Loss of regulation of Cysteine synthetic pathway in Entamoeba histolytica

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Serine acetyltransferase (SAT) (EC 2.3.1.30) is the part of two step enzyme pathway that converts L-serine to L-cysteine. This pathway is found in bacteria, protozoa, yeast and plants. SAT is a hexameric molecule that binds with 2 dimers of O-acetylserine sulfhydrylase (OASS) and form a decameric cysteine synthase (CS) complex. This association also doubles up as regulatory mechanism to control the synthesis of cysteine. We have investigated the structures of SAT and OASS from protozoan Entamoeba histolytica and found that no CS complex formation takes place in this organism. The crystal structure of EhSAT in native as well in complex with its substrate L-serine and feedback inhibitor L-cysteine were solved and both molecules were seen binding to the same active site residues confirming the competitive inhibition. The EhSAT also remains in trimeric arrangement and does not form a hexamer. EhSAT and EhOASS does not interact with each other and thus the CS complex formation does not take place in E. histolytica [1]. The loss of regulation process from this pathway helps E. histolytica to better overcome the host oxidative stress and establish infection. E. histolytica have three isoforms for SAT and each one displays varying degree of feedback inhibition by cysteine making sure that the supply of cysteine is never short as it plays the role of main anti-oxidant for the protozoan parasite. The computational and subsequent site directed mutational studies proved that the organism has modified these isoforms of SAT for better counter of the oxidative stress [2]. Therefore this pathway presents a crucial target for drug related studies.


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