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Teleocidin-producing genotype of *Streptomyces clavuligerus* ATCC 27064

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Abstract:

Streptomyces clavuligerus is an industrially important producer of clavulanic acid (CA), a β -lactamase inhibitor which is used together with amoxicillin in one of the most widely prescribed antibacterial medicines, the co-amoxiclav. In a mid-eighties ATCC vial of *S. clavuligerus* ATCC 27064 culture, we have found a new genotype, which was apparently lost from the subsequent ATCC collection stocks, and has remained obscure to the scientific community. Most importantly, this genotype harbors teleocidin (lynbyatoxin) biosynthetic genes, which are located on an enigmatic 138 kb chromosomal region and support accumulation of significant amounts of these highly toxic, tumor-promoting secondary metabolites in cultures of *S. clavuligerus*. While this genomic region is completely absent from all published sequences for *S. clavuligerus* ATCC strain, at least one of the industrial strains for commercial production of CA, originating from ATCC 27064, retained the genetic potential for production of teleocidins. The origin of teleocidin biosynthetic cluster can now be traced back to early *S. clavuligerus* stocks at the ATCC. Our work provides a genome sequence and a deposited monoisolate of this genotype. Given the scale of industrial use of *S. clavuligerus* world-wide and toxicity of teleocidins, we also discuss the environmental and safety implications and provide a method of abolishing teleocidin production without affecting productivity of CA.

Keywords: Clavulanic acid, teleocidin, *Streptomyces clavuligerus*, lynbyatoxin, genome, secondary metabolism, toxin