# 006

## 2'OmethylRNA *EFG1* antisense oligomer to control *Candida albicans* filamentation

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Antisense oligomers (ASO) and their analogues have been successfully utilized to silence gene expression for the treatment of many human diseases, however the control of yeast´s virulence determinants have never been exploited before. In this sense, this work is based on the key hypothesis that if a pathogen's genetic sequence is a determinant of virulence, it will be possible to synthesize a nucleic acid mimic based on antisense therapy (AST) that will bind to the mRNA produced, blocking its translation into protein and consequently reducing the pathogen virulent phenotype. *EFG1* is an important determinant of virulence that is involved in regulation of *Candida albicans* switch from yeast to filamentous form. Thus, our main goal was to design and synthesize an ASO targeting the *EFG1* mRNA and to validate its *in vitro* applicability in order to control *C. albicans* filamentation.
For that, an ASO against *EFG1* was designed, including 2'OMethylRNA chemical modification, through bioinformatic tools. The fluorescence in situ hybridization (FISH) was performed and demonstrated that the ASO was able to penetrate *Candida* cell wall with high sensitivity and specificity. To determine the effect of anti-*EFG1* 2'OMe, the gene level expression, protein translation inhibition and reduction of filamentation reduction were analysed. The results show that the anti-*EFG1* 2'OMe oligomer was able to significantly reduce the levels of *EFG1* gene expression (around 58%) and of Efg1p protein translation (approximately 56%), as well as effectively prevent filamentation of *C. albicans* cells (by 80%). Moreover, it was verified that anti-*EFG1* 2'OMe keep the efficacy in different simulated human body fluids.

Undeniably, this work provides potentially valuable information for future research into the management of *Candida* infections, regarding the development of a credible and alternative method to control *C. albicans* infections, based on AST methodology.

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