Subversion of immune cell signalling by parasites

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Preface

One of the most studied fields within the discipline of parasitology in the 20th century was immunoparasitology. Although the work undertaken extended into areas such as immunodiagnosis, the main emphasis was on understanding the interaction between the host immune system and the invading parasite in order that information could be gained that would aid parasite control and hence improve human health. Ultimately, the goal was to produce safe and effective vaccines against diseases such as malaria and schistosomiasis. This has proved much more difficult than originally anticipated but a wealth of data was generated some of which can help us understand the difficulties associated with vaccine development. For example, we came to learn of parasite immune system evasion strategies, including fascinating mechanisms such as acquisition of host antigens in schistosomes and antigenic variation in trypanosomes. However, an alternative approach to successful parasitism, rather than to avoid the host immune system, is to actually target it for manipulation. Eukaryotic parasites have proved equally adept at this.

A strategy facilitating survival that has been described for virtually every form of eukaryotic parasite in which it has been sought is the induction of some form of 'immunosuppression'. This term tends to be used by immunoparasitologists when some form of impaired immune response has been witnessed. Its possible existence has been remarked on since the beginning of the 20th century when it was observed that people infected with eukaryotic parasites often appeared more susceptible to bacterial infections or were more difficult to vaccinate. Furthermore, numerous studies, some going back many years, have shown that animals infected with eukaryotic parasites, demonstrate impaired immune responses to heterologous antigens. Analysis of the mechanisms underlying these defects has revealed that a number of effector mechanisms of the immune system are targeted and indeed the identity of particular cells that are affected has been reported.

This supplement is specifically concerned with the actions parasites must take to control the activities of cells of the host immune system. However, whereas in the past research has been concerned with measuring the effect of parasites on immunological parameters, advances in biochemistry and cell biology in the last two decades have permitted a molecular dissection of the functionalism of cells. The main focus here is thus on how parasites have evolved strategies to subvert the pathways that immune system cells employ to transduce signals pertinent to parasite elimination.

The six articles that the supplement contains were produced by speakers (and their colleagues) at the 2004 British Society for Parasitology Autumn Symposium on 'Subversion of immune cell signalling by parasites'. The first article by Goodridge and Harnett (M.) represents an introduction to the topic by familiarising readers with the principles of intracellular signal transduction and outlining the major immune signalling pathways triggered following the ligation of antigen receptors, cytokine receptors and Toll-like receptors (TLRs). It thus gives an overview of the cellular targets for subversion by parasites. The next article by Haga and Bowie is concerned with subversion of immune cell signalling in a very well defined system, *Vaccinia* virus. By taking note of what has been learned in such a system, parasitologists may acquire ideas of relevance to studying their own particular parasites. The remainder of the chapters focus on immune subversion mechanisms employed by eukaryotic parasites. Gregory and Olivier write on inhibition of macrophage signal transduction, describing a role for the host tyrosine phosphatase SHP-1 in the induction of macrophage

Parasitology (2005), **130**, S1–S2.
doi:10.1017/S0031182005008334 Printed in the United Kingdom

dysfunction by *Leishmania* parasites. Langsley and colleagues discuss the reversible transformation of host lymphocytes by *Theileria* parasites and the roles that casein kinase II may play in this. Schofield and colleagues focus on the malarial GPI toxin and its interaction with host receptors. Structural requirements for interaction are discussed and the role of TLR-2 as a receptor highlighted. In the last article, Harnett (W.) and colleagues describe how the filarial nematode-secreted product ES-62 modulates the activity of various cells of the immune system by selectively targeting signal transduction pathways involved in activation, proliferation and polarisation.

Finally, I would like to thank the following people: all the presenters at the symposium and/or authors who agreed to write the articles; Les Chappell in his role as co-ordinator for the supplement; the accommodating staff at the Linnean Society where the meeting was held, members of the Harnett labs for their assistance on the day and each of Active Motif, Cambridge University Press, Miltenyi Biotec, Pfizer Ltd. and 'Trends in Parasitology' for financial support.

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May 2005

https://doi.org/10.1017/S0031182005008334 Published online by Cambridge University Press