

# The orphan regulator Aor1 and its possible histidine kinase in the antibiotic regulation of *Streptomyces coelicolor*<sup>†</sup>

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*Streptomyces* is the largest genus of Actinobacteria and the main producer of natural antibiotics used in clinical treatment, which makes *Streptomyces* an interesting tool to combat the increase of antibiotic resistant bacteria. *Streptomyces* spp. have large genomes with several biosynthetic gene clusters (BGCs), but most of them are cryptic under laboratory conditions [1]. This secondary metabolism is strictly regulated by regulatory cascades, so it is important to understand this regulatory network to discover new molecules and enhance their production [2].

Typical two-component systems are composed by a histidine kinase (HK) and a response regulator (RR) and they play a crucial role in antibiotic regulation. Several of them have been studied in the model organism *S. coelicolor* [3] and among them the orphan RR Aor1 is a key regulator that controls several genes of secondary metabolism, including some cryptic BGCs [4].

As an orphan RR, the HK related to Aor1 remains unknown. By bioinformatic prediction, the HKs encoded by the genes *SCO3750* and *SCO6424* seem to be the partners of Aor1. In this work, we study the deletion mutants of these genes and their similarity with the  $\Delta aor1$  phenotype. Our objective is to unravel the signals that control Aor1 to better understand how antibiotic production is regulated in *Streptomyces*.

The  $\Delta 3750$  mutant presents a delay of differentiation on LB, like the  $\Delta aor1$  mutant, and the same phenotype as  $\Delta aor1$  on YEPD. On the contrary, the  $\Delta 6424$  mutant does not have any similarity with  $\Delta aor1$ . These results suggest that *SCO3750* is the HK that controls Aor1.

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