RELATIONSHIP OF PARASITE SPECIFIC ANTIBODIES AND HEART SPECIFIC AUTOANTIBODIES IN MICE INFECTED WITH TRYPANOSOMA CRUZI.

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Immunization of inbred mice with the Corpus Christi strain of T. cruzi increases resistance to Brazil strain challenge as indicated by enhanced survival in C3H and lowered parasitemia in C3H and C57 mice. Previous adoptive transfer studies have shown this protection is a B cell mediated phenomenon. Mice which survive acute infection develop characteristics of cardiac histopathology, such as inflammation, muscle necrosis and connective tissue replacement, up to day 300 post infection. Examination of parasite immunogen specific antibodies in the sera from these mice by Western Blot analysis reveals reactions to a variety of parasite extract antigens. Of interest, sera from mice surviving acute infection consistently show a strong reaction to a 75-77 Kd glycoprotein suggesting a protective function.

To examine the presence of autoantibody in the antisera, an ELISA was performed using normal syngeneic cardiac tissue extract as the target antigen. Sera from C3H and C57 mice contain anti-heart antibodies during acute and chronic infection. The specificity of this response was indicated by C3H sera reacting with cardiac and striated but not smooth muscle preparations, and C57 sera reacting only with cardiac muscle. This autoantibody reactivity consists of both IgG and IgM isotypes throughout infection. Immunoaffinity purified heart-specific antibodies were found to cross-react with parasite extract in an ELISA. The use of these purified antibodies in Western Blots indicated that they do not bind to the 75-77 Kd antigen of the parasite extract. The specific heart antigens bound by the mouse antisera were shown to be a 150, a 120 and, most prominently, a 67 Kd polypeptide by SDS PAGE examination. The possibility that the autoantibodies were directed toward the beta adrenergic receptor, also reportedly 67 Kd, was examined using Turkey erythrocytes (TRBC), which are rich in beta receptors. Infected mouse sera was found to react strongly with TRBC in ELISA. Similarly, adsorption of this sera with TRBC reduced its reactivity to heart extract. Addition of the beta blocker alprenolol inhibits antisera binding to TRBC and heart extract in a dose dependent manner. Similar results found with sheep RBC controls suggested a carbohydrate moiety as the target of the autoantibodies. The involvement of carbohydrates was further indicated by the ability of N-acetylglucosamine or galactose to decrease the binding of the mouse antisera to heart, TRBC or parasite antigens. Similarly, the cleaving of carbohydrate from heart extract by N-glycanase treatment resulted in a reduction of antisera binding in ELISA.

The results suggest that some of the autoantibodies present in the infected mice are directed against a carbohydrate epitope on a heart protein, perhaps the beta adrenergic receptor. This glycosylation is likely similar to one found on a nonprotective T. cruzi glycoprotein, which induces the production of the cross-reactive autoantibodies during infection. This work is supported by NIH grant AI 23704.