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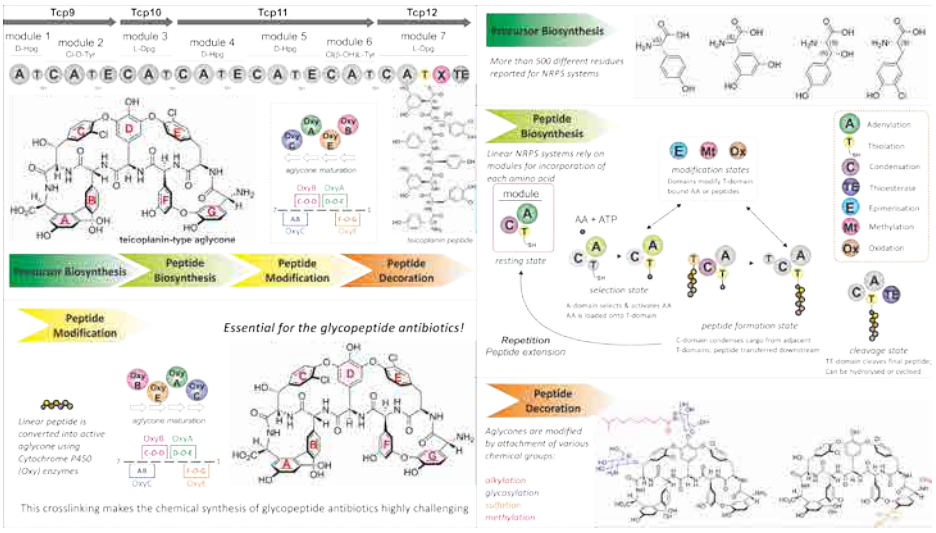
My group investigates the biosynthesis of the glycopeptide antibiotics (GPAs): these compounds include vancomycin and teicoplanin and are clinical treatments of last-resort for Gram-positive bacterial infections. Their biosynthesis centres on a fascinating enzymatic peptide assembly line known as a non-ribosomal peptide synthetase (NRPS) and the cyclisation of this NRPS precursor peptide into a rigid, active antibiotic through the action of Cytochrome P450 monooxygenases. My group investigates these enzymatic systems using a combination of approaches (chemical synthesis, X-ray crystallography, enzymatic catalysis & protein engineering) in order to reengineer these and produce new, more effective antibiotics. Furthermore, my group is identifying new cellular targets for novel antimicrobial therapies as well as developing novel approaches to treat antibiotic-resistant bacterial pathogens such as MRSA.

Research Projects

1. **Development of a bio-enabled synthesis route to the glycopeptide antibiotics**
2. **Generating novel glycopeptide antibiotics via enzymatic redesign of peptide synthetases**
3. **Structural analysis of non-ribosomal peptide synthetase from teicoplanin biosynthesis**



Schematic representation of the steps involved in teicoplanin biosynthesis: we study both the peptide synthesis and modification machineries in order to allow us to produce novel antibiotics using these biosynthetic machineries.

Selected significant publications:

1. Haslinger K, Peschke M, Brieke C, Maximowitsch E, **Cryle MJ**. 2015. X-domain of peptide synthetases recruits oxygenases crucial for glycopeptide biosynthesis. *Nature* 521, 105-109
2. Brieke C, Peschke M, Haslinger K, **Cryle MJ**. 2015. Sequential in vitro cyclization by Cytochrome P450 enzymes of glycopeptide antibiotic precursors bearing the X-domain from nonribosomal peptide biosynthesis. *Angew. Chemie*, Int. Ed. 54, 15715-15719.
3. Haslinger K, Brieke C, Uhlmann S, Sieverling L, Süssmuth R, **Cryle MJ**. 2014. The structure of a nonribosomal peptide synthetase and a Cytochrome P450 monooxygenase. *Angew. Chemie*, Int. Ed. 53, 8518-8522.
4. Brieke C, **Cryle MJ**. 2014. A facile Fmoc solid phase synthesis strategy to access epimerization-prone biosynthetic intermediates of glycopeptide antibiotics. *Org. Lett* 16, 2454-2457.
5. **Cryle MJ**, Schlichting I. 2008. Structural insights from a P450 carrier protein complex reveal how specificity is achieved in the P450BioI-ACP complex. *Proc. Nat. Acad. Sci USA* 105, 15696-15701.