BCR-ABL: CANCER PROTEIN STRUCTURE AND FUNCTION

ABOUT THIS WORKSHEET

This worksheet complements the Click and Learn “BCR-ABL: Protein Structure and Function,” which focuses on how a chromosome translocation (i.e., a type of mutation) results in a mutated protein that causes chronic myeloid leukemia (CML). You will then hear and read the story of how understanding the structure of the mutated protein, called BCR-ABL, led to the development of an effective treatment for CML.

PROCEDURE

Start the Click and Learn at http://media.hhmi.org/biointeractive/click/bcrabl/. As you read through the slides and watch the animations and film clips, answer the following questions. Be sure to read each slide, even if there aren’t questions from that slide.

QUESTIONS

Slide 4:

1. What are kinases and what do they do?

2.

Slide 5:

3. What molecule provides the phosphate for the kinase to transfer?

________________________

Slide 6:

4. Describe the mutation that results in the BCR-ABL gene and draw a diagram to illustrate the events that lead to the formation of this gene.

Slide 7:

5. How does the BCR-ABL protein differ from the normal ABL protein?
Slide 8:
6. How does the BCR-ABL protein promote the development of CML?

7. You have been asked to design a drug to inhibit BCR-ABL in an effort to treat CML. Using your knowledge of enzyme catalyzed reactions and the BCR-ABL kinase, propose a drug development strategy to combat CML.

Slide 9:
8. Describe the drug that the scientists developed.

Slide 10:
9. What is the name of the drug? ________________________________

10. Why might a general ATP-binding inhibitor be a bad idea? Was this a problem with the drug that was developed?

11. What kind of inhibitor is the drug? __________________

Slide 12:
12. Did Gleevec work? ______

13. What evidence supports this claim?

Slide 13:
14. What happened to the white blood cell counts of the patients represented by the red line, and what are the implications?
Slide 14:
  15. Why did some patients develop resistance?

Slide 15:
  16. What does the mutation that converts threonine to isoleucine cause to happen?

  17. What kind of DNA mutation would result in a single amino acid change?

Slide 16:
  18. What is a conformation change mutation?

  19. What was the next step in solving the problem of Gleevec resistance?

Slide 17:
  20. How long did it take researchers to develop Gleevec after the genetic mutation that causes CML was first found?

  21. Once the mutations that conferred resistance to Gleevec were identified, how long did it take for the next drug to be developed?

  22. What accounts for the difference in development time between the first and second drug?