

Cryptic Biosynthetic Pathways in *Streptomyces curacoii*  
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The Nobel Prize winning discovery of streptomycin, produced from *Streptomyces griseus*, in the 1940's by Selman Waksman initiated the golden age of antibiotic discovery. Over the next 75 years thousands of new antibiotics were discovered with many produced by the same streptomycin-producing genus *Streptomyces*. Genome sequencing of these organisms has revealed that each strain hosts the biosynthetic machinery capable of producing dozens of potential secondary metabolites. However, under typical fermentation conditions only a few compounds are realized; this has led to great interest in activating these silent or 'cryptic' gene clusters. One curious regulatory mechanism in *Streptomyces* depends on the translation of TTA codons within genome. These codons are rare in the GC rich genomes of *Streptomyces* and are often found in biosynthetic clusters and regulatory genes. The *bldA* gene codes for a Leu-tRNA that is responsible for this translation and is facultatively expressed in a growth dependent manner.

Isolated from a soil sample in Argentina, *Streptomyces curacoii* abundantly produces a chlorine containing glycoside antibiotic, curamycin. When complemented with a constitutively expressed *bldA* gene the biosynthetic profile changes resulting in the production of two new metabolites. A chlorinated hexapeptide from an NRPS cluster and a rare ribosomally synthesized and post-translationally modified peptide.