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Nanobiotechnological approaches to delivery of conventional antifungal drugs, DNA vaccine or peptides against fungal infection

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Human mycosis are infections that are usually difficult to treat, for different reasons, including the generally chronic state of the disease at the moment of diagnosis, the great resistance of the pathogens to many of the available drugs, and/or the long period of therapy that represents high costs in terms of antifungal agents. Likewise the growing number of the pathogen's resistance mechanisms to conventional drugs significantly increased in the last decade, in part because of the increase of the immune-compromised patients. In some cases, due to the resistance problem only few drugs present the potency necessary to treat these opportunistic infections however some of these drugs, such as amphotericin B, have the disadvantage of excessive toxicity. During the last years my group has been working to develop new alternatives of treatment to fungal infections. One of these strategies is the sustained delivery system based on nanotechnology. The treatment of mice experimentally infected with *Paracoccidioides brasiliensis* with desoxycholate amphotericin B (D-AMB) coated on poly(lactic-co-glycolic acid) (PLGA) and dimercaptosuccinic acid (DMSA) polymeric blends (Nano-D-AMB) showed the same antifungal efficacy than free D-AMB but with reduced numbers of AMB administrations and genotoxicity and cytotoxic effects. Itraconazol is another antifungal drug that has been used in fungal therapies. Our results using itraconazol entrapped in PLGA showed increased antifungal activity and lower cytotoxicity compared with free drug. Another strategy used by our group is the utilization of plasmid DNA encoding sequences to express foreign antigens as DNAhsp65 from *Mycobacterium leprae*. The DNAhsp65, that can elicit a powerful immune response, was entrapped within liposomes or PLGA systems to deliver DNAhsp65 to treat paracoccidioidomycosis. Both formulations modulated a protective immune response and reduced the pulmonary fungal burden even in the groups receiving less than four times the amount of the DNAhps65. Similar results were observed when the treatment has done with combined chemotherapy and P10 nanotherapy. P10 is a 15-amino acid peptide that carries the T-cell epitope of the glycoprotein 43 kDa glycoprotein, the major diagnostic antigen secreted by *Paracoccidioides brasiliensis*. Our results showed a marked reduction of fungal load after the treatment. During the treatment schedule, the P10 entrapped within PLGA was more effective than 'free' P10 emulsified in Freund's adjuvant. The combination of sulfamethoxazole/trimethoprim with the P10 peptide entrapped within PLGA demonstrated increased therapeutic efficacy against paracoccidioidomycosis and dramatically reduced the peptide amount necessary to elicit a protective effect. In summary, our results suggest that nanoscale-controlled release systems represent a promising approach to deliver vaccines and present advantages over administering the conventional form of the naked plasmid DNA vaccine or conventional antifungal drugs.

Biography

André C. Amaral is adjunct professor at Universidade Federal de Goias, Center East of Brazil, teaching Nanobiotechnology and Introduction to Biotechnology classes. He began his career as a research on the Biological Sciences while developed his graduation in Biology, and completed his Ph.D. at Catholic University of Brasilia, when he won the "2009 - Young Investigator Award" (FAP/DF, Distrito Federal, Brazil). He developed a postdoctoral stage at the University of Brasilia with the work plan "Technological development of amphotericin B-PLGA-DMSA nanoparticles: characterization (physical-chemical, morphology, biodistribution, and pharmacokinetics) and analysis for scaling up".He has experience on investigating nanostructured sustained delivery systems for antifungal drugs and on the experimental murine models for fungal diseases (paracoccidioidomycosis and vaginal candidiasis) and bioprospection of new bioactive molecules. His interests are on nanostructured delivery systems, pharmaceutical technology, drug development, identification of bioactive molecules, and experimental murine models of infectious diseases.

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