Heterologous Gene Expression of N-Terminally Truncated Variants of LipPks1 Suggests a Functionally Critical Structural Motif in the N-terminus of Modular Polyketide Synthase - DTU Orbit (26/12/2018)

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Streptomyces genomes have a high G + C content and typically use an ATG or GTG codon to initiate protein synthesis. Although gene-finding tools perform well in low GC genomes, it is known that the accuracy in predicting a translational start site (TSS) is much less for high GC genomes. LipPks1 Streptomyces-derived, Well-characterized modular, polyketide synthase (PKS). Using this enzyme as a model, we experimentally investigated the effects of alternative TSSs using a heterologous host, Streptomyces venezuelae. One of the TSSs employed boosted the protein level by 59-fold and the product yield by 23-fold compared to the originally annotated start codon. Interestingly, a structural model of the PKS indicated the presence of a structural motif in the N-terminus, which may explain the observed different protein levels together with a proline and arginine-rich sequence that may inhibit translational initiation. This structure was also found in six other Modular PKSs that utilize noncarboxylated starter substrates, which may guide the selection of optimal TSSs in conjunction with start codon prediction software.

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