HETEROTRIMERIC Gα PROTEIN Aga1 OF *ACREMONIUM CHRYSOGENUM* REGULATES DEVELOPMENT AND ITS ACTIVITY IS REQUIRED FOR CEPHALOSPORIN PRODUCTION

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Introduction. In fungi, heterotrimeric GTP-binding proteins (G proteins) play an important role as signal transducers, controlling cellular processes such as cell growth, differentiation, virulence and secondary metabolite production [1,2].
In this work we studied the Gα subunit Aga1 of *Acremonium chrysogenum*, and analyzed its role in developmental processes of the fungus and in the production of the β-lactam antibiotic cephalosporin.

Methods. The Gα subunit encoding gene *aga1* was cloned by PCR and a genome walking strategy from the *A. chrysogenum* genome. The gene was mutated *in vitro* to generate dominant activating (*aga1*^{G42R}) and dominant inactivating (*aga1*^{G203R}) alleles, as described [3]. The wild type *A. chrysogenum* ATCC 11550 was transformed with the mutated alleles, to obtain strains expressing a constitutively active (Aga1^{G42R}) and constitutively inactive (Aga1^{G203R}) Gα subunit respectively.

Results. Sequencing of gene *aga1* showed that it encoded a Gα subunit from a heterotrimeric G protein, and that it belonged to group I of the three fungal groups of Gα subunits described by Bölker [2]
The morphology of the strains expressing the mutant *aga1* alleles indicated that constitutive activation of Aga1 inhibits differentiation and conidiation, whereas constitutive inactivation causes strong development of conidiophore-bearing aerial mycelium and production of a higher number of conidia, which changed their morphology from fusiform (typical of the wild type) to round (Fig. 1)
We then analyzed cephalosporin production in submerged cultures of the different strains. Absence of Aga1 activity (strain Aga1^{G203R}) abolished cephalosporin production, whereas constitutive activation of the Gα subunit (strain Aga1^{G42R}) did not significantly affect the level of cephalosporin production with respect to the wild type (Fig. 2).

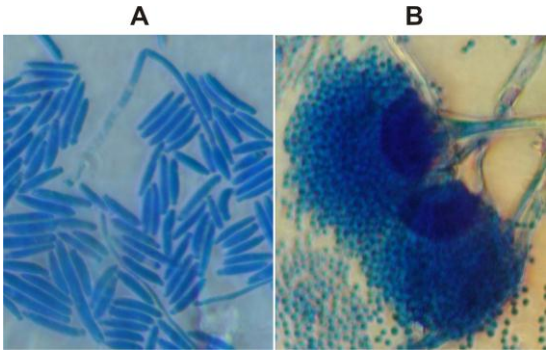

Fig.1 Conidiophores and fusiform (left) or round (right) conidia from strains ATCC 11550 (A) and Aga1^{G203R} (B).

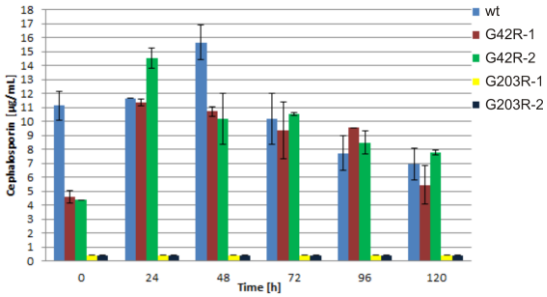

Fig.2 Cephalosporin production in submerged cultures of strains with different genetic backgrounds of gene *aga1*: wild type, Aga1^{G42R} and Aga1^{G203R}.

Conclusions. The heterotrimeric Gα protein Aga1 regulates negatively differentiation and conidia production, and its activity is required for production of the antibiotic cephalosporin in *Acremonium chrysogenum*.

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