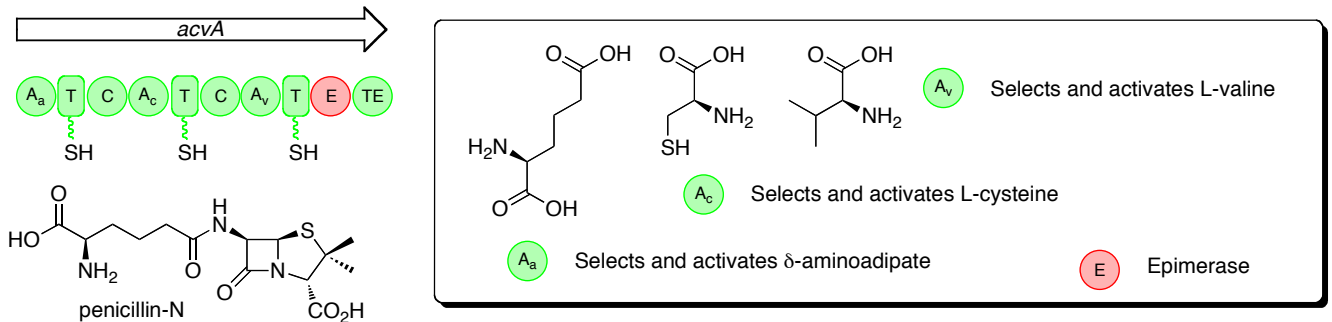


Workshop 5

1. The enzyme ACV synthetase, encoded by the gene *acvA*, is a nonribosomal peptide synthetase which makes the tripeptide precursor of the penicillins and cephalosporins.



- Which cofactor is used by each Adenylation (A) domain? Why is this necessary?
- Redraw the ACV synthetase, showing each Thiolation (T) domain carrying its selected amino acid as a thioester. Show the correct stereochemistry of each amino acid at this stage.
- Show the mechanism of the peptide bond formation catalysed by each Condensation (C) domain.
- Show the mechanism of the TE domain and the final product of ACV synthetase.
- What reactions are necessary to convert the ACV peptide into the penicillin-N skeleton? Speculate about their mechanisms....

2. For the following molecules:

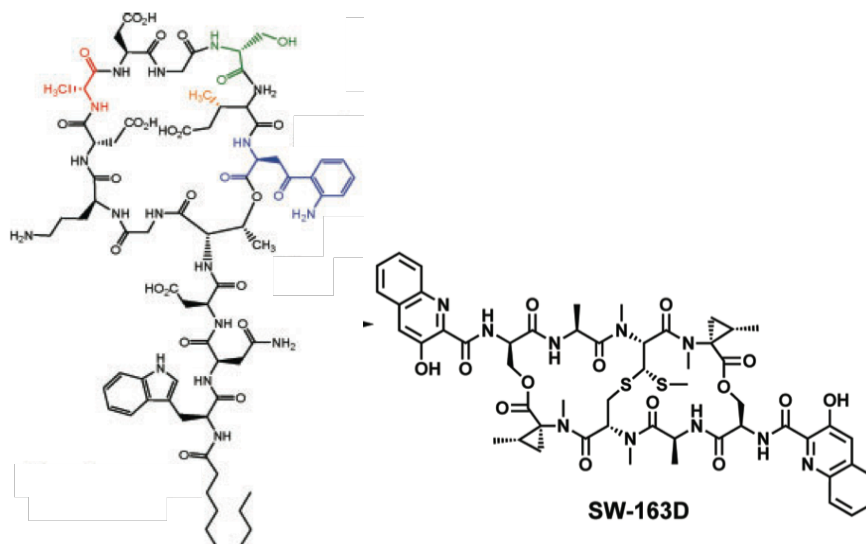
(a) State if they are likely to be Ribosomal (RiPP) or non-ribosomal Peptides.

