Functions of BldD Respressor in Teicoplanin Producer Actinoplanes teichomyceticus

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Actinoplanes teichomyceticus is a producer of antibiotic, teicoplanin, which acts against multi-resistant G+ pathogens. There are few industrial teicoplanin-overproducing strains with increased level of biosynthesis compared to wild-type. These strains were obtained by canonical mutagenesis and selection. Little information is available on global regulation of secondary metabolism and sporulation in A. teichomyceticus. One of the key repressors of sporulation and secondary metabolism in Streptomycetes spp. is a pleiotropic regulator BldD. The aim of our study was to show the presence of possible bldD homolog in A. teichomyceticus and to elucidate its functions. Analysis of the Actinoplanes genome sequence indicated presence of a homologue of the bldD gene with 68% homology to BldD from S. griseus. This gene, bldDAT, was subcloned into integrative vector pSET152 and transferred into S. coelicolor and A. teichomyceticus via intergeneric conjugation with E.coli ET12567 pUZ8002. Obtained S. coelicolor and A. teichomyceticus strains with overexpression of bldDAT were unable to form visible aerial mycelium on solid media. Detailed morphological analysis, using SEM, indicated that germination of individual hyphae of aerial mycelium of A. teichomyceticus is still happening, but sporangia are not forming; in S. coelicolor oebldDAT repression had only minor morphological effects with evident spores development in some hyphae of the aerial mycelium. Both strains also produced less antibiotics. We have shown the influence of pleiotropic regulator, bldDAT, overexpression on morphogenesis and repression of antibiotic production. Further studies should involve knockout of bldDAT that possibly will result in teicoplanin-overproducing strains.

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