Proteomic tools for the study of protozoa parasites

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In terms of mortality and morbidity, diseases caused by protozoa parasites are devastating, especially for tropical and subtropical regions of the world where they represent both a threat and challenge for the human public health. According to the World Health Organization, only malaria, leishmaniasis and trypanosomiasis account for 1.4 million of deaths annually and 50 millions disability adjusted life years (DALYs) in the economically active population. Diagnostic tools for most of the protozoa parasites are limited and the current available drugs are old-fashioned, toxic and frequently require long-term schemes with low adhesion to the treatment by the patients. The emergence of natural drug resistance in distinct world regions is summed to this picture. Complete or on-going genome sequencing of approximately 30 protozoa species represent an important advance for the understanding of the parasite biology and their pathogenic action. In most of the yet sequenced organisms, about half of the predicted proteome has no known function, and therefore the resulting proteins are currently annotated as "hypothetical". In this context, the application of proteomic technologies makes feasible the development of functional studies of these organisms, providing experimental evidence for gene expression at the protein level. Proteomic studies aim to perform detailed descriptions of the structure, function, and control expression of biological systems, moving from the study of isolated proteins to a global protein expression analysis. Wide protein studies in protozoa parasites started three decades ago but they were limited by the lack of reproducibility and could barely identify proteins of interest. Recent developments in analytical techniques for protein separations as well as in mass spectrometry enable high sensitivity and automation of protein identification. These technological developments and the availability of parasite genomic sequences have changed the scenario of proteomic analysis in the study of parasitic diseases. Considering the complexity of life cycles of most of the protozoan parasites, proteomic studies on these organisms are aimed at identifying and quantifying proteins unique to a particular life-cycle stage or specific organelle, proteins enriched in cellular fractions of parasites associated with distinct clinical manifestations, and proteins involved in immune modulation and signaling. These patterns of protein expression may lead to new routes for vaccines and drugs development, which could be targeted to stage-specific factors. In addition, these data will contribute to the functional annotation of proteins. Altogether, these approaches have allowed the accumulation of protein evidence of gene expression for several parasites under distinct experimental conditions. They also have contributed to assign functions to hypothetical proteins, to identify potential diagnostic markers, drug targets and to describe specific mechanisms related to the biology of a particular parasite species. Finally, the potential of mass spectrometry for direct identification of intact parasites, as well as for characterizing species- or strain-specific metabolites, an area well developed for bacterial species, remain to be explored in protozoa parasites.