

Hot Spots Encyclopedia Article

Hot Spots

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Hot Spots

Hot spots are regions of the prokaryotic and eukaryotic genomes that are prone to mutational alteration. These regions are often associated with cytosine, one of the four **bases** comprising **deoxyribonucleic acid**. Cytosine residues are commonly methylated-- a CH₃ group is incorporated onto carbon 5 of the cytosine molecule. The formation of 5-methylcytosine may have a role in regulating the rate of **transcription**. As well, the methylated cytosine can disintegrate into another molecule, methyl uracil. Since cytosine normally pairs with its complementary base, guanine, and methyl uracil pairs with a different base, adenine, the coding sequence of the **DNA** is changed. Mutations in the **gene** product can result.

Numerous clinically relevant examples of hot spot mutations exist in prokaryotes and **eukaryotes**. The herpes simplex **virus**, whose infection causes a serious health threat to those afflicted with **AIDS**, can persist because it is resistant to the antiviral agent acyclovir. Acyclovir resistance is due to a deficiency in the activity of an enzyme called thymidine kinase. Molecular studies of acyclovir-resistance clinical isolates have shown that the resistance is the result of frame shift mutations within two **nucleotide** regions of the viral DNA.

Hot spots are of crucial importance in the generation of skin **cancer**. With over a million new cases annually in the United States alone, skin cancer rivals the incidence of all other types of cancer combined. Researchers have shown that the **carcinogenic** factor in sunlight is ultraviolet B radiation. UVB causes mutations at points on a DNA strand containing a specific arrangement of nucleotide bases-- a pyrimidine base, where cytosine or thymine lies adjacent to another pyrimidine. The UVB most often changes the cytosine to thymidine, which affects the protein that is ultimately produced. Researchers have shown that a gene designated p53 is most susceptible to the mutagenic action of UVB. The p53 gene is also a hot spot for mutations associated with other cancers, such as breast, colorectal, liver, lung and ovarian cancers.