

L-threonine 3-dehydrogenase protects *Trypanosoma cruzi* from genetic damage and oxidative stress

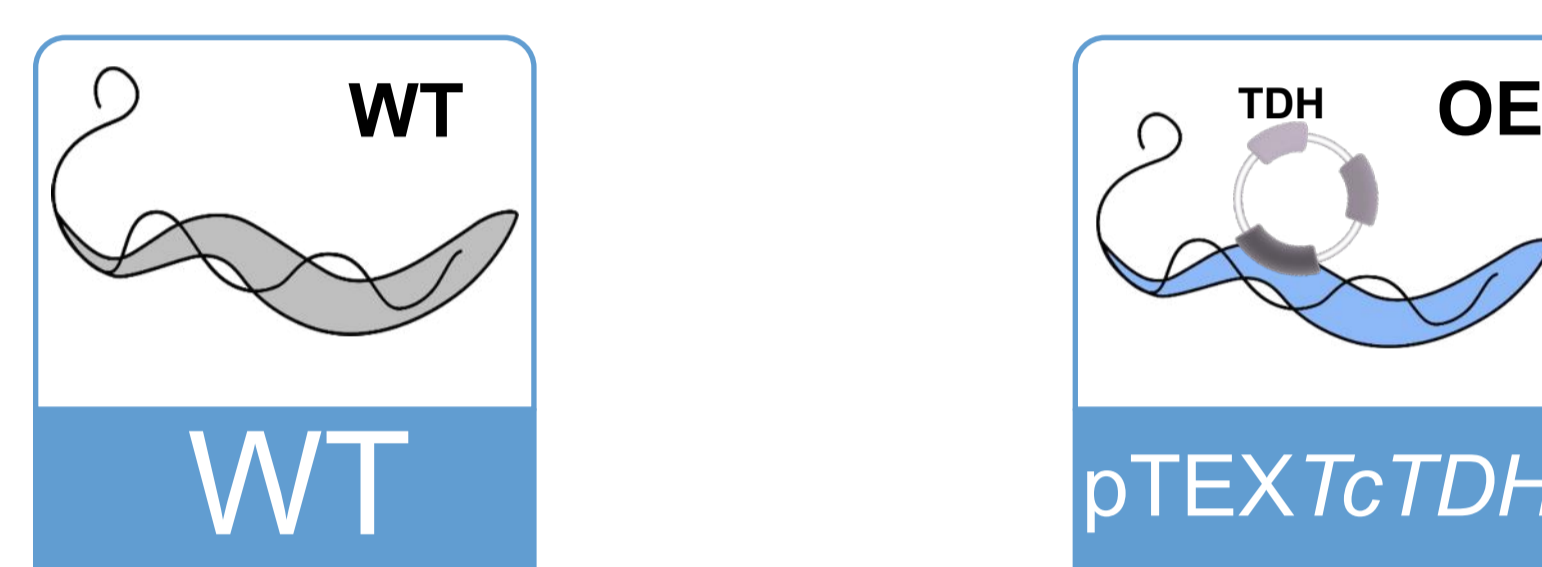
Paola García-Huertas¹, Ana María Mejía-Jaramillo¹, Carlos Renato Machado², Omar Triana-Chávez^{1*}

¹Biología y Control de Enfermedades Infecciosas-BCEI, Universidad de Antioquia, Medellín, Colombia.
²Departamento de Bioquímica e Inmología, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

