CHAPTER 16

# THE GENETIC CODE

## THE BILINGUAL DICTIONARY IS tRNA

The final trick consists of being able to translate the code. After all, it does not help much if, in a war, you have intercepted an enemy's message and you recognize that it is encrypted (in a coded language) if you cannot read it. The bulk of our functioning body is protein. How do we get from the DNA code to the protein? By the 1960's, this was a critical question. Beyond Crick's hypothesis of a triplet code and experiment (see page 205) various scientists attempted to find evidence that the hypothesis was correct. For instance, it became possible to get the amino acid sequence of readily available and easily purified proteins such as hemoglobin. Normal and sickle-cell hemoglobin were analyzed, and it became apparent that the two differed by only one amino acid. The changed amino acid in sickle-cell hemoglobin is much less soluble in water than the normal amino acid, making the hemoglobin less soluble as well and causing the sickle-cell hemoglobin to precipitate in the red blood cell under certain circumstances. The red blood cell is then deformed and catches in the smallest blood vessels, causing clogs and clots that can cause considerable pain and damage.

This is not an analysis of sickle-cell disease (but see Chapter 32, page 425) but for geneticists there were two very important lessons to be learned: first, that a mutation could be as small as one amino acid, which might theoretically result from a single base change. (The single base change was subsequently confirmed, see page 247 and page 231). Second, a severe change in characteristics (phenotypic change) could be produced by the change of a single amino acid.

To understand how the DNA was decoded, we need to know a little bit about how proteins are made, and we can explain this by the use of a few analogies. The problem is that the DNA is in the nucleus of a cell, separated from where the proteins are made, in the cytoplasm. So the first question is how we connect the two. The analogy is as follows: Everyone has seen the stockboys or stockgirls in supermarkets. They are the ones who bring materials from the storerooms to the shelves for the consumers. This is not quite the image that we need. A better image is from factories, or at least from factories in which manufacturing is not fully automated. For instance, let's describe how a fender of a car might be made. It starts as a flat sheet of metal that is placed into a large machine called a press. The press does exactly that: A large and very heavy upper part moves downward and presses

the sheet against a mold or template, bending the sheet into the form of a fender. The *press* is non-specific; it is simply a machine that exerts enormous pressure on a sheet of metal. It could bend the metal into any shape desired, depending on the shape of the *template* (Fig. 16.1). Such a machine of course is very heavy and is not movable. To make the fenders, *stockboys* bring to the machine and its operator a continuous supply of fresh metal sheets and take the finished fenders to the next station, where, for instance, holes might be cut for lights. This image now includes all the components that we need: The *press*, which is a complex collection of molecules in the cytoplasm called a *ribosome*; the *stockboys*, which are small molecules called *transfer RNAs*, which serve to bring fresh amino acids (unbent steel) to the ribosome (press) so that they may be linked together to form proteins; and the *template* for the press, which is a molecule called *messenger RNA*. The messenger RNA is what carries the information from the DNA in the nucleus to the ribosome. To picture what is happening, we need two other terms: *transcription* and *translation*. To transcribe something is to copy it as you hear it, without necessarily understanding. For instance, suppose that you are in France and want directions to the train station. You ask a native, making gestures and sounds to imitate a train, and the native tells you, "Vous allez au coin, tournez à droite, et la gare est à deux cent mètres sur votre gauche." You dutifully *transcribe* what you hear: "Vou zalley zo kwan, tourney za drwat, eh la gar eh tah duh sont

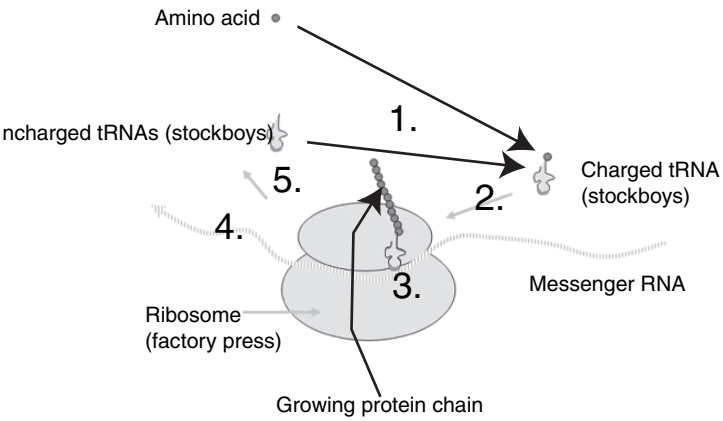


*Figure 16.1.* Protein synthesis. 1. An amino acid is attached to a specific tRNA , which has a specific anticodon and accepts only one type of amino acid. It acts as the stockboy. 2. The charged or loaded tRNA moves to the ribosome (equivalent to the press) which has bound mRNA (equivalent to the template). 3. The tRNA binds to the mRNA codon that matches its anticodon. Thus it is in a position to move its amino acid onto the end of a growing protein chain. Its act of transfering its amino acid ratchets or nudges the mRNA along the ribosome so that the next codon will be in position to donate an amino acid. 4. Once the tRNA has released its amino acid, it detaches from the ribosome and returns to pick up a new amino acid. Ultimately, the mRNA, chugging along the ribosome, will present a codon for which there is no code and no tRNA is attached (a "stop codon"). The additions will cease and the finished protein will be released

