Name:
Date:

WA4 – Mutations and Protein Structure

Download and open the file **1tyn_inhibitor_mutated** using PyMOL. This is a protease protein which is bound to an inhibitor. Protease is an enzyme which breaks down other proteins and polypeptides into shorter strands.

1. Using the following words, describe the relationship between the protease enzyme and the inhibitor.
   The protease enzyme is a **globular protein**, which contains an **active site**. Under normal conditions, the protease will break and **metabolise polypeptides** into shorter chains. However, in this case, there is an **inhibitor** present. An inhibitor is a molecule which binds to, and blocks, the active site of the protein. This prevents any of the **target substrates** from entering the active site, and stops the enzyme from working **effectively**. The inhibitor is **complementary** to the active site, as it has a complementary shape and structure. This can be considered similar to the model of a **lock-and-key**, although the **induced fit model** is more accurate, as the active site of the enzyme has some **flexibility**.

2. A DNA change has caused the protein to mutate. Select the **Mutated Protease** to show the mutation. Predict the effect that this mutation will have on the inhibitor's effectiveness.
   Although the mutation occurs **near to the active site**, it **doesn't appear to be interfering** with the inhibitor. This means that the mutation s**houldn't affect the strength of the inhibitor**, and therefore the inhibitor should act as normal. It is worth remembering that **not all mutations are inherently bad**, some may have no effect at all! A mutation could even help the inhibitor bind more strongly.

3. Explain how a change in the primary structure of polypeptide can stop an inhibitor from binding.
   Changing the primary structure will change the **sequence of amino acids** in the polypeptide. This will affect the **folding of the polypeptide chain into secondary structures** such as α-helices. Because the amino acid sequence will be different, it will also affect the **tertiary structure** of the polypeptide, which is its **3D organisation in space**. It does this by changing the way in which the protein folds, by **altering the interactions between the amino acid residues**. The tertiary structure is critical in **generating the active site** of the protein, and therefore any change in the primary structure, could affect the **shape of the active site**, and **affect the binding strength of the inhibitor**.