Explain your reasoning;

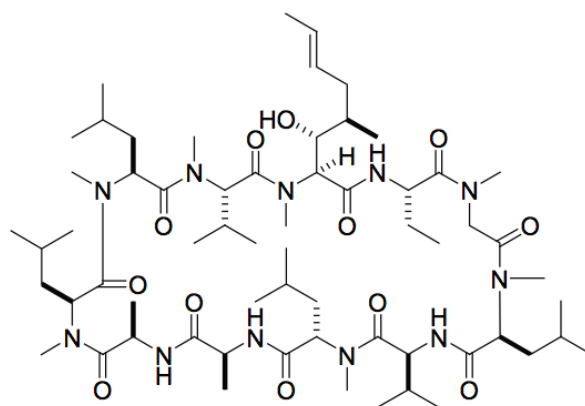
(b) Identify the component amino acids;

(c) Identify the non-proteinogenic amino acids;

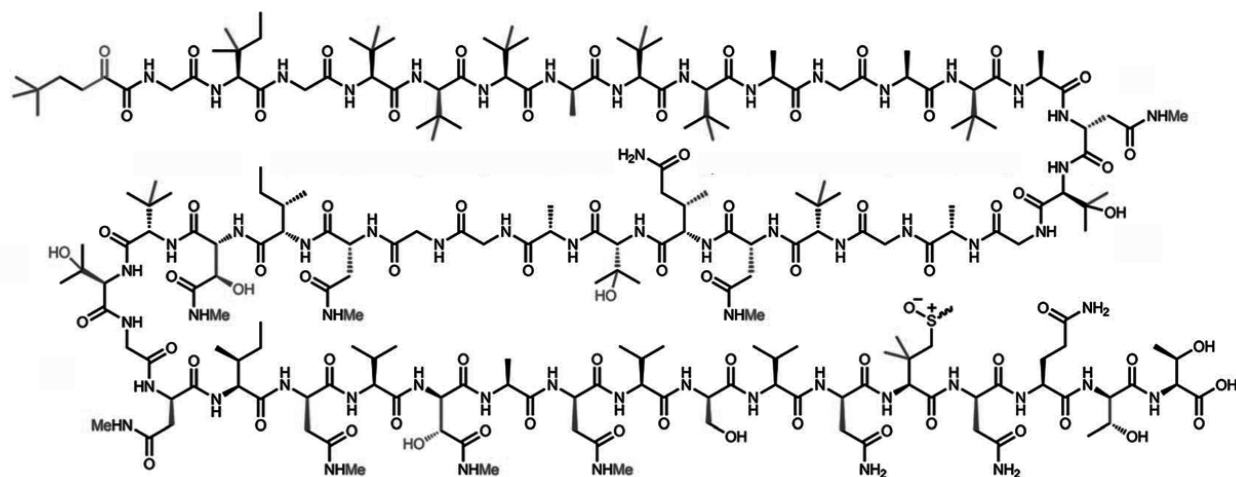
(d) Identify any chemical modifications of proteinogenic amino acids.



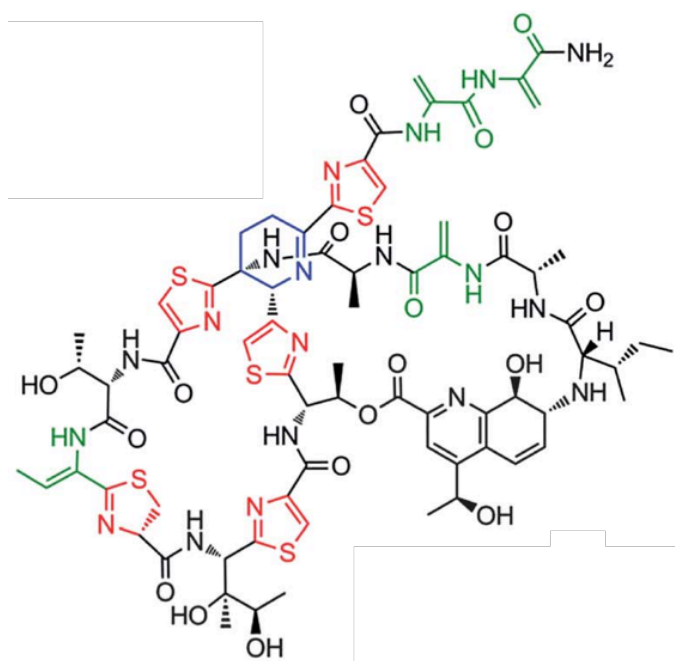
Daptomycin



Cyclosporin A



Polytheonamide A



Thiostrepton A