Abstract

Topoisomerases are ubiquitous enzymes, involved in all DNA processes across the biological world. These enzymes are also targets for various anticancer and antimicrobial agents. The causative organism of amoebiasis, *Entamoeba histolytica* (*Eh*), has seven unexplored genes annotated as putative topoisomerases in AmoebaDB. One of the seven topoisomerases in this parasite was found to be highly upregulated during heat shock and oxidative stress. The bioinformatic analysis shows that it is a eukaryotic type IIA topoisomerase. Its ortholog was also highly upregulated during the late hours of encystation at both mRNA and protein levels in *E. invadens* (*Ei*), the encystation model of *Eh*. Immunoprecipitated endogenous EhTOPOII showed relaxation of negative supercoils and decatenation activity *in vitro*. During the early hours of encystation and glucose starvation, *Entamoeba* TOPOII was exported from the nucleus and degraded in the cytoplasm. The migration of *Entamoeba* TOPOII was mediated by a nuclear export protein, JAB1. Under glucose starvation, JAB1 was found to migrate to the nucleus, interact with TOPOII, and transport it to the cytoplasm. Silencing JAB1 impaired with the TOPOII migration under glucose starvation. A similar phenomenon was also observed during the early hours of encystation. Immunolocalization studies show that EiTOPOII colocalized with newly forming nuclei during encystation, which is a significant event in maturing cysts. Double-stranded RNA mediated down-regulation of the TOPOII both in *Eh* and *Ei* reduced the viability of actively growing trophozoites and also reduced the encystation efficiency in *Ei*. Drugs that target eukaryotic topoisomerase II, e.g., etoposide, ICRF193, and amsacrine, show 3-5 times higher EC_{50} in *Eh* than that of mammalian cells. Interestingly, inhibitors of prokaryotic DNA gyrase, like ciprofloxacin, showed about six times less EC_{50} value in *Eh* than that of human cells. The parasite's difference in susceptibility to various prokaryotic and eukaryotic topoisomerase drugs, in comparison to human cells, opens the scope to study this invaluable enzyme in the light of an antiamoebic target.