bread wheat (*Triticum aestivum*), which is an allohexaploid containing three distinct sets of chromosomes derived from three different diploid species through tetraploid intermediaries (**Figure 7.38**).

Many microbes too were domesticated, and in the case of the lager-brewing yeast, *Saccharomyces pastorianus*, the domestication involved an allopolyploid species. There are two broad categories of beer: ale, which is produced by the top-fermenting yeast