metruhs seur vohtra gosh." This is not very helpful to you, but you take it to an English-speaking friend who knows French well, and she looks at it and *translates*, "You go to the corner, turn right, and the station is six hundred feet on your left." Your step was transcription: not changing the language, but putting the French into written form. Her step was translating, converting the meaning from one language to another. Similarly, messenger RNA is made from DNA in a base-pairing manner very similar to that in which a second strand of DNA is made. This is transcription. We are still in the language of nucleic acids. RNA differs slightly from DNA; its sugar is ribose, not deoxyribose (ribonucleic acid, not deoxyribonucleic acid) and instead of the T (thymidine) in DNA, it has U (uridine) (Fig. 16.2). Messenger RNA, or mRNA, is copied from the DNA strand, carrying the code, and is transported from the nucleus to the cytoplasm, where it serves as the template or mold on the ribosome press. The translation is handled by the marvelous stockboys, or transfer RNAs (tRNAs). There are approximately twenty tRNAs, one for each amino acid. They are marvelous because one end of each tRNA has a triplet codon that will match a three-base sequence on the mRNA (and therefore resembles the original DNA), while the other end is specific for a single amino acid. The transfer RNA is therefore the bilingual dictionary. On one end of the molecule it has the French word (vous, mRNA) and on the other the English word (you, protein). The tRNA translates from nucleic-ese to protein-ese (Fig. 16.2).

We are telling this story in a linear sequence, but of course the role of the tRNA could not be understood until coding was better known. Many scientists were trying to identify the code, using many different tricks. One of the most original was a mathematical biologist name Martinas Ycas, who reasoned as follows: To get the code, one would have to have a protein with a highly unusual composition, so that one could determine from the unusual composition of the RNA what the code was. Certain moths produce a silk for their cocoon that is made almost exclusively of only two amino acids, glycine and alanine. Ycas presumed that the base ratio of the RNA would be highly distorted. He flew to Africa, collected the caterpillars, and extracted the RNA from their silk glands. However, the base ratio was not distorted, leading Ycas to suggest that the coding RNA must be a very small portion of the total. He was correct: the bulk of the RNA is the press, rRNA, and mRNA makes up only about 1% of the total. Meanwhile, laboratories in France, England, and the US were producing biochemical evidence for the existence of mRNA. However, the code was still not known.

The first breakthrough was almost accidental, in the sense that, as Pasteur said, "In the field of experimentation, fortune favors the prepared mind". Marshall Nirenberg and H. Matthaei was studying how an enzyme called ribonuclease digested RNA. To have a clean and easily measurable material to work with, he made a synthetic RNA consisting of only one base, U (the equivalent of T in DNA). Poly-U, a chain of riboses containing nothing but U, could not be confused with DNA, which would have to have T. To determine what happened to his synthetic RNA, he decided to test if it had any biological function, since it was known that adding RNA to a mixture of several other components would allow the mixture to synthesize protein.

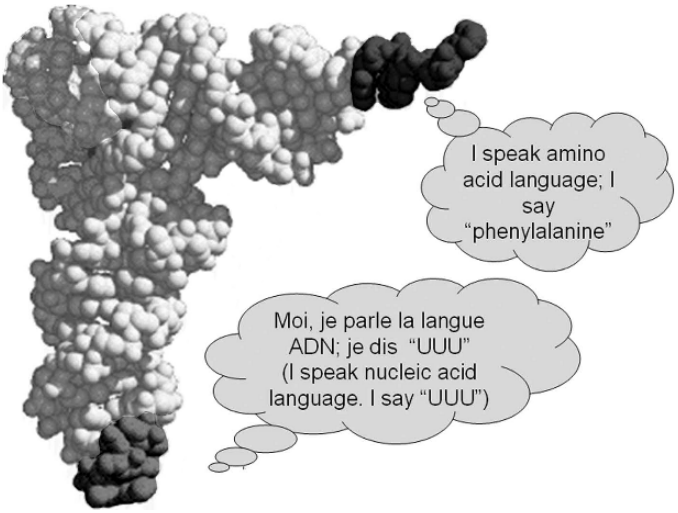


*Figure 16.2.* Transfer RNA is the translator. At one end it speaks amino-acid-ese, and identifies a specific amino acid. At the other end, too far away to strongly influence the other end, it speaks nucleic-ese, and carries a specific anticodon. Thus the lower end binds to mRNA at a specific location, and the upper end offers a specific amino acid to be incorporated into the protein, in the same sense that a good bilingual dictionary will give the English equivalent of a foreign word. Here the anticodon AAA on the tRNA binds to the UUU on the message, while the other end of the tRNA binds phenylalanine. Credits: Wikipedia: This image has been (or is hereby) released into the public domain by its author, Vossman. This applies worldwide

Therefore they added their undigested poly-U and their digested poly-U to this protein-synthesizing mixture to see how well they would work. They found, to their disappointment, that something precipitated or settled out from the mixture. Precipitation in an experiment like this generally means that something has gone wrong (see comments on stability of macromolecules in Chapter 17). However, Nirenberg and H. Matthaei decided to find out what had happened by analyzing the precipitate. What they found was a considerable surprise. The precipitate was a single compound, an artificial protein consisting of nothing but the amino acid phenylalanine. (Phenylalanine is a very poorly soluble amino acid, and therefore the chain was insoluble.) Nirenberg and H. Matthaei realized that they had conversed with molecules: They had spoken to the protein synthesizing machinery, saying "UUU, UUU, UUU, UUU…", and the machinery had responded, saying, "Oh, I see, phenylalanine-phenylalanine, phenylalanine, phenylalanine…" This was the first codon identified.

