THE CONSERVED FLY DOMAIN OF THE GP85/TRANS-SIALIDASE FAMILY FACILITATES INFECTION BY *TRYPANOSOMA CRUZI* AND MODULATES HOST IMMUNE RESPONSE *IN VIVO*.

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Trypomastigote forms of *T. cruzi* are coated with glycoproteins of the gp85/trans-sialidase superfamily, all members containing the FLY sequence (VTVXNVFLYNR) at the carboxyl terminus. This sequence binds *in vitro* to cytokeratin 18 (CK18) on the surface of LLC-MK_2 cells increasing parasite entry. The effect of the FLY sequence was investigated in mice pre-inoculated with the corresponding synthetic peptide and intra-peritoneally challenged with *T. cruzi* bloodstream forms. Animals pre-treated with FLY showed a 2-fold higher parasitemia and increased mortality rates in comparison with infected mice treated with control peptide (FAY) or PBS. Analysis of tissue sections revealed amastigote nests in almost all tissues analyzed, irrespective from pre-treatment with FLY, FAY or PBS. Nonetheless, FLY-treated animals showed an increase in amastigote nests in heart, bladder and intestine. Mice treated with FLY displayed diffused inflammation with rare inflammatory foci in all tissues studied in contrast with control mice. Analysis of cytokine secretion in the spleen of mice pre-treated with FLY and infected with *T. cruzi* revealed a decrease of the pro-inflammatory cytokine IL-12 and an increase in TNF-α. Together, our data suggest a FLY-mediated mechanism of susceptibility to *T. cruzi* that may be dependent on TNF-α and IL-12 production.

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