

Application of antisense oligomers based approaches to control candidiasis

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Candidiasis is the primary fungal disease, with a mortality rate of about 40% and costs associated with hospitalized patients that range from €5700 to €85000 per episode. This important clinical, social and economic problem is due to the recognized phenomenon of *Candida* species multi-antifungal resistance, associated with the indiscriminate use of traditional antifungal agents. In clinical practice, *Candida albicans* continues to be the most commonly encountered member of the genus *Candida* with an incidence of approximately 47% in all infections caused by *Candida* species. However, in recent decades the number of candidiasis due to non-*Candida albicans* *Candida* species, particularly *Candida glabrata*, *Candida parapsilosis* and *Candida tropicalis*, has increased significantly.

Candida species pathogenicity is facilitated by a number of virulence factors, most importantly adherence to medical and/or host cells, biofilm formation, filamentous forms development and secretion of hydrolytic enzymes [1].

Thus, new alternatives strategies/therapies, with novel mechanisms of action, improved pharmacokinetics, and less toxicity, are urgently needed to reach the marketplace to control *Candida* species infections.

Antisense therapy holds great promise for the treatment of many human diseases. The concept underlying antisense therapy is relatively straightforward: the use of a complementary sequence to a specific mRNA that can inhibit expression of the latter and induce a 'blockage' in the transfer of genetic information from DNA to protein. The antisense oligomers are a short strand of nucleic acids, which is complementary to the target mRNA, and generally composed by short sequences with 13-25 nucleotides of unmodified or chemically modified molecules [2].

Our key hypothesis is that, if in a pathogenic microorganism, the genetic sequence of a particular gene is known as a determinant agent of pathogenicity, synthesizing a strand of nucleic acid that will bind to the mRNA produced and inactivating it, in its translation into protein, we will be able to control its virulence.

In this sense, it is intended to develop cocktail(s) of therapeutic antisense oligomers to be used in drug nano-carrier formulations against the most pathogenic *Candida* species in order to control its virulence. Coating of medical surfaces, as well as, the antisense oligomers exploitation as new nano-drugs for *in vivo* administration, are exciting examples of future medical applications that will contribute for decreasing of candidiasis in the worldwide.

References

- [1] Silva, S, Negri M, Henriques, M, Oliveira, R, Williams, W, Azeredo J. Adherence and biofilm formation of non - *Candida albicans* *Candida* species, *Trends Microbiol* 19(5), 241-247, 2011.
- [2] DeVos, SL, Miler TM. Antisense oligonucleotides: treating neurodegeneration at the level of RNA, *Neurotherapeutics*, 10(3), 486-497, 2013.