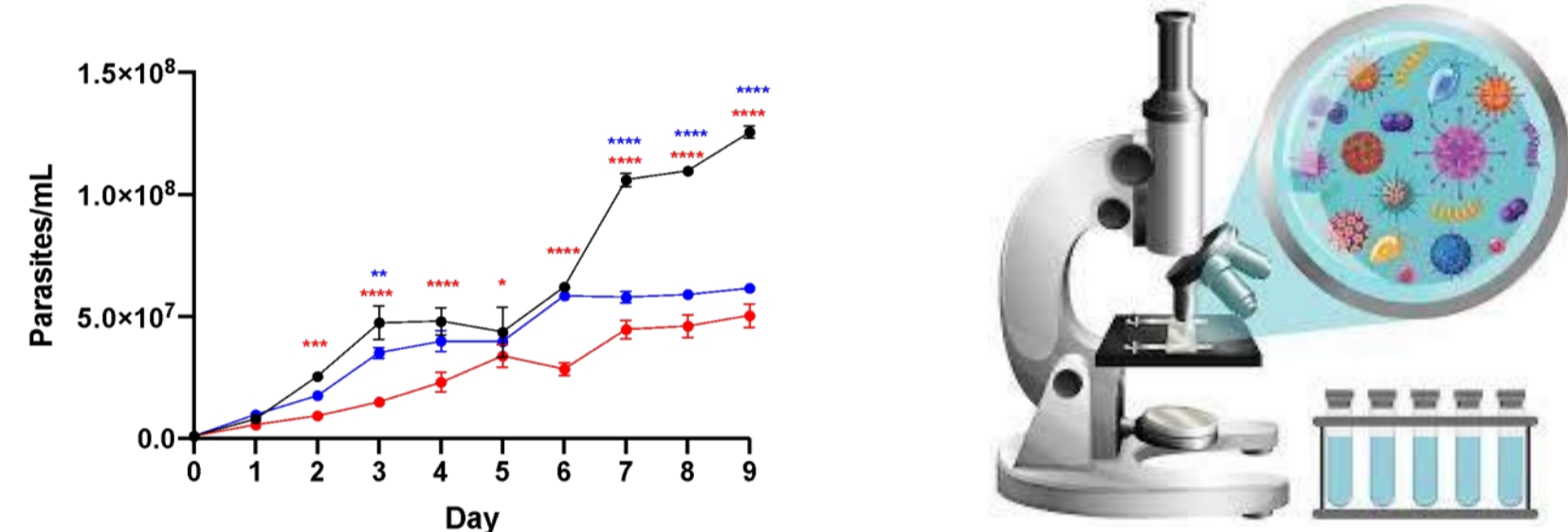
INTRODUCTION

Benznidazole and nifurtimox are the front-line drugs used to treat *Trypanosoma cruzi* infections. The resistance of *T. cruzi* to these drugs has been reported as one of the leading causes of treatment failure against Chagas disease. L-threonine 3-dehydrogenase (TDH) plays an essential role in L-threonine catabolism. It catalyzes the NAD(P)+-dependent oxidation of L-threonine to 