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**New Cancer Drug Affects Cell Cycle**

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A scientists research the checkpoints of the cell cycle, they recognize the importance of understanding these cell cycle controls. After all, cancer is a disease of uncontrolled cell division, and thus a disease caused by malfunctioning checkpoints. Traditional anti-cancer treatments, like radiation or chemotherapy, sometimes stop cell division in the cancer cells, but they can stop cell division in normal cells as well. That leads to unfortunate side effects including nausea, hair loss, and immune suppression. The hope is someday will develop treatments that will more successfully target cancer cells, and not harm normal cells.

In 2001 Novartis began to market the drug Gleevec® as a therapy for one type of cancer, chronic myelogenous leukemia. Gleevec inhibits a kinase that is normally activated in response to a growth factor binding to its receptor (remember that a kinase is an enzyme that transfers a phosphate group from ATP to a target protein).

Chronic myelogenous leukemia is one type of cancer of the white blood cells, and is caused by a translocation between chromosomes 9 and 22. A translocation is the interchange of chromosome segments between nonhomologous chromosomes. The gene for the kinase that is normally activated in response to growth factor signaling is translocated to a new place on another chromosome. The translocation results in the fusion of two genes, as the translocated kinase gene fuses with a gene at the new location. Remarkably, the gene fusion event results in a fused protein; following fusion, the codons remain in frame and are able to be translated by the ribosomes to produce a functional protein. These cells now synthesize a new protein that has kinase activity. However, rather than being switched on or off in response to growth factor, the fused kinase remains in the "on" position, and is not regulated. Cells containing the fused protein gain the ability to divide in the absence of growth factor, and this activity contributes to the development of cancer. Gleevec only binds to, and inhibits, the fused version of the kinase. Gleevec does not bind or inhibit the unfused version of the kinase.

Animation of Gleevec: <http://www.hhmi.org/biointeractive/cancer/gleevec.html>

**A.** Why could Gleevec be a successful anticancer treatment?

**B.** Explain why Gleevec differs from radiation or general cell cycle inhibitors often used for cancer therapies. What do you predict about side effects in an individual treated with Gleevec as compared to a more traditional anticancer treatment?