To say that there was a race to get other codons is putting it mildly. Nirenberg and H. Matthaei had made the announcement at a meeting of biochemists in Moscow. He stopped in Europe to repeat the talk two or three times, and a month or so later gave the talk at Harvard, in Cambridge, Massachusetts. At the talk, a gentleman not known to the audience stood up, literally with a laboratory notebook in hand,

and read from the notebook, saying that they had identified several other codons by synthesizing other simple nucleic acids. He had flown from New York to Boston to confront Nirenberg and H. Matthaei with the announcement. We learned later that Severo Ochoa, a biochemist from New York, had been at the Moscow meeting and had telephoned his laboratory—not an easy or inexpensive task in those days!—to report how Nirenberg and H. Matthaei had done it, and they had immediately begun the experiments to determine other codons. We now know that, of the 64 possible codons, some are punctuation. A triplet code for which there is no tRNA is called a "stop codon" meaning that the amino acid chain ends where this codon appears. Some of the other codons are "degenerate," meaning that more than one codon can be used for the same amino acid. Thus it took a little time to identify them all correctly. Once the codons were known, other scientists returned to the sickle-cell mutation and a few other similar mutations. Sure enough, there was a one-base change in the sickle-cell DNA, and it was exactly the change to produce the abnormal amino acid of the mutation. This served as an independent verification of the hypothesis of the genetic code. We can now produce synthetic DNAs to change specific amino acids at will, in a process called "site-directed mutagenesis".

The mechanism of coding should now be clear. Because of how we handle it, we tend to call the mRNA sequence the code. Therefore, the DNA anticode sequence AAA produces the code sequence in mRNA, UUU. The tRNA anticodon AAA binds to the template UUU, and the amino acid carried by what we will now call phe-tRNA, phenylalanine, is contributed to the growing protein chain (Fig. 16.1).

There is a final very important point to be learned from the coding hypothesis. Protein-synthesizing kits are now sold to research scientists. They consist of ribosomes, tRNAs, and other necessary ingredients; one needs only to contribute the mRNA to produce the protein encoded by the mRNA. mRNAs from many animals, plants, bacteria, and viruses have been tested. With very few and relatively minor exceptions, the code is universal. In other words, if UUU = phenylalanine in humans, then it also = phenylalanine in frogs, sequoia trees, bees, mosses, bacteria, and viruses. Physically, this does not have to be so. The tRNA molecule is big enough that what it has on one end, where it binds the amino acid, does not impose any requirement on the other end, where it carries the three-base sequence called the anticodon. You can perhaps picture this more effectively if you imagine a set of keys, each of which has been tagged to indicate to which lock it corresponds. There is no reason why the tags on the keys cannot be switched around. Thus the tag AAA on the tRNA corresponds to the amino acid key phenylalanine, but an impish biologist could switch the tag so that you try to insert the key in the wrong lock. In fact, artificial tRNAs have been constructed, in which the anticodon has been altered (Fig. 16.3). For instance, if the AAA of the phe-tRNA is altered to GAA, the anticodon will recognize the codon CUU, which represents the amino acid leucine. Sure enough, the synthetic tRNA with the anticodon GAA dutifully inserts a phenylalanine into a protein where a leucine belongs. It would obviously be very dangerous to have a mutation in a tRNA, and it is not surprising that the coding has been conserved throughout evolution. But the take-home lesson is more

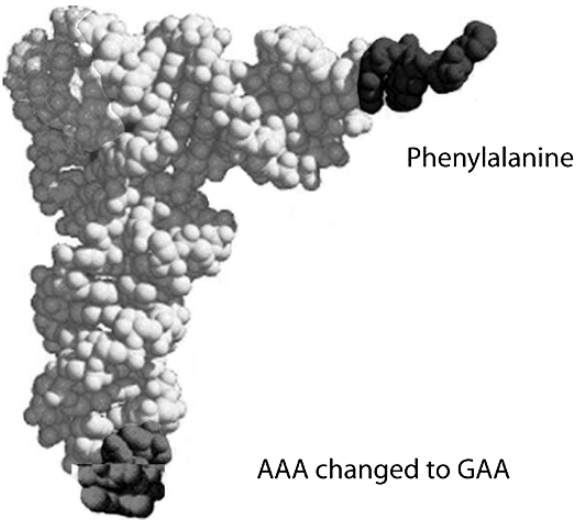


*Figure 16.3.* Proof of the hypothesis. The first proof was that the DNA sequence that produced the change in a single amino acid that was responsible for sickle-cell anemia was analyzed, and it proved to be a change in a single base in DNA. The change was exactly what was predicted to produce the change of the amino acid. A more elaborate proof consisted in altering a tRNA such that, while it still bound the amino acid phenylalanine, its anticodon was altered so that it bound to inappropriate locations on mRNA. The protein made by this construct incorporated phenylalanine in these incorrect locations. The experiment was done in a test tube. As you might expect (see study questions) such a situation would be catastrophic for a living animal or plant. Credits: Wikipedia: This image has been (or is hereby) released into the public domain by its author, Vossman. This applies worldwide