2-amino-3-oxobutyrate, a precursor in glycine and acetyl-coenzyme A production. Recently, TDH was found overexpressed in benznidazole-resistant parasites and was classified as exclusive in resistant parasites. Here, we characterized the TDH protein by overexpressing the gene in *T. cruzi* epimastigotes and studied different genetic and biological features.

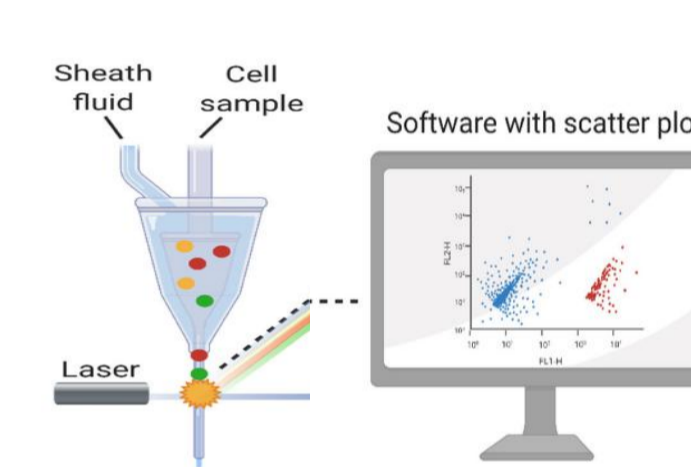
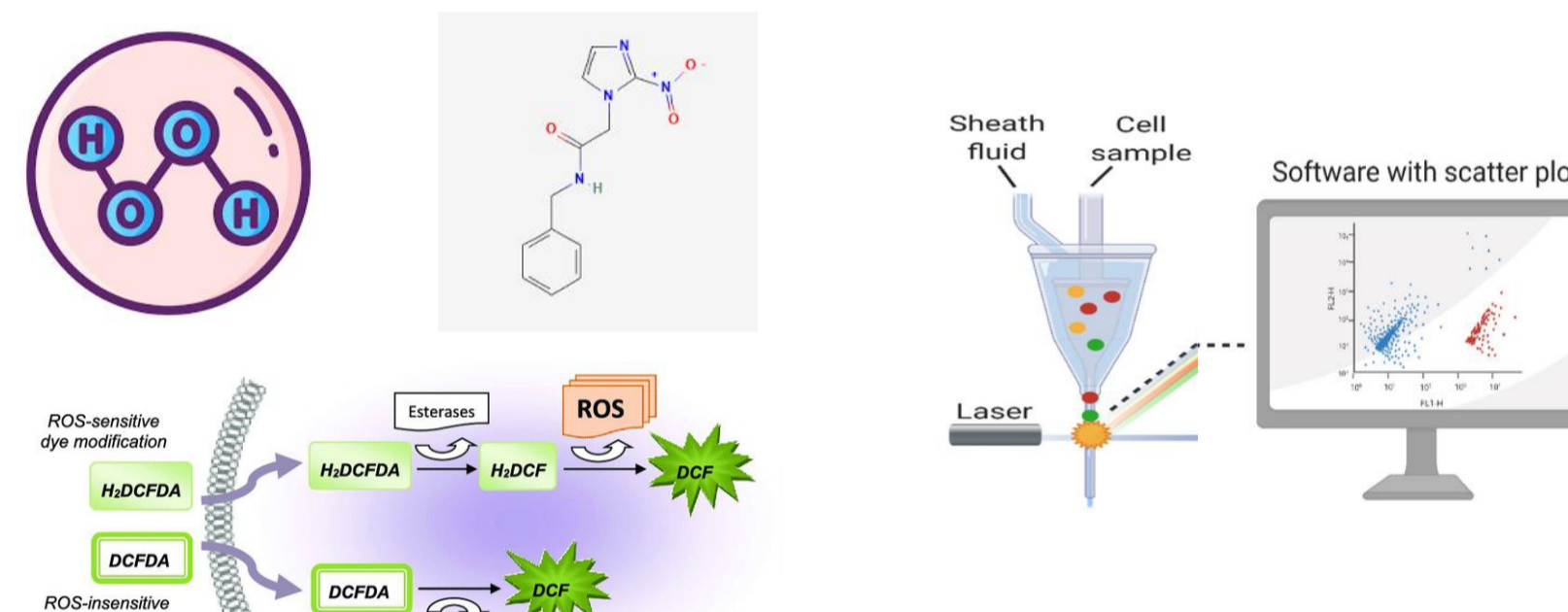
METHODOLOGY



