



EXPLOITING CRYPTIC BIOSYNTHETIC GENE CLUSTERS FOR NOVEL NATURAL PRODUCT DISCOVERY

Greg Challis; Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK; g.l.challis@warwick.ac.uk

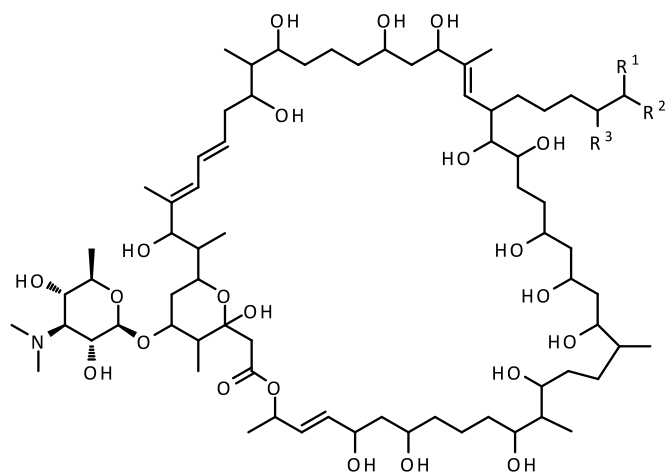
Key words: Streptomyces, antibiotic, polyketide

Bioinformatics analyses have identified gene clusters encoding cryptic natural product biosynthetic pathways, not associated with the production of known metabolites, in numerous microbial genome sequences. Discovery of the metabolic products of such cryptic gene clusters promises to unearth a hitherto untapped wealth of novel bioactive compounds.¹ However, a major obstacle to the discovery of novel natural products by this approach is that many cryptic pathways are expressed poorly or not at all under normal laboratory conditions.

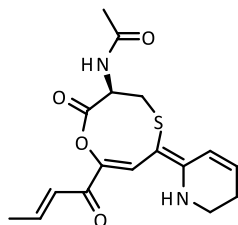
Several examples of the discovery of novel *Streptomyces* natural products via rational genetic manipulation to induce the expression of silent biosynthetic gene clusters will be presented. These include the stambomycins and the coelimycins (figure 1),^{2,3} two novel families of polyketide antibiotics produced by *Streptomyces ambofaciens* and *Streptomyces coelicolor*, respectively, as well as several as yet unpublished examples.

References.

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stambomycins



coelimycin P1

Fig.1 Structures of novel polyketide natural products discovered via rational activation of silent biosynthetic gene clusters.