profound. Basically, the fact that the code is universal would be the equivalent of Europeans arriving in the New World, stepping off the boat, and realizing that the Arawak and Carib Indians addressed them in perfect Spanish! In other words, the genetic language is universal, even though there is no physical reason why it should be. This is the strongest argument we have that all life currently on earth came from one original living type. This is not to say that others did not start and fail—we have no evidence that this did not occur—but that today's living creatures have a common source. So what does this story have to do with evolution? It is of profound interest for the one very simple and straightforward reason mentioned above: The genetic code is universal, but it does not have to be. We could imagine mechanisms to synthesize proteins other than the rather complex DNA → mRNA → export from nucleus → ribosome + tRNA → protein system described, but we do not find other mechanisms. Even where there are differences, for instance in the structure of ribosomes of bacteria compared to the structure of ribosomes of eukaryotes, the similarities are far more striking than the differences. Furthermore, the code is universal: if the code TAC means the amino acid methionine in a bacterium, it means methionine for a sequoia tree, a moss, a fish, a bee, and a mouse. We know that this code is carried by the bilingual dictionary, tRNA, and

that the structure of tRNA does not force the association between the base triplet AUG (on the mRNA) and the specific binding of methionine. Therefore, as far as we yet know, there is no physical reason to assume that TAC could not be leucine, or phenylalanine. In fact, we can make artificial hybrid tRNAs, and they can work perfectly well in a test tube, incorporating the (wrong) amino acid they carry at the location specified by the anticodon on the other end. Therefore, the argument is as follows: If there many possible codes, but we find only one, then all life on this earth derives from one source. This does not claim that there was only one origin to life—only that, if there were other attempts at starting life, only one survived to present. One may attribute that origin to any source: God, natural causes, arrival from another planet, etc., but mechanically the descent is the same. We can also conclude that all this life is related, in the same sense that one might reasonably conclude that a freckle-faced, red-haired Caucasian child in a central African village is the child of the freckle-faced, red-haired European couple working in the village rather than the child of the other residents. All life is related because it all looks alike. It is very difficult to understand why this should be so if each form of life was a special, individual creation. Thus we can conclude that the universality of the genetic code offers extremely strong support for the theory of evolution.

## CONSERVED GENES AND HOMEOTIC GENES

Equally startling, though perhaps of a different order of urgency, is the frequency of conserved genes. As is described immediately below, these are found in quite unexpected circumstances, and they provide remarkable documentation of evolutionary connectedness. The basic argument is as follows: a gene (a DNA sequence that codes for a particular protein) evolves in a lower animal or plant. The function of this protein is very important to the survival and reproduction of the organism. In the course of time, random events cause mutations, or changes in base sequence that translate to changes in the amino acid sequence of the protein. However, because the protein is very important and because the function of the protein depends heavily on the presence of particular amino acids in defined sequence, almost all mutations prove to be very deleterious or even lethal, and the bearers of these mutations do not survive. Thus the only individuals that produce young for the next generation are those that maintain the gene intact or nearly intact. The gene survives the evolution of new species over a very wide and long period.

The survival of the gene indicates not only the importance of the gene. Where conserved genes are found, one can trace the lineage among organisms, and detect relationship where it is otherwise not obvious. In this manner one can identify an evolutionary history that connects insects and humans and some of the lowliest threadworms or roundworms and humans. These relationships were quite unexpected and are best explained by illustration. We will use three examples, all of which illustrate important principles of evolution. The examples include a group of enzymes known as caspases; genes controlling the development of eyes; and a group of genes known as homeotic genes.

*Caspases*: There are many ways to make an enzyme that can digest other proteins. We can digest proteins in our stomachs and intestines; inside of cells one can degrade damaged or improperly formed proteins; and in other cases some proteins are intentionally made to be quickly used, rapidly degraded, and built anew. The decomposition of a dead animal ultimately is a process of digestion of the proteins by bacteria and molds. There are well over 100 different types of protein-digesting enzymes (proteases), and there is no particular reason to assume that others could not be designed. Thus it came as a considerable surprise when Junying Yuan and H. Robert Horvitz, looking for a mechanism by which cells in a roundworm commit suicide, identified a gene that produced a protein-digesting enzyme. It was gratifying but not particularly surprising to find the protease—this would be an effective way of destroying the cell—but what was really amazing was that they identified its function because it was very similar to an enzyme found in humans! Further research quickly revealed that not only were the enzymes similar, they had similar, previously unknown functions in controlling the death of cells in humans and other mammals. (This group of enzymes is now called caspases, a technical name that describes to the initiated their function and structure. Cell death is a very important aspect of normal development and physiology, and many diseases including congenital (present at birth) abnormalities, cancer, AIDS, Alzheimer's Disease, Lupus, rheumatoid arthritis, and others at least in part result from derangements in patterns of cell death. There are now over 200,000 papers in the field, and Horvitz was awarded a Nobel Prize in large part because of these discoveries.) Think of it: at least 300 million years separate the lowly threadworm (the miniscule wriggly strings that you sometimes see in stagnant standing water) from us, and yet we use the same enzymes, and the same mechanisms of controlling cell death, to assure the appropriate placement and survival of our cells. Since one could imagine an infinite number of other means to assure proper development, the only possible conclusion is that the first evolutionary appearance of the caspase-based means of regulating cell survival proved wildly successful, and all organisms that derived from that first creature that used it have depended on maintaining it intact.

