# ENGINEERING THE BIOSYNTHESIS OF NON-RIBOSOMAL PEPTIDES

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Non-ribosomal peptides are a class of natural product that exhibit diverse properties and function as toxins, antibiotics, siderophores, and pigments. Their range of activity means they have roles in medicine, agriculture and bioremediation. Non-ribosomal peptides are biosynthesised by linking monomers together via peptide bonds. They are assembled from a pool of hundreds of monomers, and often contain cyclisation or other modifications not found in ribosomally-synthesised peptides. Their structural diversity means they can be expensive and/or difficult to synthesise. Consequently, many non-ribosomal peptides are produced using fermentation and then modified to generate compounds suitable for medical or industrial applications. Modifying the biosynthetic pathways could provide a cheap and scalable source of new compounds but attempts to engineer them have previously had a low success rate. Using pyoverdine as a model system, this study investigated how to rationally engineer non-ribosomal peptide biosynthesis and generated modified pyoverdines in 6/9 cases. The results of modifying pyoverdine were then used to engineer a second pathway to make dipeptides with a 3/5 success rate. The high success rate and similar results using two biosynthetic pathways suggest this approach is highly transferable and will be valuable for engineering other pathways.