

Cancer agents - Problem set #1 - Solutions

1. Mutagenesis is defined as a change (or alteration) of genes in DNA. Oncogenes are defined as genes or changes in genes that cause or promote cancer. Tumor suppressors are defined as the opposite, they inhibit or slow cancer growth. Some examples of oncogenes are: bcr-abl, bcl-2, ret, HER2, N-myc, and c-Myc. Some examples of tumor suppressors are APC, BRCA-1, BRCA-2, CDKN2A (p16 INK4), VHL, p53, pRb, and PTEN.

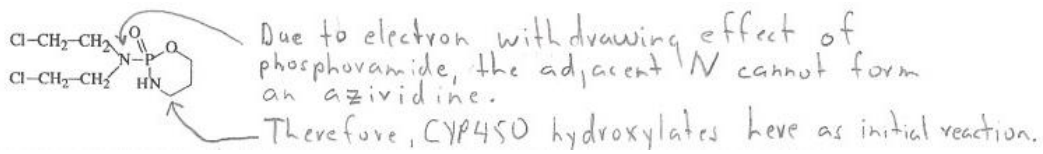
2. The process is called hematopoiesis. The least abundant blood cells are leukocytes or WBCs. RBCs have a life span of about 120 days.

3. Drug resistance in cancer chemotherapy arises because the cancer cells within any tumor are not truly identical. Therefore, the cells will have different levels of sensitivity to a given drug. Those most sensitive to the initial drug will die first, while the less sensitive cells will survive and proliferate. This process is called clonal selection. The effect of drug resistance on a patient's therapy is that resistance forces a change to a new drug (or drugs) so that different cell killing mechanisms can be used against the cancer cells.

4. True.

5. Specific toxicities of cisplatin include ototoxicity and nephrotoxicity. Amifostine can be administered to reduce the ototoxicity and sodium thiosulfate is useful to reduce the nephrotoxicity. If other drugs are cleared by the kidneys, then the renal toxicity of cisplatin can interfere with the clearance of these other drugs.

6. Cyclophosphamide belongs to the class called alkylating agents. Due to the electron withdrawing effect of the phosphoramidate, the adjacent nitrogen (the tertiary nitrogen) cannot form an aziridine. Therefore, CYP450 hydroxylates at the carbon shown below as the initial reaction.



7. 5-FU belongs to the class of drugs called antimetabolites. The enzyme 5-FU inhibits is thymidylate synthetase. The sulfur atom in the Cys residue of the enzyme attaches to the double bond in 5-FU near the fluorine atom. The electron pair of the double bond then attaches to the methylene carbon of 5,10 MethyleneTHF. The reaction cannot proceed any further and activity of the enzyme is terminated.