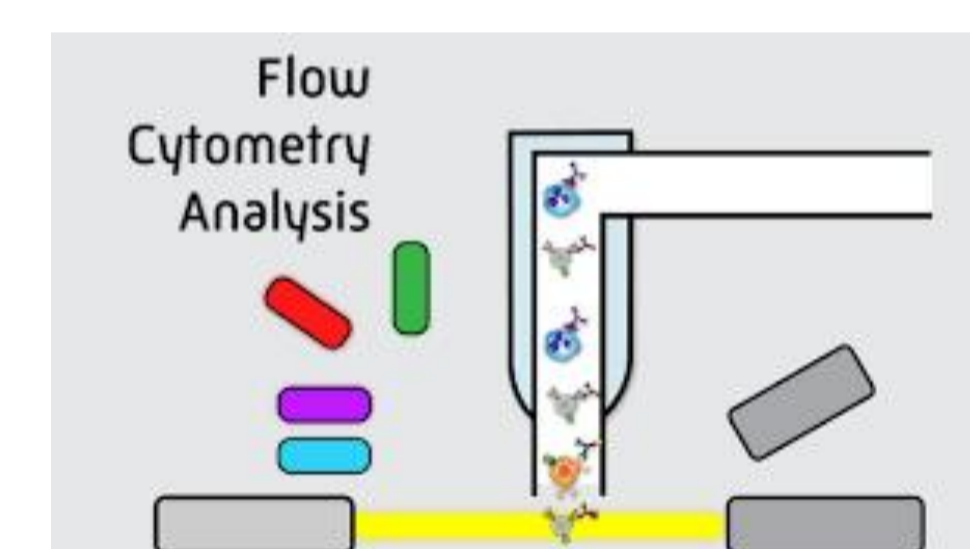
1. Growth curves and cell infection



2. Response to ROS and Benznidazole

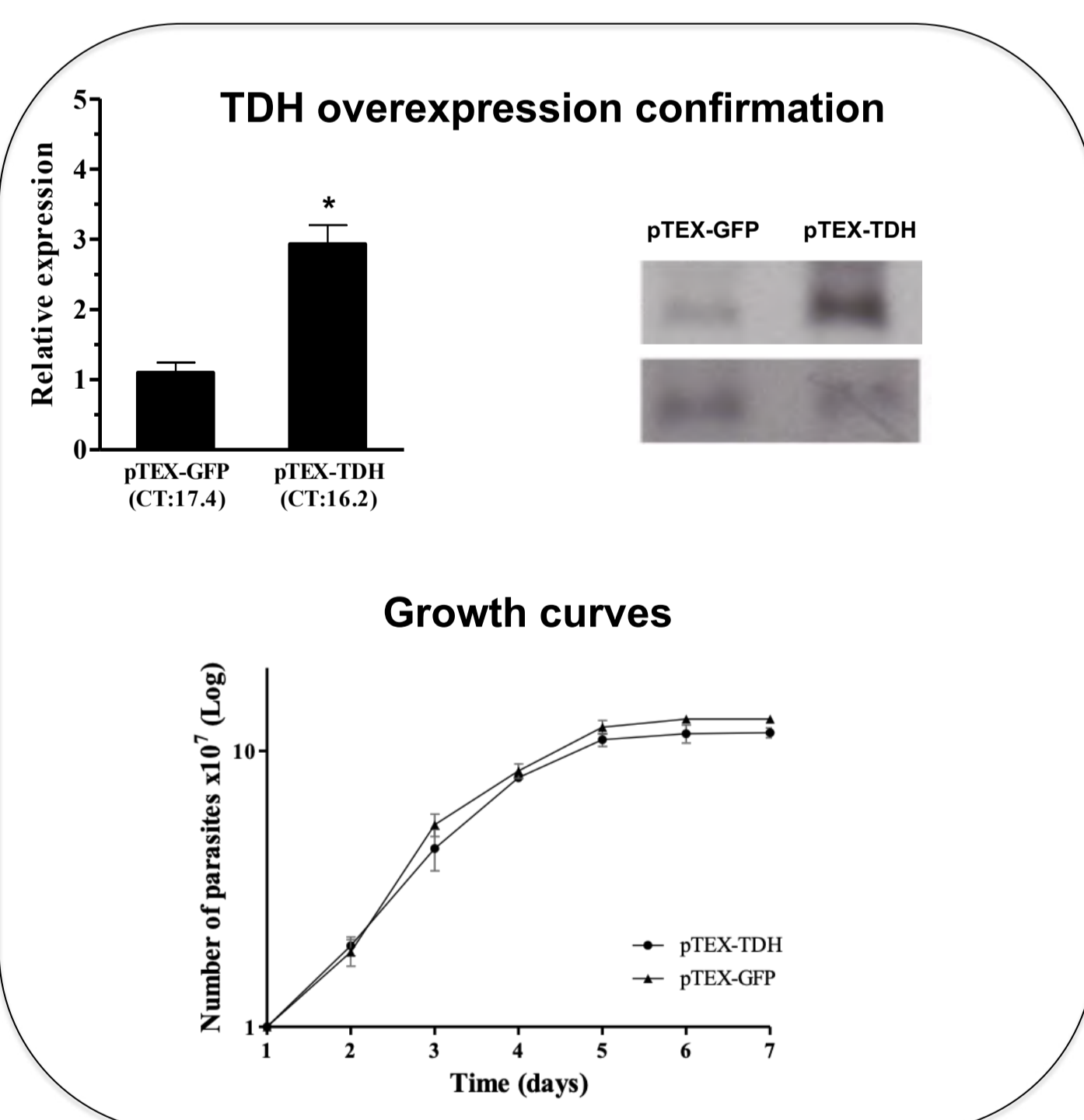


3. Mitochondrial potential and genetic damage

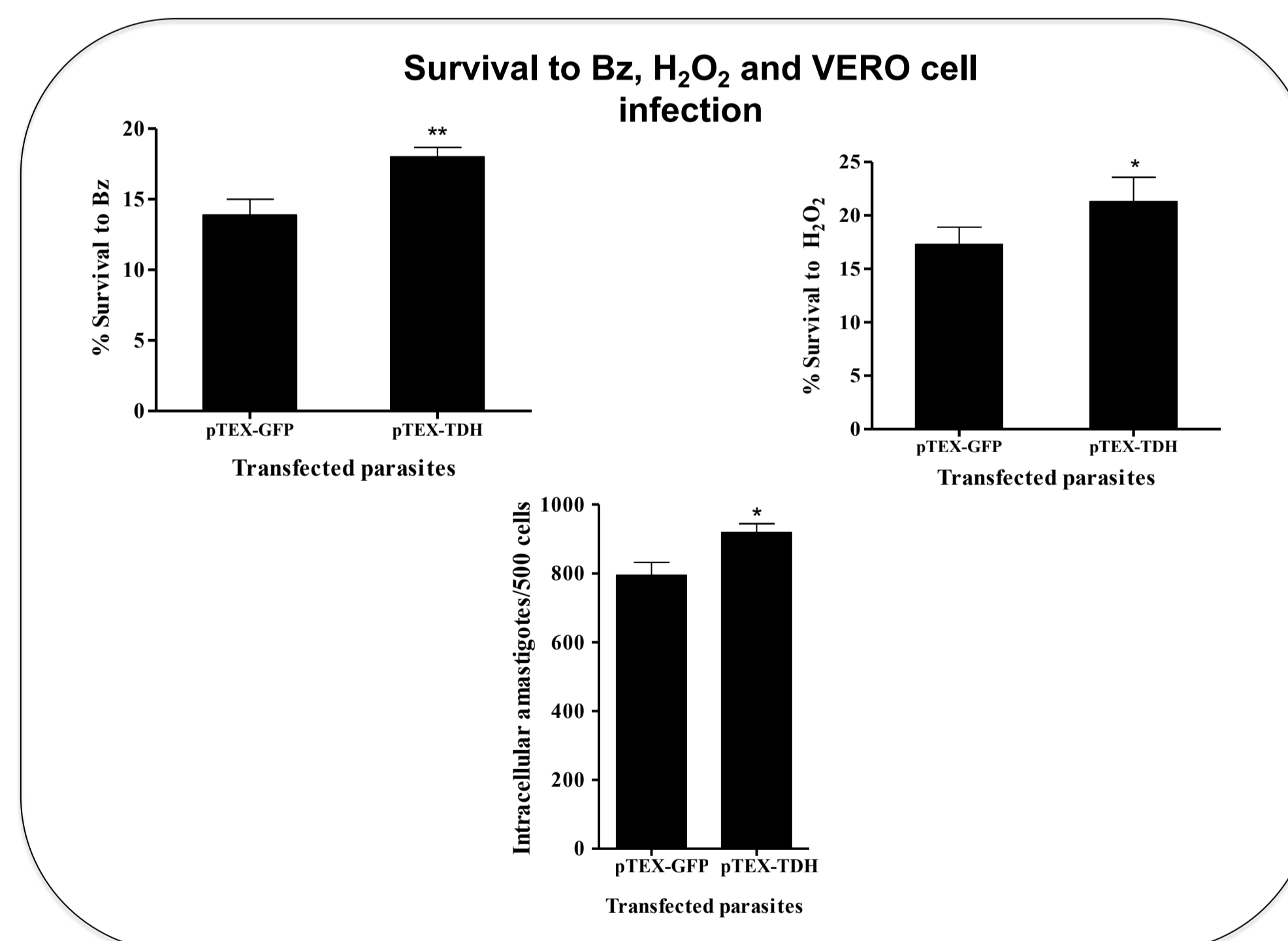


RESULTS

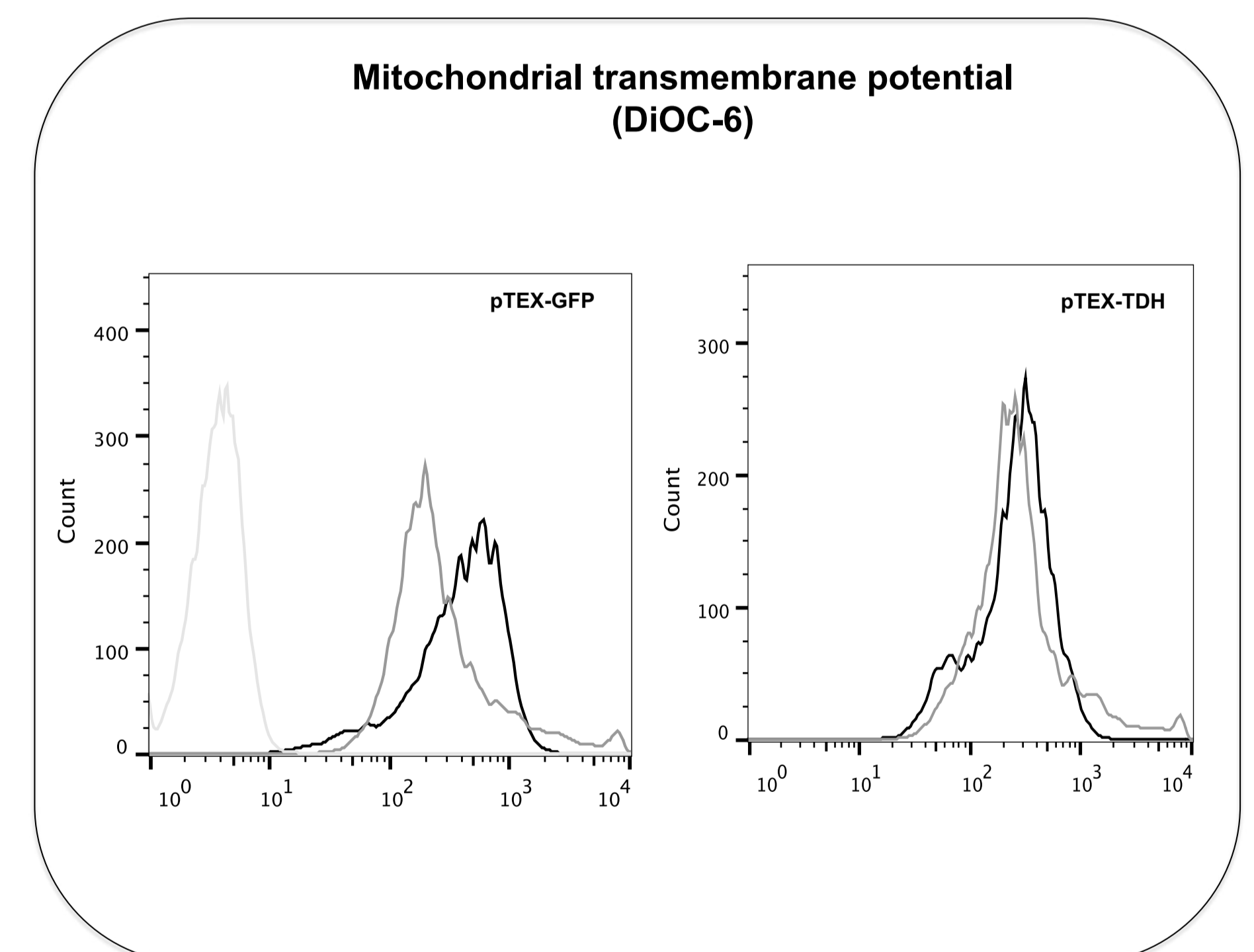
