FILARIAL ANTIGENS : TARGETS FOR DIAGNOSIS, PROTECTION AND PATHOLOGY

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ABSTRACT

A range of surface, secreted and somatic antigens from filarial parasites have been studies in order to analyse the response of human infected with these pathogens, and to develop reliable diagnostic and prophylactic agents. Diagnostic procedures, which are urgently required for targetting chemotherapy, are being developed by two techniques. Firstly, detection of host antibody is carried out using selected, specific parasite antigens in the form of recombinant peptides from a filarial DNA library. Secondly, measurement of parasite by a monoclonal antibody "antigen-capture" assay. In addition, a longer-term objective of our collaborative study is to isolate molecules which may stimulate the immune system to mount a protective immune response against filarial parasites. A major focus has been a parasite surface glycoprotein known to be closely conserved between adult worms of *Brugia malayi, B. timori* and *Wuchereria bancrofti*. This antigen has been cloned from a cDNA library, and its primary sequence established; in addition to being a constant feature of the adult surface, it is expressed by developing larvae and represents an attractive target for vaccine production. Finally, one of the most intriguing questions in filariasis relates to the genesis of pathological reactions. Although this is a difficult problem, we are now beginning to compare the immune responses of individuals of differing clinical status to certain defined parasite antigens, in an attempt to correlate disease development with particular categories of immune response in infected patients. In this way there is hope to advance the basic understanding of filarial disease, while providing practical means for controlling filariasis at the individual and community levels.

QUESTIONS AND ANSWERS :

1. Question: What do you think about chyluria patients ?
   Can we use your technique (two site ELISA) to differentiate filarial patients from non filarial patients by utilizing their urine ?

   Answer : The two site ELISA should be tested in these patients. Other investigators have reported circulating antigen in urine of filarial patients, and levels of antigen in urine may be higher in individuals with lesions causing chyluria.

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2. Question: As P.C. is produced by other nematodes how would this be excluded when the test is used in areas where other nematodes than filarids also exists ?

   Answer : This is the most critical question, but surprisingly few problems have arisen in our and others' studies measuring PC antigens. However, for this reason I am suggesting that the PC test should not be used as the sole diagnostic criterion.

3. Question:
   1. Dealing with the immunological diagnosis, what kind of relationship did you observe in respect to the disease stage ? Didn't it influence the detection of circulating Ag ?
   2. What is the current status of the role of cell mediated immunity ?
   3. What is the significance of the recombinant antigen which were recognized only by Mf negative?

   Answer :
   1. All microfilaremic cases were strongly antigen positive, but not all individuals with filarial symptoms but without microfilariae showed circulating antigen. Presumably these were cases where the infection had gone but lesions persisted. In addition some asymptomatic, amicrofilaraemic "endemic normals" were antigen-positive, presumably reflecting an occult infection.
   2. We are only just beginning to examine the T cell populations in filariasis. Perhaps the greatest advance in this area has been reported by Dr.T. Nutruan of the NIH, USA : he found T cells from microfilaraemics were specifically *less* responsive to parasite antigens compared to T cells from endemic normals.
   3. If an antigen were consistently recognized by amicrofilaraemics but not by microfilaraemics, it may be implicated in antibody-dependent clearance of microfilariae. However, we found that individuals varied significantly in all anti-peptide responses so that no single correlation between antigen recognition and carrier status emerged.

4. Question: In view of the presence of considerable crossreactivity in filariasis sera, how much of this response could be due to polyclonal immune response(s) (eg.antibody) and how could such "upscale" regulation of the immune response impact on sorting out the "best"peptides/epitopes for serology.

   Answer : These does not appear to be nonspecific, polyclonal immune activation in filariasis, and in fact microfilaraemic individuals often show very low antibody responses. Otherwise, a generalised stimulation would certainly obscure any analysis of responses to single peptide epitopes.