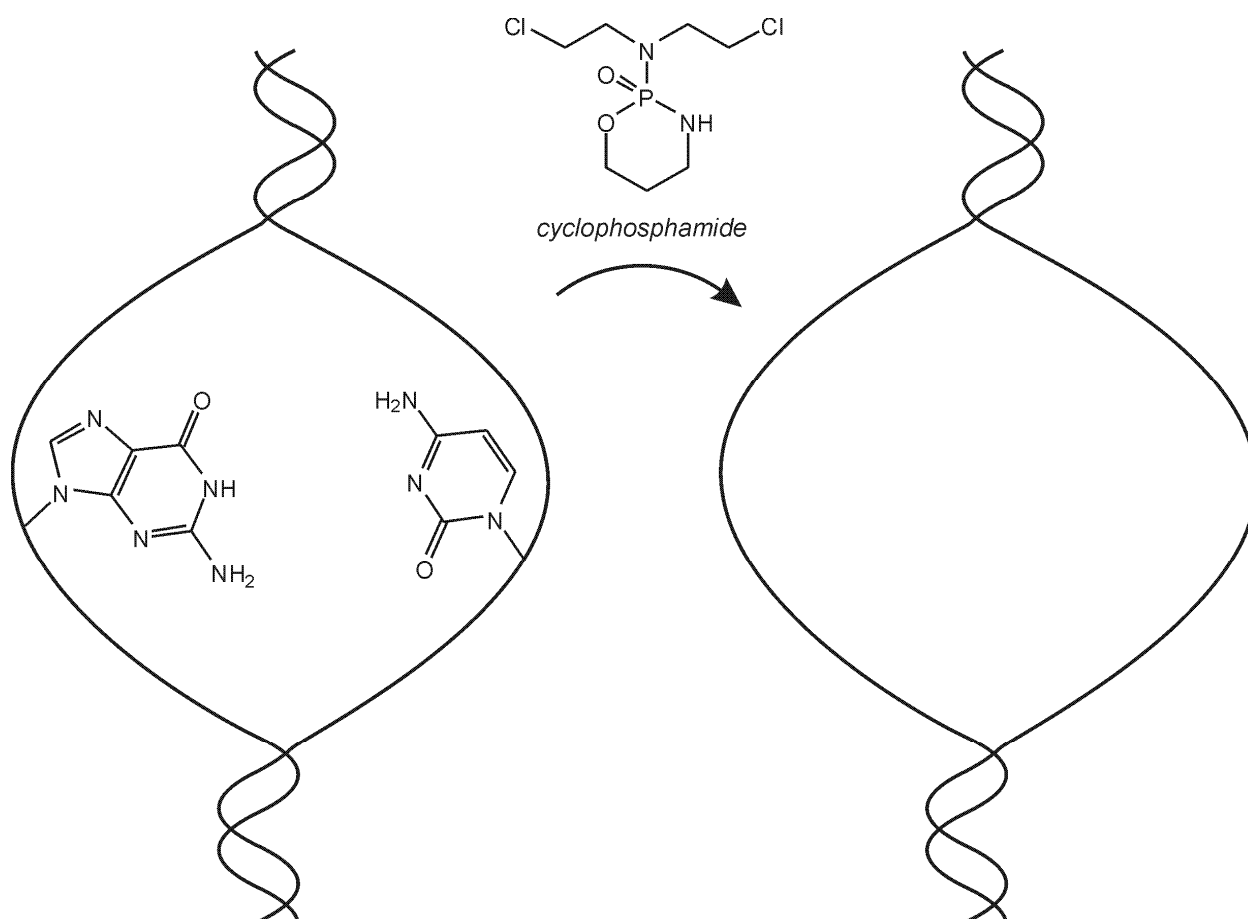


Workshop 13 Chemotherapeutic Alkylating Agents

Though there are many types of cancer, cancerous cells have two characteristics in common: (1) they multiply more rapidly than normal cells, resulting in tumor growth; and (2) they absorb more nutrients than normal cells to fuel this growth. When cancer patients are treated with cyclophosphamide, a chemotherapy agent, the molecule is rapidly absorbed by cancer cells, and then reacts with the cell's DNA via two successive S_N2 reactions.¹ After the reaction is done, the cancer cell's DNA can no longer replicate because its double helix is tied together.



- The cartoon on the left shows two fragments of the DNA helix—guanine and cytosine—that might react as nucleophiles with cyclophosphamide. Which electron pairs from these two fragments will be most reactive as S_N2 donors?
- Draw a multi-step mechanism for one possible reaction between cyclophosphamide and both fragments. Then, draw the result of your reaction in the DNA helix on the right. (The molecules are flexible—don't worry about trying to “fit” the reaction into the hole I've drawn.)

¹ I lied here, but just a little. Cyclophosphamide is actually converted in the cytoplasm to a few different molecules, all of which look a lot like cyclophosphamide. For simplicity's sake, we'll pretend that cyclophosphamide is the active agent.