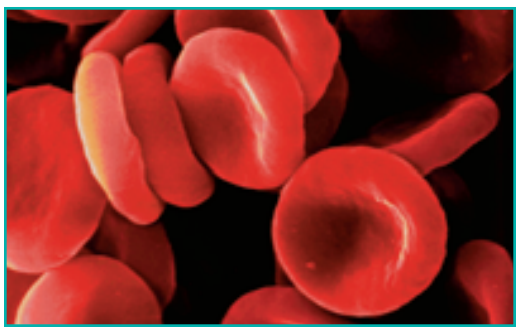
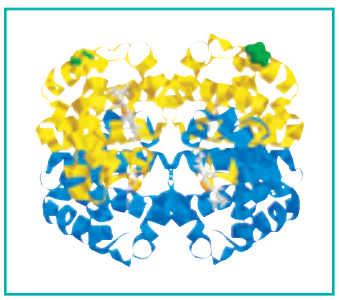
Amino Acid Substitution

A protein's amino acid sequence determines its three-dimensional structure, which in turn determines its function. Even a single substitution of one amino acid for another can change the shape and function of a protein. For example, the genetic disease sickle cell anemia can happen when one amino acid—glutamic acid—is replaced by a molecule of valine. This change in only 1 of 146 amino acids in one of the two protein chains in the hemoglobin molecule causes a major change in the shape of the molecule. This change in the shape of the hemoglobin molecule causes the red blood cells to sickle when oxygen levels are relatively low (as is the case in most body tissues). The sickled cells tend to clog small blood vessels, which prevents the transport of enough oxygen to tissue cells. As a result, people who have sickle cell anemia suffer from shortness of breath. **Figure 11** shows the shape of normal red blood cells and sickled cells. The sickle cell gene is more common in some groups of people than it is in others. In areas where the disease malaria is common, scientists have discovered that sickled cells are more resistant to malarial infection than other cells are. So, people who have sickle cell anemia are more resistant to malaria than other people are.

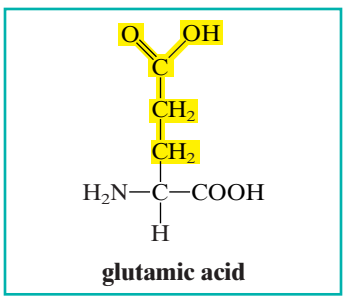
FIGURE 11



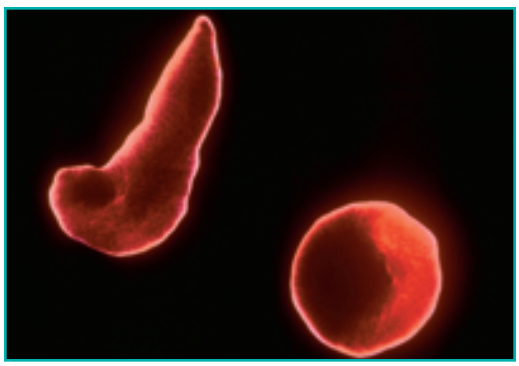
(a) The round, flat shape of healthy red blood cells shows they have normal hemoglobin molecules.



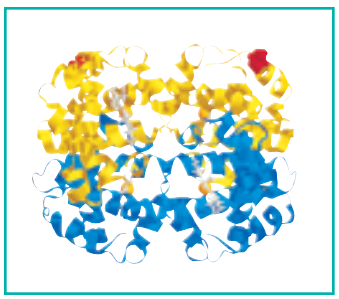
(b) Hemoglobin consists of four polypeptide chains; the area where the change in sickle cell hemoglobin occurs is shown in green.



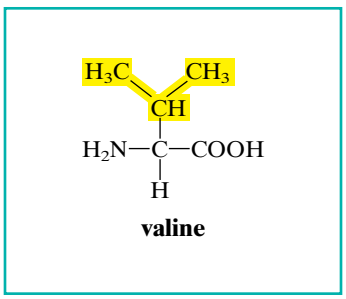
(c) Each of the chains is a polymer of 141 or 146 amino acid units, such as the glutamic acid monomer shown here.



(d) Because of their shape, sickle cells clog small blood vessels.



(e) A genetic mutation causes one glutamic acid to be replaced by valine in the hemoglobin molecules, as shown in red.



(f) The sickle shape of the cell comes from the different shape of the hemoglobin caused by the substitution of valine for glutamic acid.