Perhaps a less abstruse example is that of *eye development*. Insects and vertebrates have gone their separate evolutionary ways almost as long as threadworms and vertebrates have and, although many insects can see very well, their eyes are extremely different from ours (Fig. 16.4). Our eyes are designed like a camera (or rather, a camera is designed like our eyes): a lens focuses light on a retina (film or light sensor); the lens adjusts to change focus; and the orientation of the eye changes to take in different views. It is a very complex instrument, and its complexity has been occasionally used as an argument against evolution. In fact, there is ample documentation for the evolution of the eye from a simple light-sensitive tissue into its present form (Fig. 16.5). An insect's eye is very different. It is more like a bundle of fiber-optic cables, each fiber capturing and carrying a fragment of the entire image. The LED (light-emitting diode) traffic lights and advertising signs that are now appearing in many cities give a sense of the image captured by insects:

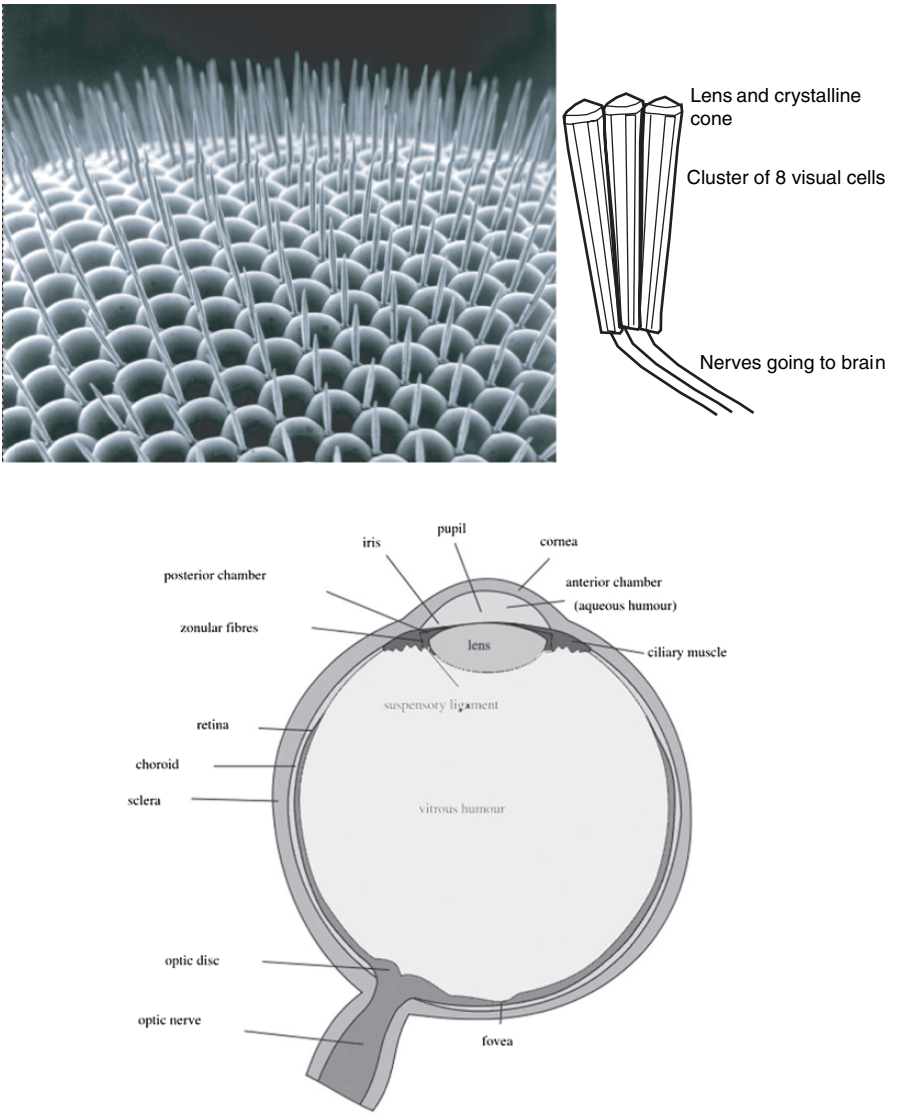


*Figure 16.4.* Insect eyes and vertebrate eyes. Upper: an insect compound eye. Each unmovable lens provides a fragment of the total image to a cluster of visual cells. No focus is possible, but near images are resolved fairly well. In contrast, in the vertebrate (here mammalian) eye, the lens takes in the entire image, and focus is adjusted by muscles that change the shape of the lens. Also, the shape of vertebrate eyes is maintained by fluid- and gel-filled chambers, which is not the case for invertebrate eyes. Credits: http://remf.dartmouth.edu/images/insectPart3SEM/source/26.html; (Wikipedia)

