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# THE CENTER FOR STRUCTURAL MOLECULAR BIOTECHNOLOGY

CBME

RESEARCH, INNOVATION
AND DISSEMINATION CENTERS (RIDC)

*Crystal structure of the enzyme glyceraldehyde-3-phosphate dehydrogenase from Trypanosoma cruzi, one of the targets for anti-parasitic drug discovery at CBME*

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National Synchrotron Light Laboratory (LNLS)

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The major goal of the Center for Structural Molecular Biotechnology (CBME) is to perform both applied and basic research, as well as technological development in all areas that depend on Structure Based Molecular Design, specifically in the rational design of new structure-based compounds (drugs, vaccines, pesticides, herbicides) and in protein engineering. Our center promotes an integrated multidisciplinary approach including Molecular Biology, Biochemistry, Structural Biology, Medicinal Chemistry based on both Synthetic and Natural Product Chemistry, Molecular Immunology, Cell Biology and Pharmacology. Maximum integration and collaboration with the private sector is always sought, particularly with pharmaceutical and biotechnology companies and research institutes within the health and agricultural sectors. The integration of biological sciences with the facilities of the National Synchrotron Light Laboratory (LNLS) represents a major advantage for the center.

The research projects of CBME are selected by their focus on areas which are socially highly sensitive, such as human health, agriculture and the environment. The center aims to achieve maximum integration and partnership with both public and productive sectors, particularly national and international pharmaceutical companies, biotechnology industry, research institutions dedicated to human health and the agricultural sector. The large majority of the projects currently being developed are related to tropical parasitic diseases endemic in Brazil, as well as cancer, HIV and agricultural related diseases.

On the educational front, the center strongly invests in training programs for students and researchers in the area of Structural Biology in all institutions involved. Furthermore, the CBME will closely work with the Center for Scientific and Cultural Diffusion, which interacts with the community, through strong programs directed towards high school students, school teachers, libraries of experiments for school demonstrations, education at a distance via internet, videos, science fairs, lectures and so on.

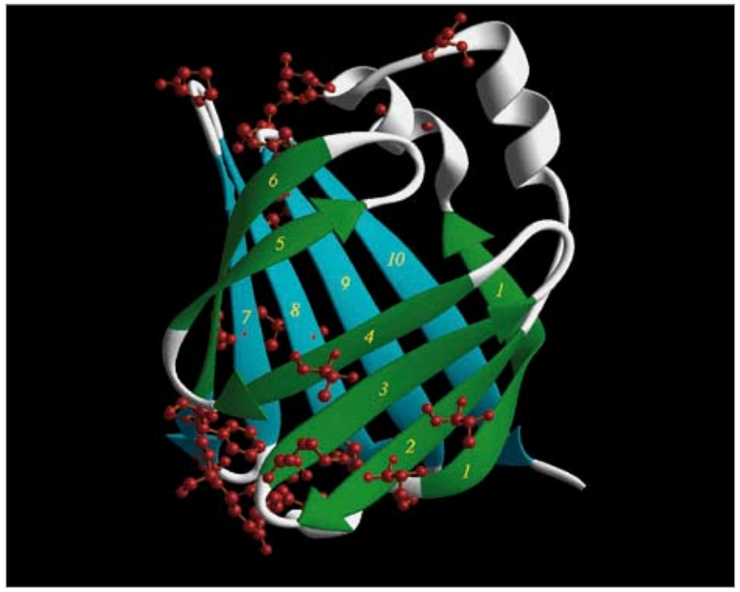
## MAIN RESEARCH TOPICS

*The laboratories of CBME integrate top technologies in molecular biology, biochemistry, protein crystallography and medicinal chemistry*

The common issue on the research projects of CBME is the molecular approach, in atomic detail, of biological systems related to demanding areas of society, such as human health, agriculture, and environment. The team members are researchers with solid formation and background in different aspects of molecular and structural biology CBME's mission is to develop high-quality basic research in strategic areas for the country. The current main projects are related to endemic infectious diseases in Brazil, like Chagas' disease, leishmaniasis, schistosomiasis, yellow fever, malaria, and diarrhea. Other projects investigate proteins associated with cancer like septins, tubulin, Nek kinases and nuclear receptors; genetic diseases (Shwachman-Bondian-Diamond syndrome); anti-inflammatory drugs; plant-pathogen interactions; matrix metalloproteinases; disintegrins; myotoxins; and neurotoxins from Brazilian snake venoms; biological models of inflammation; and cellular signaling. The CBME research organization adopts a matrix arrangement, in which the heads of projects utilize all the available facilities, competences and skills, according to the projects' needs, thus optimizing the chances to achieve the established goals. These extensive external collaborations enable CBME to cover all the demanded methodologies and specialized techniques on developing projects.

By virtue of the strategic nature of CBME in pursuing partnerships with industry and research institutions, we are permanently open to set new challenges.

## SUMMARY OF RESULTS TO DATE AND PERSPECTIVES




*The antigenic protein SM14 is a vaccine candidate for the treatment of schistosomiasis. A model for its three-dimensional structure, built by CBME researchers in collaborations with Fiocruz (RJ), has aided in better understanding its immunological properties, and the development of novel immunogenic peptides*

During its existence CBME has contributed significantly to the current body of knowledge in structural biology of many different systems. These include studies on proteins from human parasites (such as *T. brucei, T. cruzi, P. falciparum, S. mansoni, L. major* among others) many of which are related to essential metabolic processes within the parasite and therefore potential targets for chemotherapy. Equally important have been studies on proteins related to non-infectious human diseases, such as nuclear receptors, where the classical methods of structural biology have been complemented by medicinal chemistry approaches towards the design of novel ligands with potential therapeutic benefit. Other projects have an alternative emphasis, for example on the design of peptides for vaccination trials or for diagnostic purposes or for better understanding of the molecular mechanisms behind the disease process itself. Overall, the research team of the CBME has solved tens of different protein structures and their complexes over the last seven years of existence.

Not all effort is devoted to research in human health. The discovery of a large number of cysteine protease inhibitors, coded by sugar cane has led to the development of transgenic plants resistant to common plagues that severely damage crops. Such experiments are currently ongoing involving researchers from the CBME together with studies aimed at better understanding the molecular mechanisms involved in plant/pathogen relationships.

Such efforts in the research field have limited impact without corresponding attempts to make them relevant to the academic community and to society in general. The CBME has become renowned both nationally and internationally for its outreach department, which involves the development of novel teaching aids, games, videos as well as for running teacher-training courses and for motivating high school children towards a career in the biomolecular sciences. Furthermore, the Center has collaborated with many industrial partners over the years including well-known national pharmaceutical companies such as Eurofarma, Cristalia and EMS, and its members are always aware of potential patenting possibilities. Indeed, several patents have been filed both nationally and internationally over the last few years. Licensing of some of those to private partners is under advanced negotiations.