Carvedilol inhibits *Trypanosoma cruzi* autophagic pathway affecting parasite replication and survival.

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Introduction

Chagas disease is caused by the protozoan parasite *T. cruzi*. Pathogenesis of Chagas heart disease (CHD) involves low-grade incessant systemic infection and triggered autoimmune reaction. Cruzipain is a key virulence factor of *T. cruzi*.

Autophagy is an intracellular pathway that can affect survival and/or virulence of parasites. A recent study showed that Carvedilol (Carve) was effective to reduce oxidative damage in CHD. K777 is a Cruzipain inhibitor with antiproliferative effect on *T. cruzi* but hepatotoxic. A virtual screening of K777-similar structures selected Carve as a candidate (Novick P. and Trosin S. Stanford University, USA). Although Carve didn’t inhibit Cruzipain, we observed some effect of Carve on *T. cruzi* autophagy and continued studies in this regard.

Results

1- Carvedilol affects proliferation of *T. cruzi* epimastigotes (p<0.001).

2- Carvedilol affects proliferation of *T. cruzi* amastigotes inside host cells (p<0.001).  

![Graph showing Carvedilol affects proliferation of T. cruzi epimastigotes](image)

3- Carvedilol displays abnormal vacuolization and accumulation of multivesicular structures in *T. cruzi*.

4- Carvedilol induces autophagosome accumulation and inhibits lysosomal degradation in *T. cruzi*.

![Graph showing Carvedilol affects proliferation of T. cruzi amastigotes](image)

Conclusions

- Carve inhibits proliferation of *T. cruzi* axenic epimastigotes and intracellular amastigotes.
- Carve affects the *T. cruzi* autophagic pathway leading to accumulation of autophagic non-degradative compartments affecting its growth and vitality.
- This study shows that Carve has a direct effect on *T. cruzi* and should be explored as a possible treatment for CHD.

Acknowledgements

Rivero Cynthia thanks to UNO Medios Foundation for travel funding.  
Romano Patricia thanks to CONICET, ANPCyT and SeCyT-UNCUYO for funding.