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Amino acid and polyamine membrane transporters in Trypanosoma cruzi: Biological function and evaluation as drug targets.

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Abstract

Amino acids and polyamines are involved in relevant processes for the parasite Trypanosoma cruzi, like protein synthesis, stress resistance, life cycle progression, infection establishment and redox balance, among others. In addition to the biosynthetic routes of amino acids, T. cruzi possesses transport systems that allow the active uptake from the extracellular medium; and in the case of polyamines, the uptake is the unique way to obtain these compounds. The TcAAAP protein family is absent in mammals and its members are responsible for amino acid and derivative uptake, thus the TcAAAP permeases are not only interesting and promising therapeutic targets but also could be used to direct the entry of toxic compounds into the parasite. Although there is a treatment available for Chagas disease, its limited efficacy in the chronic stage of the disease, as well as the side effects reported, highlight the urgent need to develop new therapies. Discovery of new drugs is a slow and money-consuming process, and even during clinical trials the drugs can fail. In this context, drug repositioning is an interesting and recommended strategy by the World Health Organization since costs and time are significantly reduced. In this article, amino acids and polyamines transport and its potential as therapeutic targets will be revised, including examples of synthetic drugs and drug repurposing.

KEYWORDS: Chagas disease.; Trypanosoma cruzi; amino acid transport; drug repositioning; drug discovery; new therapies; polyamine transport; therapeutic target

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