THE EXPANDED GLYCOLYTIC NODE ON STREPTOMYCETES (PGM-ENO-PYK) COULD BE LINKED TO CARBON CATABOLIC REPRESSION

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Introduction. *Streptomyces* are proficient producers of Natural Products (NPs). The biosynthesis of these compounds depends on the supply of common precursors which are also important for biomass production and development. Since these organisms have evolved to become specialized in the production of NPs, their central metabolic network may be also specialized in order to promote their production. We undertook a comparative genomic analysis to explore this hypothesis.

Methods. The enzyme expansions on the central metabolism of actinobacteria were identified using metabolic reconstructions and publically available genome sequences (1). Phylogenomic analyses were used to identify core and expanded homologs of central enzymes and their evolutionary history. Gene knock-out, over-expression, transcriptional analysis and phenotyping was used for the characterization of glycolytic expansions on *Streptomyces coelicolor*.

Results. We found that the last enzymes of the glycolytic pathway (Phosphoglyceromutase, Enolase and Pyruvate kinase) are expanded in most *Streptomyces* species with available genome sequences. The phylogenetic reconstructions of these enzymes indicated that the last common ancestor of *Streptomyces* must have acquired this set of expansions before speciation, indicating that the evolution of this expanded glycolitic pathway is concomitant with the specialization in Natural Product biosynthesis. Therefore, we suggest that the conserved enzyme expansions on *Streptomyces*, especially those in the glycolytic pathway, are highly important for the production of Natural Products. To explore this hypothesis we characterized the glycolysis on *S. colicolor* by gene knockout construction, transcriptional analysis, over-expression, and phenotyping, among other studies. These results indicate the involvement of the expanded node on the glycolityc pathway on carbon catabolic repression; interestingly, over-expression of the expanded enzymes induced the overproduction of pigmented NPs .

Conclusions. Our results support the idea that the expansion of the glycolytic enzymes on Streptomycetes has a bearing on their extraordinary ability to produce Natural Products

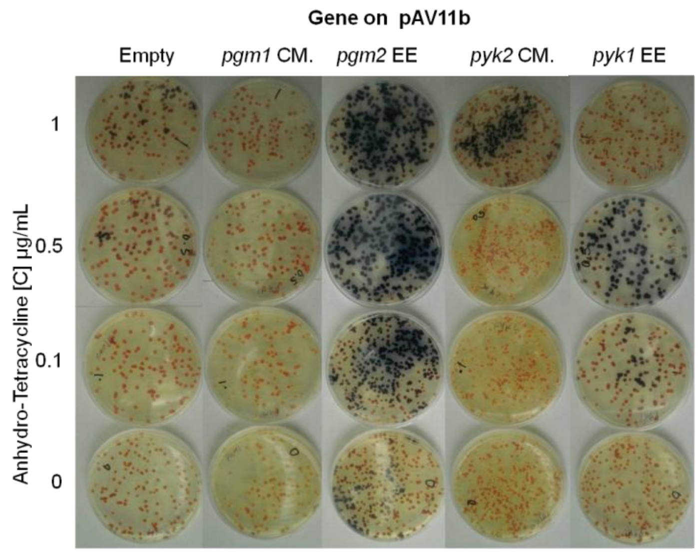

Figure 1. Over-expression assay of *pyk1* and 2 and *pgm1* and 2 on *S. coelicolor* at 72 hours .Transformant strains carrying the each gene cloned on pAV11b were plated on R2YE media with 0, 0.1, 0.5 and 1 µg of anhydro-tetracycline. *Pgm2* and *pyk1* over-expression seem to induce the overproduction of actinorhodin and faster development than their counterparts. CM= Central metabolism homolog, EE=Enzyme expansion

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References.

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