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Current Opinion in Microbiology

Trying to get rid of protozoan parasites

Editorial overview

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Hugo D Lujan is a full professor of biochemistry and molecular biology at the School of Medicine, Catholic University of Cordoba, and director of the Center for Research and Development in Immunology and Infectious Disease of the National Council for Science and Technology of Argentina (CONICET). His principal research interest focuses on the adaptive mechanisms developed by the intestinal parasite *Giardia lamblia* to survive both inside and outside its host.

Over the last few decades, extensive scientific research has been focused on the molecular and cellular mechanisms controlling host–parasite interactions. A recurrent topic of interest among microbiologists is the fascinating ability of parasitic organisms to adapt to changes in their environment. Most parasites inhabit different niches during their life cycles, developing important adaptive responses that allow them to survive under hostile conditions. For that reason, the life cycles of parasitic protozoan are excellent systems to study many molecular mechanisms involved in cell differentiation and adaptation, such as the regulation of gene expression, the activation of signal transduction pathways, and the biogenesis of organelles involved in some aspects of parasite pathogenesis. The study of these processes can also provide new targets for the development of better therapeutic tools and information regarding the minimal set of molecules and structures associated with the parasitic life style of such organisms.

During an infection, however, colonization and survival of pathogenic parasites depend on their capacity not only to adapt to the environment provided by the new host but also to neutralize the innate and adaptive immune defenses generated by the infected individual.

For these reasons, with the combination of different approaches to study both parasites and hosts, including genetics, biochemistry, cell and evolutionary biology, immunology, and physiology, new insights regarding host–parasite interactions are coming to light. The results not only continuously surprise scientists but also contribute with exciting progress in our fight against pathogenic microorganisms. The importance of this scientific field is evident for *Current Opinion in Microbiology*, because each year a special issue is committed to show the most recent advances and perspectives regarding host–parasite interactions.

In this issue, we bring together some of the most prestigious scientists who are leaders in the field, working on diverse microorganisms and specializing in different aspects of host–parasite interactions. I found no reason to limit the scope of a special issue on this topic to a particular parasite or host, since our experience dictates that the knowledge generated in a particular model can be easily extrapolated to another, particularly in early-branching eukaryotic microorganisms. I have also chosen not to limit the authors to a particular biological aspect, again, so that the information provided in this series of reviews can reach a large variety of readers.

In the first of these reviews, David Sibley discusses an essential characteristic of Apicomplexan parasites, which is their ability to invade host cells in a very active manner. Invasion of host cells by this group of parasites is a

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complex process that requires first, host cell attachment; second, protein secretion; third, parasite motility. Here, Sibley pays a great deal of attention to a structure called the 'moving junction', which plays a central role during cell invasion. What surprises most is the fact that this tight connection between invading parasite and host cell membranes, which is used by the parasites to enter the host cell, was recognized microscopically many decades ago, but the molecular characterization of this structure has been determined only recently. In this review, David Sibley analyzes the molecular components of the moving junction and provides exciting ideas that combine composition and organization of this neglected structure.

One important adaptive mechanism developed by many pathogenic microorganisms is the so-called antigenic variation, a clonal phenotypic variation involving surface antigenic determinants. Antigenic variation has been demonstrated in a variety of bacterial, fungal, and parasitic organisms, but is highly relevant in many deadly parasites such as *Plasmodium* sp. In a review by Deitsch's group, they extensively discuss the genetic basis underlying antigenic variation in malaria parasites, beginning with the description of large families of genes that encode erythrocyte surface antigens and early studies that suggested that antigenic variation in *Plasmodium* was transcriptionally regulated. They also analyze more recent findings demonstrating that alterations in chromatin structure and subnuclear localization of surface molecule-encoding genes play fundamental roles in mutually exclusive gene expression, gene activation and/or gene silencing, and epigenetic memory of member of these families. Moreover, they provide new insights about the mechanisms responsible for the generation of sequence diversity within these genes, a process that remains poorly understood not only in malaria, but also in all parasites that undergo antigenic variation.

James Bangs' group review the most recent advances in secretory biology of African trypanosomes. The secretory pathway of parasitic organisms is fascinating from the cell biology point of view. Many parasites lack secretory organelles, which are 'essential' components of the secretory pathway of more evolved cells, whereas many pathogens also have additional secretory structures that play major roles in pathogenesis. Protein transport in *Trypanosoma brucei* is fundamental for membrane localization of the major antigenic variants of this parasite, the variable surface glycoproteins or VSGs. Here, the authors discuss how VSG transport in the early and post Golgi compartments is selective and dependent on glycosylphosphatidyl inositol anchors. They also focus on the reorganization of the secretory pathway, which includes reduced organelle abundance and association of ER exit sites with the Golgi apparatus and with the flagellar pocket cytoskeleton. The signals for post-Golgi sorting of both lysosomal and endocytic molecules are also described. The authors suggest that secretory organelles such as the multivesicular body and the acidocalcisomes need more attention from researchers in the field.

On the other hand, despite being highly prevalent worldwide, infection by intestinal parasitic protozoan is not a major focus of research in parasitology. For example, research on *Entamoeba histolytica*, which is one of the leading causes of dysentery worldwide, is conducted by few groups around the world. Although identified as the causative agent of amebiasis in the 19th century, the molecular mechanisms by which the parasite causes disease are still not fully understood. Here, Upinder Singh and coworkers indicate that studies of *Entamoeba* may reveal insights of a eukaryotic cell that differs in many ways from better-studied model organisms. In this review they discuss selected topics on *Entamoeba* research and pay attention to the development of molecular biological techniques that are needed to better understand the biology of this important human parasite. They also highlight many important biological questions that remain unresolved regarding several aspects of this parasite and its relationship with the host.

Last, but not least, is the review by Ricardo Gazzineli's group regarding the rationale for designing a vaccine against leishmaniasis, taking into account both the biology of the parasite and the host immune defenses. Visceral leishmaniasis is a major health problem in Latin America and some regions of Europe and Asia. This group developed a vaccine against visceral leishmaniasis targeting the intracellular amastigote specific antigen A2. The immunological basis of cell-mediated immunity and protection against visceral leishmaniasis is deeply discussed in this interesting work.

All these outstanding reviews summarize and put into perspective the most relevant areas of research and the still unanswered questions regarding the pathogenesis of different parasitic infections. The information and opinions of these prestigious authors will contribute to the progress in the field of host–parasite interactions.

I would like to thank the authors, reviewers and staff of Elsevier's Editorial Office for their invaluable work to complete this special issue.

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