Antibodies produced against the catalytic domain of congopain complexed with α_2-macroglobulin inhibit congopain activity

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The protozoan parasite *Trypanosoma congolense* causes trypanosomosis in cattle. The major lysosomal cysteine proteinase of T. congolense, congopain, contributes to pathogenesis of the disease, and antibody-mediated inhibition of this enzyme may contribute to mechanisms of trypanotolerance[1]. Congopain has thus been identified as an anti-disease vaccine candidate. The vaccine potential of congopain was evaluated in the present study by producing antibodies in rabbits against the catalytic domain of congopain, called C2. To this end the adjuvant potential of bovine and rabbit α_2-macroglobulin (α_2M) was investigated[2]. Inhibition of congopain activity by these antibodies was assessed[3].

C2 interacted with α_2M, producing bait region cleavage visualised by SDS-PAGE, and congopain activity was inhibited. Recombinant C2 was used to immunise rabbits with Freunds adjuvant, or complexed with bovine or rabbit α_2M. Rabbits immunised with C2 and Freunds adjuvant produced sustained anti-C2 antibody titres. Antibodies produced at different times enhanced or inhibited C2 and congopain activity against Z-Phe-Arg-NHMec, with maximum inhibition of 40%. Rabbits receiving C2-α_2M complexes produced initial anti-C2 antibody titres comparable to those obtained using Freunds adjuvant, but these titres were not sustained over the immunisation period. These antibodies inhibited 65% of C2 and congopain activity against Z-Phe-Arg-NHMec.

Immunisation of rabbits with C2 complexed to either rabbit or bovine α_2M led to the production of antibodies that were better able to inhibit the activity of C2 and congopain in vitro. Immunisation of cattle with C2 complexed to bovine α_2M therefore has the potential to neutralise congopain, thus constituting an anti-disease vaccine against African trypanosomosis.

[1]Authie E, Boulange, A, Muteti DK, Lalamanch, G, Gauthier, F and Musoke, AJ. (2001) Immunisation of cattle with cysteine proteinases of *Trypanosoma congolense*: targeting the disease rather than the parasite. Intl. J. Parasitol. 31, 1429-1433. [2]Cianciolo, G. J., Enghild, J. J. and Pizzo, S. V. (2002) Covalent complexes of antigen and α_2-macroglobulin: evidence for dramatically-increased immunogenicity. Vaccine 20, 554-562. [3]Troeberg, L, Pike, R.N., Lonsdale-Eccles, J.D and Coetzer, T.H.T. (1997) Production of anti-peptide antibodies against trypanopain-Tb from *Trypanosoma brucei brucei*. Effects of antibodies on enzyme activity against Z-Phe-Arg-NHMec. Immunopharm. 36, 295-303.