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Structural insights of SIR2 proteins from T. cruzi as promising targets to fight against Chagas disease

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Abstract

Trypanosoma cruzi is a protozoan pathogen responsible for Chagas disease. Current therapies rely only on a very limited number of drugs, most of them inadequate because of severe host toxicity or drug-resistance phenomena. In order to find therapeutic alternatives, the identification and the study of new biotargets is highly recommended. Recent findings suggested that the inhibition of the silent-information regulator 2 (SIR2)-like proteins, commonly called sirtuins, can cause kinetoplast alterations and cell cycle arrest of the parasite. Therefore, these parasitic sirtuins have emerged as promising new anti-parasitic targets. In the absence of crystallographic data, reliable homology models of sirtuins SIR2rp1 and SIR2rp3 from *T. cruzi* have been generated. *In silico* structural analyses revealed important features for the design of novel and selective candidate drugs. Moreover, a library of phytochemicals with a growth inhibitory activity against *T. cruzi* has been screened against the modeled sirtuins, highlighting the potential mechanism of action of four trypanocidal natural compounds. Taken together, this information on *T. cruzi* sirtuins may be useful in the research of novel therapeutic strategies against Chagas disease.

Biography

In 2006, Dr. Nurisso graduated from the University of Turin (Italy) with a Master Degree in Industrial Pharmacy. She then completed her Ph.D. in Structural Biology and Nanobiology from the University of Grenoble (France) as a Marie-Curie fellow. In 2010, she joined the Pharmacochemistry laboratory of the School of Pharmaceutical Sciences of the University of Geneva (Switzerland), working two years as a post-doctoral fellow. Dr. Nurisso is currently Assistant Lecturer at the School of Pharmaceutical Sciences and also the winner of the Scholarship of Excellence of the University of Geneva (Switzerland), working on inter-disciplinary projects related to epigenetics.