<u>DNA Proofreading and Repair</u>

Slide 2 DNA replication is an amazingly accurate process. As DNA polymerase adds nucleotides to a growing strand of DNA, it inserts an incorrect base on average only once in every 10^4 to 10^6 bases. This is an error rate of one in ten thousand to one in one million bases. Even more astonishing, DNA polymerase maintains this low error rate while working at an incredible rate of speed. In *E. coli*, for example, DNA polymerase builds new strands of DNA at rates of over one thousand nucleotides per second! Remember, though, that the majority of mutations, or changes in DNA, have a neutral or negative effect on the organism. It is essential, then, that organisms minimize the number of mutations occurring in their DNA as much as possible.

Cells utilize numerous repair processes to safeguard their DNA from damage. Some of these processes are found in all types of cells, while others may be highly specific to certain cell types. All repair mechanisms are energy-requiring, which perhaps underscores the importance to organisms of maintaining the integrity of DNA in a cell. In this lesson, we will discuss three of the basic mechanisms that organisms use to reduce the error rate of DNA replication: proofreading, mismatch repair, and excision repair.

Slide 3 As DNA replication proceeds, the replication complex through which DNA is threaded simultaneously builds a new strand of DNA and proofreads its work. Proofreading involves many of the enzymes of the replication complex, but DNA polymerase III plays perhaps the most important role. When DNA polymerase III inserts an incorrect nucleotide in a growing strand of DNA, it usually recognizes its mistake immediately, removes the nucleotide, and replaces it with the correct nucleotide. This proofreading mechanism alone greatly reduces the error rate of DNA replication.

Slide 4 After DNA replication is completed, a second mechanism similar to the proofreading mechanism scans the new strand of DNA for errors missed by proofreading. When errors are found, incorrect nucleotides are removed and replaced by DNA polymerase. This mechanism is called mismatch repair. Together with the proofreading mechanism, mismatch repair reduces the error rate of DNA replication to around one incorrect base pair in a billion.

Slide 5 During the life of a cell, there is always the potential for damage to the cell's DNA, which in turn could result in the production of non-functional proteins. The DNA may be exposed to different mutagens, for example, such as chemicals or ultraviolet light, which can chemically alter nucleotides. To guard against this type of damage, specialized enzymes continuously scan the cells DNA for any damage such as mismatched base pairs or even extra nucleotides. When damage is encountered, short stretches of DNA may be removed, or excised. These stretches are then replaced with the proper nucleotides through the activity of DNA polymerase and DNA ligase. This type of repair is called excision repair.

Slide 6 Considering the highly effective, and energy-consuming, repair mechanisms that cells use to repair their DNA, one might ask why errors in DNA occur at all, or why evolution hasn't produced absolutely perfect proofreading and repair mechanisms. Recall, however, that mutations are truly the source of novel genetic material. Without mutations constantly altering the DNA of organisms, species could not evolve and adapt to changing environments. And without evolution, a species ultimately would not be able to survive. On the other hand, since many mutations have adverse effects, a mutation rate that is too high could have disastrous consequences for individual organisms. It is believed, therefore, that mutation rates have evolved over time to fall in between the extremes of no mutations, hence no evolution, and too many mutations, hence the death of individual organisms. In this way, mutation rates allow a balance between the evolution of species and the survival and reproductive success of individual organisms.