Reading Guide for “Exposing Cancer’s Soft Spot,” HHMI Bulletin, November 2010

<http://www.hhmi.org/bulletin/november-2010/exposing-cancer-s-soft-spot>

1. What type of lung cancer did Bill Schuette have? What is the prognosis for this type of cancer?
2. What was Schuette’s prognosis after taking seven rounds of chemotherapy drugs?
3. How did Schuette find out about the new drug crizotinib?
4. Crizotinib is part of a new class of drugs that target \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. How do these drugs work?
5. How did the development of the first member of this class of drugs, imatinib (Gleevec) affect the prognosis for patients with Chronic Myelogenous Leukemia (CML)?
6. Initially, gene fusions were found mostly in blood cancers. Since 2005, gene fusions have been found in solid tumors such as …….
7. Charles Sawyers refers to a “gold rush” among cancer researchers. Explain the significance of this.
8. Explain the meaning of the term “translocation.” Describe the translocation found in CML, what it produces, and its effects on cells.
9. Imatinib (Gleevec) blocks the BCR-ABL fusion protein in leukemia cells. Why is it not a “panacea” or cure?
10. Not all cancer-causing genes form fusion proteins. Some cancer-causing genes are \_\_\_\_\_\_\_\_\_\_\_\_\_\_, \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, or \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
11. In 2007, Hiroyuki Mano’s team discovered the *EML4-ALK* gene fusion in some lung cancer patients. What did this fusion encode, and how was this discovery important to the treatment of these lung cancer patients? *(AP)*
12. When Schuette and other lung cancer patients with the *EML4-ALK* fusion started taking crizotinib as part of the clinical trial, what were the results?
13. Why don’t mice that have the most common prostate cancer fusion, *TMPRSS2-ERG*, develop prostate cancer? *(AP)*
14. Describe the three steps in forming a translocation. How could understanding the pathways involved affect cancer treatment? *(AP)*
15. Chinnaiyan’s team hypothesized that testosterone might be involved in forming the *TMPRSS2-ERG* fusion in prostate cancer. How did they confirm their hypothesis?
16. How could correlating patients’ genetic fingerprints with their clinical outcome help guide treatment of prostate cancer?
17. It has been difficult to develop drugs which directly block the action of transcription factors formed by gene fusions. Describe a strategy researchers are using to try to overcome this obstacle. *(AP)*
18. Why is new drug development so important to Bill Schuette? *(AP)*
19. Explain the diagnostic (identifying a disease), treatment, and prognostic (predicting the progression of a disease) value of understanding mutations which can cause cancer. *(AP)*