

ABSTRACT

Giardia is a unicellular parasitic organism; it is a worldwide cause of human diarrhea. It has minimalistic genome equipment and simplified molecular and metabolic pathways. In this respect, it is a suitable model organism for studying cell cycle regulation and to define the minimal genetic and protein equipment required for the functional reproduction of the eukaryotic cell. Its life cycle comprises of two stages; a pathogenic trophozoite and an infective cyst, which can survive in outer environment. New knowledge about encystation can be therapeutically important because this process is a target for vaccine and drug development. Since cell cycle analysis requires a synchronized population, we studied the effect of the synchronization drug aphidicolin on individual cell characteristics during the cell cycle of *Giardia* trophozoites. Our results showed that aphidicolin caused inhibition of DNA synthesis and trophozoites were aligned according to their DNA content in G1/S border. Subsequent inhibition of entry into mitosis and cytokinesis indicates, that *Giardia* has functioning DNA damage checkpoint. Extensive treatment with aphidicolin causes side effects. We detected positive signals for phosphorylated histone H2A which, in mammalian cells, is involved in a signaling pathway triggered as a reaction to double stranded DNA breaks. Reversibility of this posttranslational modification after inhibitor removal indicates that *Giardia* possesses DNA damage reparatory mechanisms. Aphidicolin treatment causes dissociation of the nuclear and cytoplasmic cycles. While DNA synthesis and entry to mitosis are stopped, the cytoplasmic cycle and its processes continue. We also focused on characterization of nuclear division during *Giardia* encystation with respect to cyst wall formation and flagellar apparatus arrangement. Nuclei are divided by semi-open mitosis in early phase of encystation in a precyst before cyst wall formation. After the karyokinesis, nuclei stayed in pairs and were interconnected with several inter-nuclear bridges formed by fusion of nuclear envelopes. Each interconnected nuclear pair is associated with one basal body tetrad of the undivided diplomonad mastigont.

Keywords: *Giardia intestinalis*, cell cycle, encystation, flow cytometry, mitosis