Name:
Date:

QA5 - Inhibitors

1. Thermolysin is an enzyme which can break down peptide bonds. A new inhibitor has been discovered which stops thermolysin from working. Explain how an inhibitor does this.
   Inhibitors work by **blocking the active site of an enzyme**. They will **bind strongly** to the active site, so that the **substrate cannot**. For this to happen, the inhibitor must have a **complementary shape** to the active site of the enzyme.

2. Which two factors are most important in considering the complementarity between a ligand and a substrate?
   Shape complementarity, and the **complementarity of interactions** within the active site. A drug may appear to have the perfect shape, but if it cannot bind, then it may not interact.

3. Why might it be important that a drug doesn't bind too strongly to the active site?
   Because it may create a **very large response**, or it **may not leave the active site**, effectively blocking it, and acting as an inhibitor, which may not be the desired effect.

4. Explain the difference between an inhibitor and an allosteric modulator.
   An inhibitor works by **binding to the active site directly**, thus blocking the substrate from doing so.
   An allosteric modulator works by **binding to the enzyme at a position away from the active site**. In doing so, it causes a **conformational change in the tertiary structure** which **changes the shape of the active site**. The active site is **no longer complementary** to the substrate, so the substrate is unable to bind.

5. Explain the advantage of using computational modelling when designing drugs such as inhibitors.
   Computational modelling helps to **reduce the time, money, and energy** used in traditional lab-based studies. Instead of having to design, produce and then test many drugs and drug targets, it is possible to **model interactions** and narrow down the possibilities. Computational medicinal chemistry can **consider many factors** in drug design, such as solubility, active site complementarity, and other interactions. This makes it much easier to select drugs which more likely to be effective.

Produced by Adam Stubbs at Newcastle University as part of a summer outreach project.