Marine-derived thiopeptide antibiotic: A genomic-transcriptomic insight for enhanced production

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Résumé

Marine derived "Thiopeptides" are promising candidates as antibiotics/antimicrobials due to their complex structure and potent activity. One such cyclic thiopeptide isolated from marine sponge associated bacterium showed very promising *in vivo/In vitro* activities against several pathogens, but its production at a large scale is held back by bottlenecks in its biosynthesis. To tackle this issue, whole genome analysis and co-culture-based transcriptomics studies were done. The genomic analysis revealed a Biosynthetic gene cluster (BGC) responsible for making this cyclic thiopeptide, along with several regulatory elements that control the production pathway. Simultaneously, in Co-culture experiment the antibiotic-producing strain was grown along with other microbes to induce stress, which was then subjected to transcriptomic analysis. This co-culture approach revealed the changes in expression of important biosynthetic genes, where expression of core biosynthetic genes increased, while genes limiting production were shown less expressed/none. In simple terms, the presence of other microbes helped the antibiotic producing strain "turn on" the necessary genes that require for the antibiotic synthesis and limit those which are not. These combined insights from genome, and the transcriptomic studies in co-culture system helped us understand how this cyclic thiopeptide is made and find its key genes for improving its production by offering clear targets for genetic engineering. We believe that by modifying the regulatory network either by boosting key genes or disabling inhibitors, it is possible to produce this potent antibiotic at a scale suitable for clinical use, thus expanding its therapeutic potential.

Mots-Clés: Antibiotic, Biosynthesis, Genomic, Transcriptomic, Therapeutic

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