

## **THE *HUS1-LIKE* GENE OF *LEISHMANIA MAJOR* PROTECTS DNA FROM PHLEOMYCIN-INDUCED DAMAGE.**

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The Hus1-like gene of *Leishmania major* (*LmHUS1*) is located in the H region, a 45 kb locus involved in drug resistance and virulence. In resistant cell lines selected in unrelated drugs, the H locus is found amplified as extrachromosomal circles. Hus1 is widely conserved and believed to be a checkpoint protein that forms a trimeric complex with Rad1 and Rad9 (the 9-1-1 complex) to encircle damaged DNA. In yeast, the 9-1-1 complex activates checkpoint signaling pathways that block cell cycle progression, regulate DNA repair, and trigger apoptosis. The precise mechanisms controlling this process remain unclear. *LmHUS1* was cloned and transfected into the parasite. The selected mutant presented resistance to Phleomycin, a radiomimetic drug. The effect of Phleomycin on chromosome integrity, as investigated by PFG-separated chromosomes, also revealed that transfectant *LmHUS1* was less affected by the drug. The possible involvement of *LmHUS1* in the cell cycle progression was investigated in synchronized cultures treated with the phleomycin. Preliminary results indicated that, after release from G1/S block by removing hydroxyurea, transfectant *LmHUS1* progress through cell cycle more rapidly when compared to wild-type cells. Our current efforts are focused on the generation of *LmHUS1* mutants and in the subcellular localization of *LmHUS1*. Keywords: Cell cycle, dna damage, *Leishmania major*. Supported by: FAPESP, CNPq, CAPES.