SINGLE-DOMAIN LLAMA ANTIBODIES INHIBIT RECOMBINANT TRANS-SIALIDASE ACTIVITY OF *TRYPANOSOMA CRUZI*

Ratier, L.[1*], Urrutia, M.[2*], Paris, G.[2], Zarebski, L.[2], Frasch, A. C.[1] and Goldbaum, F. A.[2]

[1]Instituto de Investigaciones Biotecnológicas-Instituto Tecnológico de Chascomús (IIB-INTECH), UNSAM-CONICET, Buenos Aires, Argentina;
[2]Instituto Leloir, CONICET, Buenos Aires, Argentina

* Boths authors contributed equally to this manuscript.

Trypanosoma cruzi, the causal agent of Chagas' disease, expresses trans-sialidase (TcTS) in its surface, which is a relevant factor in cell invasion and pathogenesis. Although TcTS is a potential target for the development of chemotherapeutic agents, effective inhibitor compounds are not available. Single domain camelid antibodies (VHHs) are promising sources of new enzymatic inhibitors. Llamas were immunized with recombinant TcTS (rTcTS), VHHs fragments were obtained by phage display and were screened by TcTS inhibition assay. Four VHHs displayed strong rTcTS inhibition capacity with affinities between 26-86 nM. They share the CDR3 length (17 residues) and have very similar sequences, showing a unique structural solution for tight binding to the rTcTS. These antibodies bind an epitope closer or overlapped with the active site. Despite the fact that selected VHHs clearly inhibit rTcTS, they were unable to inhibit TcTS isolated from trypomastigotes. Since active TcTS from trypomastigotes is produced from a high number of genes and all of them share the active site with rTcTS, we suggest that post-translational modifications or point mutations near to the catalytic centre could explain the lack of inhibition of the natural enzyme.

Keywords: VHHs; Trans-sialidase; *T. cruzi*;