The role of histone H4 acetylations on Trypanosoma cruzi transcription control

Thiago Cesar Prata Ramos; Bruno Pascoalino dos Santos; Sheila Cristina Nardelli; Antonio Augusto Rocha; Nilmar Silvio Moretti; Sergio Schenkman

Departamento de Microbiologia, Imunologia e Parasitologia, Escola Paulista de Medicina, Universidade Federal de São Paulo, R. Pedro de Toledo São Paulo, SP. Email: sschenkman@unifesp.br

Trypanosoma cruzi, the protozoan that is the agent of Chagas disease, belongs to an early evolutionary branch of eukaryotes. When compared with other eukaryotic histones T. cruzi sequences are highly divergent, especially when concerning the sites of post-translational modifications (PTMs), known to act as important regulators of gene expression. In trypanosomes transcription is proposed to initiate in chromatin regions enriched in acetylated histones such as histone H4, which contains acetylations in the lysines 4, 10 and 14. While the K4 is modified in 70% of the total histones, the K10 and K14 are minor modifications and, most likely, have regulatory functions. In this study, we generated parasites expressing the wild type or mutated forms of histone H4 with the lysine 4, 10 and 14 residues replaced by arginine. All modified histones were found incorporated in the chromatin, but only H4K10R and H4K14R mutations affected growth. These effects were not caused by increased damage in DNA breaks, known to depend on the K10 and K14 modifications. They are due to an increased exposition of regulatory regions in the absence of these later modifications and impairment of transcription initiation. These results indicate that acetylation of lysine 10 and 14 residues of histone H4 are required for optimal chromatin structure formation and organization.

Key words: Chromatin remodeling, histone acetylation, Trypanosoma cruzi