

Understanding the chemistry of biological processes

Education in Chemistry

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rsc.li/2AgFK6Q

Bacteria are single-celled organisms that need a strong cell wall to protect them from changes in their environment. In order to achieve this, the cell wall contains cross-linked glycan (a type of sugar) and amino acid chains.

As bacteria grow and divide the cell wall is in a continuous process of being broken down by autolysins and built back up again by transpeptidases (an enzyme that creates a covalent peptide bond between two peptides) and transglycosylases (an enzyme that creates a covalent bond between two glycan molecules).

The transpeptidase enzyme (otherwise known as the penicillin binding protein) is the target of the penicillin class of drug molecules. Penicillin, and structurally related drugs, bind in the active site of the transpeptidase and prevent it from carrying out its usual function. Computer molecular graphics can be used to visualise these reactions.

1. How enzymes work

Watch the video on how enzymes work (bit.ly/2NPVzoi) and then answer the following questions:

1. How do enzymes reduce the energy of the transition state?
2. In the reaction of citrate with the enzyme aconitase, what do you notice about where the citrate binds on the enzyme?
3. In the reaction of citrate with the enzyme aconitase, what type of bonds are used to hold the citrate in exactly the right place?
4. Was the enzyme changed by the reaction? How did it change during the reaction?
5. Explain how the term 'induced fit' describes what is happening to an enzyme when the substrate binds.

2. Effects of penicillin-like drugs on transpeptidase

There are a number of varieties of transpeptidase found in different bacteria. They all have a similar function but have small variations in their structures. This is an area of active research and a paper by Eric Sauvage and colleagues (bit.ly/2EvN2aQ) describes much of the recent work.

Figure nine in that paper (available as a MS PowerPoint slide, bit.ly/2OuXNPp) shows the arrangement of the enzymes (shown in orange, yellow and magenta) in position by the cell membrane and the growing peptidoglycan structure.

Watch these three short videos and then answer the questions that follow:

- The actions of the transpeptidase (penicillin binding protein): youtu.be/bQaV14ehq1o.
 - The binding of ampicillin: youtu.be/MFVDkZuw6AU
 - The effect of β -lactamase enzyme on ampicillin: youtu.be/fz5-0IE-v5A
6. What are the substrates and the products for the reaction involving the transpeptidase?
 7. Explain how ampicillin prevents bacterial cell wall synthesis
 8. What effect does β -lactamase have on ampicillin?
 9. What functional group(s) are important in the enzyme's active site and in the ampicillin molecule?
 10. (Extension activity) It has been proposed that there is also a lysine group in the active site that holds the antibiotic in place. Considering the structure of the lysine side chain, suggest a part of the ampicillin molecule that may be involved in this interaction.

11. Read the paragraph underneath 'Designing drugs for crafty bugs' in the main article (rsc.li/2AgFK6Q) and use this information to annotate the diagram below:

- Highlight the β -lactam ring
- In the boxes, add the functional groups for serine and lysine side chains.
- Label the amide group that withdraws electrons from the carbonyl group in the β -lactam.
- Use curly arrows to show how the nucleophile in the transpeptidase attacks the β -lactam carbonyl to open the β -lactam ring.
- Draw in the product of the reaction.

