



## “Biosynthesis of arginine and control of gene expression in *Streptomyces*”

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**Introduction.** Arginine metabolism is feedback repressed by arginine in different Gram-positive and Gram-negative bacteria. This effect is mediated by ArgR, a hexameric protein that represses arginine biosynthesis genes, using L-arginine as co-repressor, in *Escherichia coli*, *Pseudomonas*, *Bacillus subtilis* or *Corynebacteria*<sup>1</sup>. In *Streptomyces coelicolor* the *argR* gene, encoding the ArgR regulator has been deleted<sup>2</sup>. Transcriptomic comparison has been performed using microarrays between *Streptomyces coelicolor* M145 and its mutant *S. coelicolor*  $\Delta argR$  under control, unsupplemented conditions, and in the presence of 25 mM arginine<sup>3</sup>. Our objective is to know the complete set of genes controlled by ArgR in *Streptomyces*.

**Methods.** Construction of *S. coelicolor*  $\Delta argR$  was made using the Redirect Technique. Conditions for the microarrays experiments have been described previously (3). To determine more specifically the transcriptomic effect, an additional sequential transcriptomic study has been made comparing *Streptomyces coelicolor* M145 and *S. coelicolor*  $\Delta argR$  between 28 and 64 h of culture in MG medium.

**Results.** The transcriptomic analysis indicates that arginine has very low effect on gene expression in *Streptomyces coelicolor*. A recombinant ArgR protein deleted in the C-terminal end is unable to bind ARG boxes *in vitro* and is inactive as regulator *in vivo*. Genes homologous to those of the degradative pathways found in other bacteria (AST, ADI, ADC) exist in *Streptomyces* but are not clearly regulated either by arginine or by ArgR. As expected the arginine biosynthesis genes are derepressed in the *argR*-deleted mutant, as occurs to the gene for the pyrimidine

pathway. The lack of ArgR strongly affects the formation of chaplins and rodlines, as well as the expression of many genes of unknown function (i.e hypothetical proteins), secreted proteins or general regulators. However the main effect observed was on the expression of gene clusters encoding ectoin, gas vesicles, actinorhodin or undecylprodigiosin.

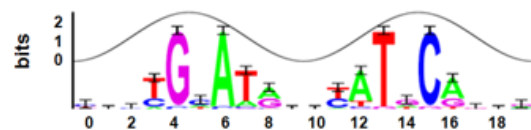


Fig. 1. Consensus ARG box in *Streptomyces*

### Conclusions.

The arginine biosynthesis genes are derepressed in the *argR*-deleted *S. coelicolor* mutant, as occurs to the genes for the pyrimidine biosynthesis pathway. Different clusters for secondary metabolism are also affected in this mutant.

A consensus ARG box for ArgR-binding has been located upstream of many ArgR-regulated genes

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