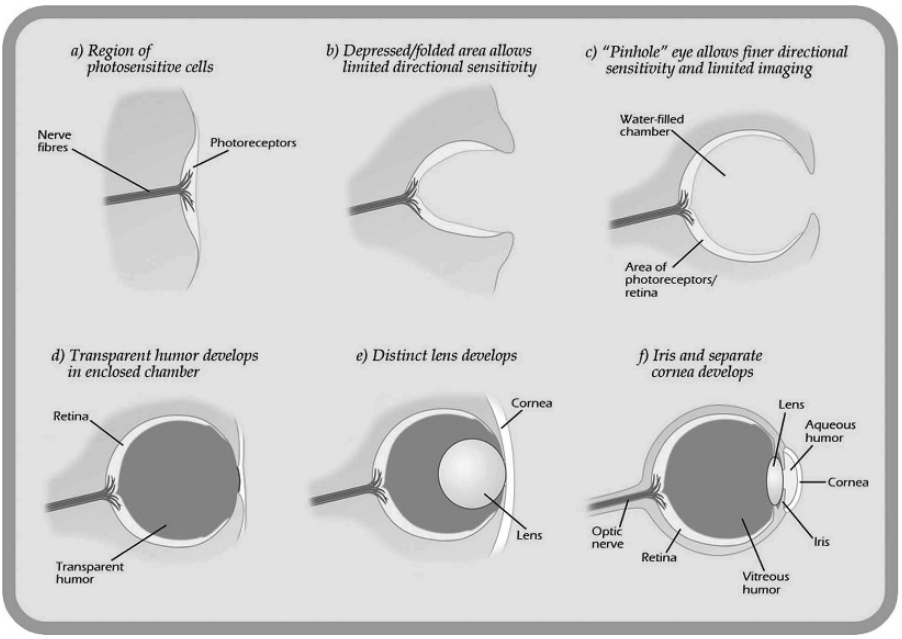


*Figure 16.5.* Evolution of the vertebrate eye. There are living creatures that have eyes similar to each of these stages. Credits: Created by Matticus78 (Wikipedia)

a series of dots that, when maintained in pattern, create an overall picture. Each "dot" is a group of seven or eight cells, with a lens, that captures a fragment of the image. The lenses do not focus, and the eyes do not rotate. Insects get their breadth of vision by having bulbous eyes, so that each mini-lens covers a different territory (Fig. 16.4). There was, originally, no reason to assume that the evolution of an insect's eye was not completely independent of the evolution of a mammal's eye. That is, there was no reason for this assumption until genetics got better and it was possible to sequence genes.

There exists, in laboratory fruit flies, a mutation called "eyeless". As one might presume, the bearers of this mutation have very poorly developed or absent eyes. In the laboratory setting, where food is readily available, the flies can get along using their other senses, but they are blind. Conversely, it is possible to make the good form of the gene turn on in other parts of the fly's body; in this case extra eyes pop up in the weirdest places. They are non-functional, since they do not connect properly to the brain, but they are otherwise structurally normal eyes. This mutation was known for quite a while. In the sometimes annoying structure of the nomenclature of genetics, the name of the gene is the effect that appears when it is not functional. Thus the eye is missing when the gene is mutated, and the normal form of the gene "eyeless" is responsible for making the eye.

During the 1980's and 1990's, it became possible to sequence genes, to read their base sequences. As the databases became larger, governmental agencies in the US, England, Switzerland, and Japan pooled the information so that researchers could compare sequences and look for common themes, in the quest to understand how genes worked. One, again startling, discovery was the realization that the fruit fly eyeless gene was structurally very similar to a human gene called aniridia. Again following the naming convention, there is a rare mutation in humans in which the eyes are exceptionally small and often non-functional. In one version of the mutation, the most noticeable feature is absence or near-absence of the iris, leading to the name aniridia (absence of iris). The normal form of the gene is necessary for the proper development of the eye. It was certainly provocative to realize that genes controlling the development of the eye in a fruit fly and in humans were similar in sequence.

Since the sequences of both genes were known, it was possible to isolate the normal form of the human aniridia gene and insert it (see Chapter 14, page 191) into fruit flies that had mutated eyeless genes and were therefore blind. This experiment was done, with the result that the human gene was able, at least in part, to restore the development of the fruit fly eye! Thus eye development in insects and humans, even though the eyes are very different, was so genetically similar that the genes were nearly functionally interchangeable! Again, there appears to be no rational explanation except for the argument that, before insects and vertebrates existed, an ancestor common to both evolutionary lines had established a genetic mechanism for building a light-sensing organ. This capability was so important—it is obvious to imagine the value of being able to detect light and darkness—that all ancestors preserved this genetic mechanism, even as they evolved into insects, lobsters, octopuses, fish, birds, and mammals. It is a further and extremely strong argument for our common evolutionary heritage.

A final and likewise important example of common lineage is the remarkable story of the *homeotic genes.* This group of genes is important at many other levels as well, since their appearance may have been one of the bases for the Cambrian explosion (Chapter 20, page 281). The homeotic genes are responsible for establishing the basic layout of the body: why our arms and legs are located at the appropriate positions; why the vertebrae of our chest connect to ribs, whereas those of the neck, lower spine, and sacrum and coccyx do not; why the heart and lungs are in the chest and the stomach, spleen, liver, pancreas, and intestines are in the abdomen. Their name comes from the description of some peculiar mutants seen in fruitflies, in which the parts are mixed up. In one, the poor fly has, where the palps or little feelers around the mouth should be, legs instead of palps. In another, the wing-bearing segment of the thorax is repeated (Fig. 16.6).

