T. Cruzi dna polymerase beta (tcpolβ) is phosphorylated in vitro by ck1, ck2 and tcauk1 leading to the potentiation of its dna synthesis activity

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Abstract

The unicellular protozoan Trypanosoma cruzi is the causing agent of Chagas disease which affects several millions of people around the world. The components of the cell signaling pathways in this parasite have not been well studied yet, although its genome can encode several components able to transduce the signals, such as protein kinases and phosphatases. In a previous work we have found that DNA polymerase β (Tcpolβ) can be phosphorylated in vivo and this modification activates the synthesis activity of the enzyme. Tcpolβ is kinetoplast-located and is a key enzyme in the DNA base excision repair (BER) system. The polypeptide possesses several consensus phosphorylation sites for several protein kinases, however, a direct phosphorylation of those sites by specific kinases has not been reported yet. Tcpolβ has consensus phosphorylation sites for casein kinase 1 (CK1), casein kinase 2 (CK2) and aurora kinase (AUK). Genes encoding orthologues of those kinases exist in T. cruzi and we were able to identify the genes and to express them to investigate whether or no Tcpolβ could be a substrate for in vitro phosphorylation by those kinases. Both CK1 and TcAUK1 have auto-phosphorylation activities and they are able to phosphorylate Tcpolβ. CK2 cannot perform auto-phosphorylation of its subunits, however, it was able to phosphorylate Tcpolβ. Pharmacological inhibitors used to inhibit the homologous mammalian kinases can also inhibit the activity of T. cruzi kinases, although, at higher concentrations. The phosphorylation events carried out by those kinases can potentiate the DNA polymerase activity of Tcpolβ and it is discussed the role of the phosphorylation on the DNA polymerase and lyase activities of Tcpolβ. Taken altogether, indicates that CK1, CK2 and TcAUK1 can play an in vivo role regulating the function of Tcpolβ.