

Effective immunization against gastrointestinal helminth infections with cDNA and/or recombinant protein of parasitic proteases

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Gastrointestinal helminths are responsible for enormous health problems and economic losses throughout the world. Chemotherapy is at present the major way of controlling these infections, however, recently the treatment has been less efficient because of the development of populations of parasitic helminths with resistance to one or more anthelmintics and this process is increasing worldwide. Therefore, in many laboratories intensive research is conducted on development of defined and effective anti-helminth vaccines.

The identification of host protective antigens represents one of the key areas of vaccine development, especially for such complex parasitic organisms as helminths. Good candidates for vaccine antigens, which would be effective against gastrointestinal helminths, seem to be cysteine and aspartic proteases. These powerful enzymes play an important role in the physiology of parasitic helminths and are responsible for various specific functions including: invasion and migration through a host, facilitation of feeding by inhibition of blood clot formation and by transformation of host tissues, cells and macromolecules into nutrients essential for parasite metabolism, evasion of host immune responses by down regulation/inhibition of effector mechanisms. The challenge is to develop a vaccine, which will neutralise the biological activities of these molecules thereby disarming the parasites' survival strategies, and impairing their capacity to survive and/or enabling the host to remove the worms through protective immune responses.

Results obtained so far in our laboratories indicate that one of the cysteine proteases of *Fasciola hepatica* which we have cloned, may induce a considerable level of protection against infection with the trematode. Mean worm burdens found in rats vaccinated intranasally with cDNA of the cysteine proteinase 5 or 10 weeks after the infection were reduced by 61-75% in comparison to the non vaccinated challenge controls, which suggests that intranasal vaccination with CPcDNA may protect hosts against *F. hepatica* infection. Also, vaccination with recombinated cysteine proteinase of the liver fluke expressed in *E. coli*, in the form of inclusion bodies, administered intragastrically to rats produced a high level of protection to subsequent infection with metacercariae of the fluke.

We also cloned cDNA of a novel aspartic protease from *Ancylostoma ceylanicum* a blood sucking nematode inhabiting the gut of many animals and humans. Immunization of laboratory hosts with *Ace-apr-1*/pCDNA 3.1, performed by lipotransfection of the nasal mucosal surface, resulted in a clear reduction in worm burden after the challenge infection in comparison to not vaccinated hosts. A slightly lower level of protection was achieved following immunization with the recombinant enzyme expressed in bacterial or eukaryotic expression systems.

We may conclude that advances in parasite genomic and new vaccine delivery systems gave a hope that genetically engineering anti-helminth vaccines will appear on the market in the not too distant future.