THE EFFECT OF GLUCOSE AND GLK ON THE *Streptomyces coelicolor* TRANSCRIPTOME

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Introduction. Carbon catabolite regulation (CCR) is a global regulatory process, where the presence of a preferential carbon source represses the expression of genes and operons whose products are involved in utilization of alternative carbon sources (1). Around 5-10% of all bacterial genes are subject to CCR. Bacteria from the *Streptomyces* genus are primarily isolated from soil and frequently found to produce a wide range of secondary metabolites accompanied by a complex life cycle. The morphological differentiation during its life cycle and the secondary metabolite production are under CCR by glucose and other carbon sources (reviewed in 2 an 3). In addition to its catalytic function, in the genus *Streptomyces* the enzyme glucose kinase (Glk) seems to have a regulatory role in CCR (4).Despite the great effort made during the last years, the CCR mechanism in *Streptomyces* is still unknown, therefore it is important to evaluate the global effect of glucose and *glk* on the transcriptional response in *Streptomyces*. The aim of this work was to evaluate the effect of glucose and *glk* gene deletion on the *S. coelicolor* transcriptome, in order to look for transcriptional regulators implicated in this process.

Methods. The culture media and methods used for *Streptomyces* manipulation were previously described (4). Culture conditions for RNA preparation were also described (4). RNA extraction was performed by a modification of the Kirby method (4). For the purpose of this study, a z-score>2 was considered as significant.

Results. Considering a z-score>2 we found 232 genes down regulated and 25 up regulated by glucose. Genes coding for putative DNA binding proteins either down or up regulated by glucose were grouped inside families of transcriptional regulators (Fig. 1) and selected for further studies. Most of the putative proteins (inside described families) are grouped inside MarR, TetR, LysR and IcIR families. Members of these families have been implicated on carbon regulation process.

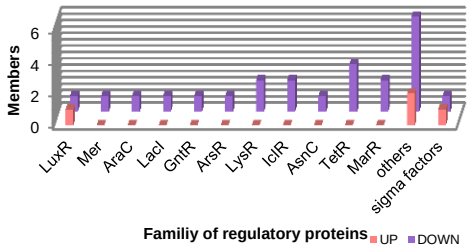

Fig. 1 Classification of DNA binding proteins in TFs families. Significantly overexpressed genes (pink, UP) or significantly repressed genes (purple, DOWN) in the presence of glucose

The expression of selected genes is evaluated either by qRT-PCR or semi-quantitative PCR. Also the genome context is analyzed in order to look for novel transcriptional regulators. To evaluate the *glk* participation on CCR a mutant deletion on that gene was made as previously reported (5). To assess the replacement, glucose kinase activity, growth and sugar consumption were determined. Additionally, the effect of the deletion over the whole transcriptional response is being determined.

Conclusions. Significant differences were found in the expression of DNA binding proteins between a repressor and a non-repressor carbon source.

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