In the 1970's and 1980's, Walter Gehring in Switzerland analyzed the genes that were responsible for some of these mutations, and he realized that they all contained a very similar short sequence. This nucleic acid sequence coded for a sequence of amino acids that would take a shape such that it would readily bind to DNA. In other words, these proteins were of a type that would be able to regulate the activity of DNA, exactly what would be needed if one were to determine that


*Figure 16.6.* The effect of mutations of homeotic genes. In the upper picture is a normal fruit fly. The fly on the lower left is a bithorax mutant. In this fly the wing-bearing segment (the second thoracic segment) is repeated, creating an extra set of wings. On the lower right is a fly with the mutation antennapedia. In this fly the antennae, which are the anteriormost appendages, are converted to the more posterior legs, which are properly found on the thorax

one region, for instance, should be the head and another the thorax. Furthermore, Gehring and his coworkers found something else quite startling and still not well explained: these similar genes were lined up on the chromosome in the order that they functioned in the body. The ones that determined what would be head came first, followed by those that determined what would be thorax, followed by those that determined the abdomen (Fig. 16.7).

At this time the structures of the six-legged insect or the ten-legged lobster, with their nerve cords along the stomach and their hearts along the backside, were so obviously different from the structures of the four-legged vertebrates, with their hearts on the stomach (ventral) side and their nerve cords along the back (dorsal) side, that there was no assumption of evolutionary connectedness. However, again referring to databases and pursuing the issue, Gehring and many others quickly realized that, not only were close relatives of the fruit fly homeotic genes found in vertebrates, they were arranged on the chromosome in the same sequence as those in the fruit fly! Not only were they similar and their arrangement similar, mutations of them in mice demonstrated that, as in fruit flies, these homeotic genes in vertebrates also established the anterior-to-posterior axis of the mouse. Thus, once again, the existence of common base sequences with common functions—conserved

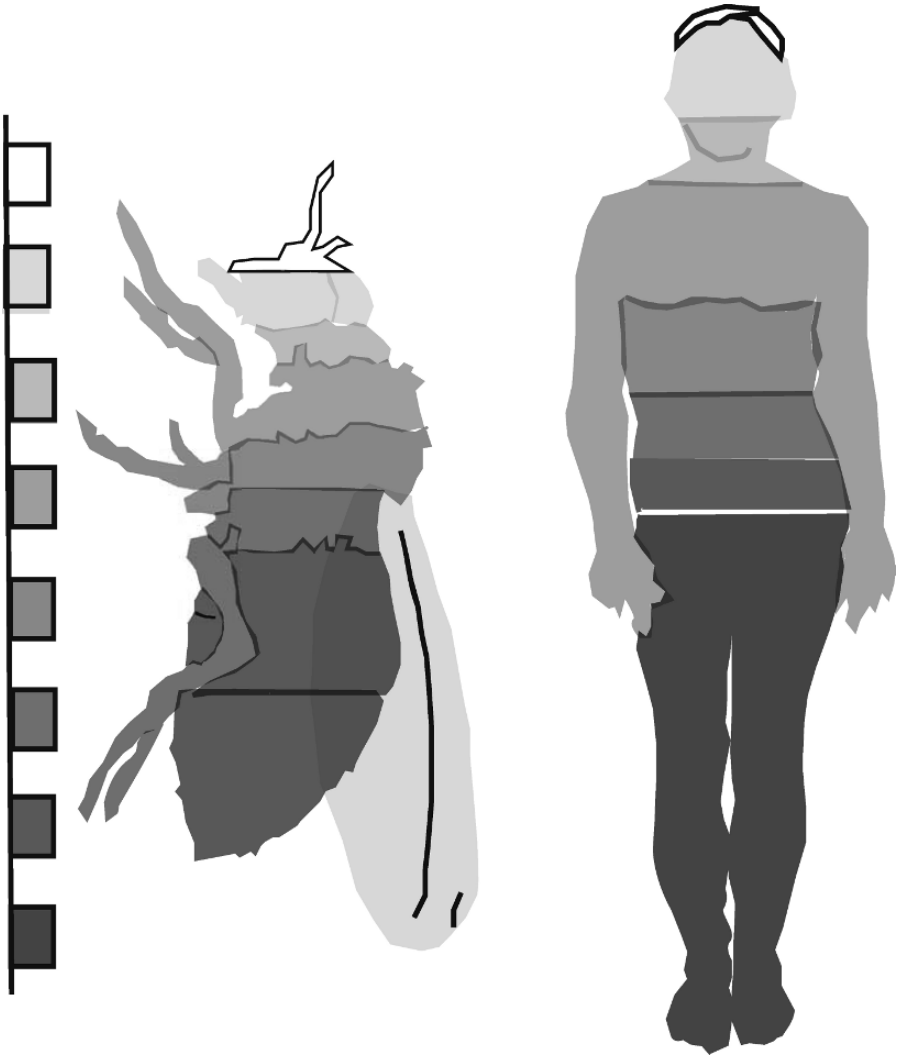

*Figure 16.7.* Conservation of homeotic complexes from invertebrates to humans. On the left is illustrated the sequence of eight homeotic genes on a fruit fly or human chromosome. On the models of the fruit fly and human the regions that these genes delineate are indicated in corresponding shades. In both humans and fruit flies, the alignment on the chromosome is the same as the anterior-to-posterior realm of action in the body

genes—in wildly different creatures not only establishes the importance of the genes and their functions, it provides a deeply compelling argument for common ancestry. An early precursor of both the vertebrates and the higher invertebrates found a means of differentiating its body parts, and this mechanism was so valuable that it was altered only at the bearer's peril.