TDH Overexpression do not affect the growth curve



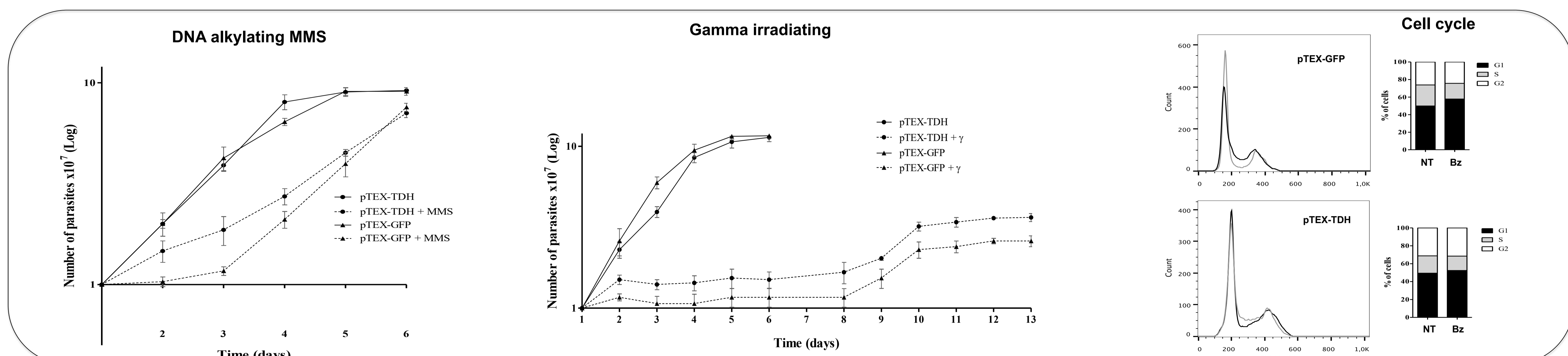
TDH produces more resistance to Bz and H₂O₂



TDH recovery the mitochondrial membrane potential



TDH protects against DNA alkylating agents and Gamma irradiation



CONCLUSION

We propose that TDH has a protective effect on oxidative stress and genetic damage caused by Bz, as well as on the impact of compounds such as H₂O₂, MMS, and gamma radiation. Likewise, we support that the Bz acts through the induction of oxidative stress and genetic damage in *T. cruzi*.