

HST.035 Homework Assignment #6

(Answer sheet)

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1. Which of the following statements best describe colorectal cancer (CRC) *staging* such as those proposed by Dukes? (choose two)
 - A. **CRC staging is a classification based on (i) the depth of invasion of tumor into the colonic wall and (ii) the presence or absence of lymph node and distant metastases.**
 - B. CRC staging is a classification based on (i) size of tumor and (ii) degree of differentiation.
 - C. **Staging is clinically important because there is a strong correlation between stage at presentation and survival from CRC.**
 - D. There is a strong association between the stage of CRC and age at presentation.

2. With regard to Hereditary Non-polyposis Colorectal Cancer (HNPCC) syndrome, all of the following statements are true EXCEPT:
 - A. CRC's associated with HNPCC demonstrate microsatellite instability.
 - B. Patients are at risk of development of cancers in colon, uterus and a variety of other organs.
 - C. **Patients typically present with hundreds of colorectal adenomas.**
 - D. HNPCC has a strong associations with germline mutations in DNA mismatch repair genes MLH1 and MSH2

3. The risk of progression from adenoma to carcinoma is related to all of the following EXCEPT:
 - A. Size of adenoma
 - B. Extent of villous architecture
 - C. Degree of dysplasia
 - D. **Age of onset of adenoma**

4. With respect to the pathogenesis of B cell lymphomas, which of the following statements are true? (choose one)
 - A. The regulated genetic instability involved in class switching and somatic hypermutation (SHM) puts B cells at risk for oncogenic translocations and mutations.
 - B. Chronic B cell stimulation increases the pool of at-risk population and the probability of oncogenic events.
 - C. B cell lymphomas commonly have translocations involving the immunoglobulin gene.
 - D. **All of the above.**

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5. Do you agree with the following statement (please briefly justify your answer)?

*“The observation that eradication of *H. pylori* infection with antibiotics results in regression of gastric MALT lymphomas suggests that infection of B cell by *H. pylori* is an important pathogenic mechanism.”*

***H. pylori* is an epithelial infection, and neither B nor T cells are thought to be directly infected. Chronic infection of the gastric mucosa by *H. pylori* results in chronic stimulation of the immune system which is thought to be associated with increased risk of clonal expansion (i.e., lymphoma). The fact that some MALT lymphomas respond to antibiotic treatment is because the antibiotics eliminate the gastric mucosal infection, thus eliminating the source of chronic B cell stimulation which is thought to be responsible for the pathogenesis of early MALT lymphomas.**

6. Gardos channels are calcium-activated potassium channels in the red cell plasma membrane.

A. Briefly describe the mechanism of (abnormal) activation of Gardos channels in sickle cell disease?

The mechanism that was specifically emphasized in lecture is as follows:

Low oxygen saturation (e.g., in venules) → abnormal hemoglobin saturation → red cell membrane damage → calcium influx → activation of the Gardos channel

B. What is the consequence of activation of Gardos channels with respect to intracellular potassium and water in the affected red blood cells?

Activation of the Gardos channel leads to the loss of potassium and dehydration of the red blood cells. Dehydration of the red blood cell leads to hemoglobin concentration and further abnormal polymerization of hemoglobin, which promotes additional cell/membrane damage.