EXPERIMENTAL APPROACHES TO STUDYING THE IMMUNOLOGY OF PARASITIC DISEASES

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OVERVIEW AND BACKGROUND INFORMATION

The immune system plays a central role in recognizing and controlling the spread and impact on the host of infectious organisms. In the case of parasitic infections this task is complicated by the fact that many eukaryotic parasites have evolved sophisticated mechanisms for evading the immune response. Consequently, many diseases caused by parasites are chronic in nature and result in prolonged and excessive immune responsiveness which in itself can be deleterious. The study of immune responses to parasites has been important not only because of the potential for improving human and animal health through immunological means such as vaccination, but also because the extreme nature of many parasite-induced responses allow insights into the functioning of the immune system itself.

The immune system
The immune response is initiated by a series of cells that include dendritic cells, macrophages, neutrophils, and natural killer (NK) cells and, which are capable of detecting and responding to foreign organisms such as parasites. The recognition occurs through various pattern recognition receptors, which either directly or indirectly in collaboration with the complement system recognize molecular structures not normally found in mammals. This early
innate response is complex and involves the expression by the responding cells of new surface and soluble molecules that serve two key functions. First, through inflammatory cascades they limit the growth and spread of the organism, and second, they play a central role in initiating the adaptive, highly specific immune response by B and T lymphocytes. These cells proliferate and differentiate and produce the molecules, antibodies (Ab) and cytokines, which act to neutralize or destroy the parasite while at the same time controlling the magnitude, longevity and nature of the immune response itself. Since many of the molecules produced by T cells or by other cells in response to signals from T cells are toxic, they can also directly cause pathologic changes. The successful response combines the production of the appropriate Ab and or cytokines to kill or at least control the parasite, with concomitant regulatory elements that prevent overt host damage.

EXPERIMENTAL APPROACHES

Different parasites elicit different types of responses
Being such a varied group of protozoan and metazoan organisms with intra- and extracellular habitats, parasites elicit the entire range of immune responses. Consequently, we have made some attempt to be comprehensive in terms of the techniques that we utilize on the Course. However, due to the nature of our own research programs, we have tended to focus on contemporary assays of innate and T cell mediated immunity and it is on these techniques that we will concentrate here.

Immune response induction
We have examined innate and early adaptive immune responses to *Leishmania major* and *Schistosoma mansoni*, and the immune response and immunopathology that develops during established infection with these pathogens. For analysis of early responses, we generally inject parasites either subcutaneously (s.c.) into the rear footpad and examine responses in the draining popliteal lymph nodes (LN), or inject parasites intraperitoneally (i.p.), and subsequently recover cells from the site of infection using peritoneal lavage. For infection studies, we often analyze the immune response ongoing in the spleen, or if the site of infection is clearly demarcated (as for example is the case in *L. major* infected mice, where parasites have been injected into the footpad), the draining LN. We have also removed sites of infection or areas of parasite-induced pathology and analyzed immune responses in these sites.