Vertebrates differ from insects in that they have more than one set of these homeotic genes, up to five sets, with each presumably adding a greater level of subtlety to the differentiation. This is an entirely different story, but it does provide one more argument for why animal life rapidly expanded approximately 400 million years ago. An earthworm has a sort of a brain at its front end, and it goes in one direction, but if you cut off the front end, the remainder of the worm really has no obvious direction or layout. Similarly, the most primitive vertebrates (we call them "chordates" or "hemichordates" because they don't have bony vertebrae) are not very impressive: picture a longish fish like an eel but without fins, cut off its head, and substitute instead a filtering mouth through which it can suck in microscopic organism as food. This would be one of these creatures (Fig. 16.8). Now picture a fast, efficient fish with keen eyes,

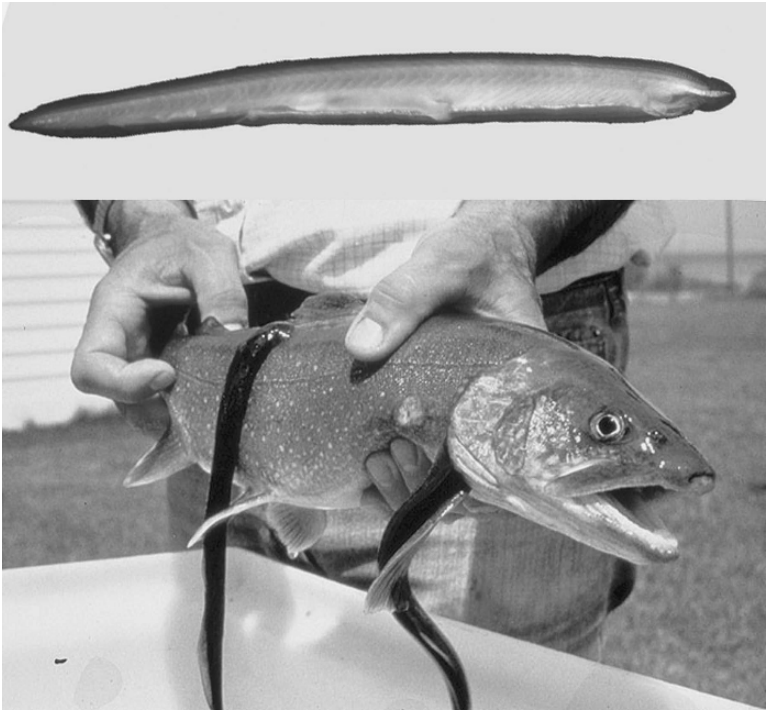

*Figure 16.8.* Upper: a lancelet. Its head is to the right. This inconspicuous creature (it is only about an inch long) has very little anterior-to-posterior (head to tail) differentiation. It has no elaborate brain or eyes, no skull or teeth. It draws in water and small organisms through its filtering mouth. This is the general appearance of a chordate that does not have a full set of homeotic genes. Lampreys and hagfishes are much larger but only slightly more elaborate. The lampreys clinging to the trout may look like eels, but they have no true fins or jaws. Credits: Amphioxis - Wikimedia Commons. Branchiostoma lanceolatum. Photo by Hans Hillewaert. Lamprey - Sea_Lamprey_fish.jpg (81KB, MIME type: image/jpeg) Licensing This image is a work of a United States Geological Survey employee, taken or made during the course of the person's official duties. As a work of the United States Government, the image is in the public domain. (Wikipedia)

well developed and specialized fins, a true skull with strong and specialized teeth, and clearly differentiated parts of the body. A trout, tuna, or barracuda would be a good example. Perhaps the most important difference between these types of creatures is the presence of one or more full sets of homeotic genes. Tracing back the lineages of these genes (Chapter 9, page 118) we can surmise that they appeared and duplicated approximately 350 million years ago. The obviously much higher efficiency of having highly specialized regions of the body, controlled by the activity of the homeotic genes, leads to the argument that the appearance of the homeotic genes created the basis for the high variety among creatures that led to their rapid expansion in the Cambrian era (page 281). Certainly the appearance of these genes was very important to the incipient animal lineages, as the genes are highly conserved, but homeotic genes do not exist in plants, which organize their structures in very different ways.

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## STUDY QUESTIONS

1. If you were to design a machine for making proteins based on information stored as a linear sequence of DNA, how would you do so? Why?
2. What do we mean, "The code is universal"?
3. Imagine an animal in which a tRNA has been mutated so that it gives a false translation. What would happen to the animal? Why?
4. Occasionally we encounter an organism that makes a unique amino acid, somewhat similar to another amino acid, but with a distinct difference. How might this come about? (Hint: consider the possibility that it is possible to modify an amino acid. At what steps might this occur?)
5. Can you think of any means by which the base sequence at the anticodon of the tRNA could determine which amino acid is attached?
6. If the code is universal, could you for instance use ribosomes and tRNA from bacteria and mix them with mRNA from humans and expect to get a human protein synthesized? Why or why not?
7. If you were to find a creature from another planet, would you expect to find a similar means of making protein and a similar code? Why or why not?
8. If you found an organism that did NOT use the universal code, but still used the tRNA, mRNA, ribosome synthesizing system, would you consider it related to everything else on earth? Why or why not?