A novel locus for mycelial aggregation forms a gateway to improved *Streptomyces* cell factories

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Abstract

Background

Streptomycetes produce a plethora of natural products including antibiotics and anticancer drugs, as well as many industrial enzymes. Their mycelial life style is a major bottleneck for industrial exploitation and over decades strain improvement programs have selected production strains with better growth properties. Uncovering the nature of the underlying mutations should allow the ready transfer of desirable traits to other production hosts.

Results

Here we report that the *mat* gene cluster, which was identified through reverse engineering of a non-pelleting mutant selected in a chemostat, is key to pellet formation of *Streptomyces lividans*. Deletion of *matA* or *matB*, which encode putative polysaccharide synthases, effects mycelial

metamorphosis, with very small and open mycelia. Growth rate and productivity of the *matAB* null mutant were increased by over 60% as compared to the wild-type strain.

Conclusion

Here, we present a way to counteract pellet formation by streptomycetes, which is one of the major bottlenecks in their industrial application. The *mat* locus is an ideal target for rational strain design approaches aimed at improving streptomycetes as industrial production hosts.

Keywords: Reverse engineering; Morphology; Genome sequencing; Pellet; Actinomycete; Antibiotic

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