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Systems Biology of *Leishmania* Differentiation

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Abstract

Leishmania spp. are causative agents of leishmaniasis, a broad-spectrum neglected vector-borne disease. Genomic studies and transcriptional studies are not capable of leading to the emergence of proteomics, solving intricate biological mysteries, which can provide insights into the field of parasite biology and its interactions with the host.

Keywords

Systems Biology; Leishmania; Systems Biology

Leishmania occurs in various developmental forms and which they undergoes complex cell differentiation events during its life-cycle. Those are required to allow the parasite to adapt to the different environmental conditions. The sequencing of the genome of *L. major* has facilitated the identification of the parasite's vast arsenal of proteolytic enzymes, a few of which have already been carefully studied and found to be important for the development and virulence of the parasite. This review focuses on these peptidases and their role in the cellular differentiation of *Leishmania* through their key involvement in a variety of degradative pathways in the lysosomal and autophagy networks.

Shape and Form of *Leishmania*

Like many protozoan parasites, *Leishmania* have a digenetic life cycle involving both a mammalian host and an insect vector. *Leishmania* parasites exhibit a variety of different cell morphologies and a number of cell types (developmental forms) that are adapted to either the host or the vector. As seen with other parasites such as *Plasmodium* and trypanosomes, some of these developmental forms are proliferative, whereas others are quiescent and pre-adapted for transmission to the next host Much of the interpretation of cellular form and function. in *Leishmania* species is derived from the more studied basic cell biology of trypanosomes. While this is a natural transfer of knowledge, one has to remain vigilant to the fact that unrecognized differences may exist between the two pathogen systems, even in their basic biology.

Cell Bilogy of *Leishmania*:

Leishmania is a digenetic parasite that shuttles between the flagellated promastigote form that resides in the midgut of the vector and an amastigote form within the phagolysosome of mammalian macrophages. Upon the bite of an infected sandfly, parasites are released into the blood stream, facilitating their colonization in macrophages in an amastigote form. The cycle continues when the sandfly bites the host during a blood meal and ingests infected macrophages.

Scope of *Leishmania* Biology

Omics technology is increasingly being used for investigations of disease phenotype, mechanism of action of drugs and parasite biology. This approach has undoubtedly refined the infrastructure of postgenomic research. Proteomics remains an essential armoury of biomedical research because proteins serve as one of the main functional units of the cell. DNA-based conventional molecular methods do not answer proteome-related queries because gene expression is regulated at transcriptional, translational and/or post-translational levels. Additionally, the dynamic nature of protein profiles accentuates the need to study protein expression as the most suited factor for understanding complex cellular behaviours. Structural mapping of genes/proteins remains the backbone for understanding gene and protein functions. Ongoing developments and improvements in proteomics technology have led to the emergence of several proteomic aspects, i.e., structural, functional and expression proteomics.

Developmental regulation of the proteome profile in *Leishmania*

The combination of genomic tools along with proteomics has shed light on the different life-stages of the parasite and its developmental regulation. Host-parasite interactions continue to be crucial determinants of disease pathogenesis and have been widely studied for centuries. Although proteomic applications remain a challenge in diverse areas of pathogen biology and provide huge datasets, current knowledge has provided a good degree of understanding regarding the mechanism of molecular pathogenesis and further paved the way for research on parasite and host proteomics defining the concept of "parasitoproteomics" to investigate global proteins of parasite and host during cross-talk. The vital question in this context continues to be the specificity of host responses during parasite infections. We will individually examine the effects of each factor on disease pathogenesis.

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