MEDCH 562 Cancer Drugs Problem Set #1

1. Define mutagenesis and discuss the difference between oncogenes and tumor suppressor genes. Provide at least two examples of each.

2. Discuss drug resistance in the context of cancer chemotherapy, focusing on how it occurs and the effect it can have on the chemotherapy regimen.

3. What are the major types of genetic mutation that can lead to formation of cancer? What specific type of mutation is responsible for the formation of the Philadelphia chromosome?

4. Please draw the structure of cisplatin below. Why should cisplatin only be reconstituted with saline?
5. What is the reactive portion of busulfan shown below? What is the mechanism of action?

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\text{CH}_3\text{S-}O\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-O}\text{S-CH}_3
\]

6. Dacarbazine is a prodrug used to treat Hodgkin’s lymphoma and must be activated initially by Cytochrome P450s. After O-dealkylation, a tautomerization step occurs which activates the molecule for nucleophilic attack. On the pathway below, please draw the reactive form of the molecule and indicate the driving force for the reaction.
7. Cyclophosphamide is an important cancer prodrug. Name the class of chemotherapy agents to which it belongs. Explain how the prodrug activation changes the reactivity of the molecule. Show the initial product of the prodrug activation pathway.

8. What type of cancers are nitrosoureas used for commonly? Draw the chemically active portion of the molecule below.

9. 5-FU is an important cancer drug. Name the class of chemotherapy agents to which it belongs and the enzyme that 5-FU inhibits. Also explain how the compound must be activated before inhibiting cancer cells.

10. What class of cancer drugs does gemcitabine belong to and what type of cancer is it commonly used to treat? Additionally, it has two mechanisms of action. Describe both. Why does it have such a long half-life compared to similar drugs such as cytarabine?
11. Despite having the same intracellular target, vincristine and paclitaxel have different mechanisms of action. Explain both mechanisms of action and how they differ as well as any important toxicological differences between the drugs.

12. What is the name of the drug shown below? Draw a dashed line showing what bond is broken to form the active metabolite. Also explain the metabolism and clearance of the active metabolite and any potential hazards.