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Commentary

Function of Proteasomes in Parasite Biology and Virulence

Heran Jastrab*

Department of Microbiology, New York University School of Medicine, New York, USA

DESCRIPTION

Proteasomes are enzymes that break down proteins to enforce quality control and manage a variety of cellular activities in eukaryotic cells, including cell cycle progression, signal transduction, cell death, immunological responses, metabolism, protein-quality control, and development. The 20S proteasome, which serves as the catalytic core of these complexes, is largely conserved in bacteria, yeast, and humans. Yet, the function of proteasomes in the biology of parasites remained completely unknown until a few years ago. Here, we provide an overview of research on the function of proteasomes in the biology and pathogenicity of protozoan parasites. The involvement of proteasomes in parasite biological processes like cell differentiation, cell cycle, proliferation, and encystation has been supported by numerous investigations. Key phases in host colonization include cell differentiation and proliferation [1-3].

Parasite proteasomes may operate as virulence factors due to their role in both processes in a variety of parasites, including *Trypanosoma*, *Leishmania*, *Toxoplasma*, and *Entamoeba*. It is strongly suggested by a number of pieces of data that the ubiquitin-proteasome pathway is potentially a potential parasite treatment target. Recent studies have demonstrated that the proteasome is a viable therapeutic target for malaria and sleeping sickness. Then, proteasomes are a crucial organelle in the biology and virulence of parasites and seem to be a promising new target for chemotherapeutics.

The lysosome and the proteasome are two self-contained proteolytic systems that carry out the majority of the turnover of intracellular proteins in eukaryotic cells. The Ubiquitin-Proteasome System (UPS) degrades the majority of proteins. Large complexes called proteasomes play critical roles in numerous cellular pathways by breaking down proteins in eukaryotic cells' cytosol and nucleus to enforce quality control and control numerous fundamental cellular activities. Proteasomes breakdown short-lived regulatory or structurally abnormal proteins during the cell cycle, signal transduction, cell death, immunological responses, metabolism, and development processes, among others. The 20S proteasome, the catalytic core of these complexes, is largely conserved across bacteria, yeast, and humans. Certain Archaea and prokaryotes also have simpler variants of this enzyme.

The barrel-shaped 20S proteasome is made up of 28 individual protein subunits. Two outer α rings and two inner β rings made up of seven structurally similar α and β subunits stack axially to form a packed particle. The three inner ring subunits of each include threonine residues that are catalytically active at their N termini and exhibit nucleophile hydrolase activity at their N termini, proving that the proteasome is a threonine protease. Protein complexes that attach to the end rings of subunits cause proteasomes to become active [4]. The most well-known activator is PA700 (proteasome activator MW 700, also known as 19S or Regulatory Complex (RC), which attaches to the 20S proteasome to produce the 26S proteasome and is substantially conserved from yeast to humans). The only proteasome activator known to promote protein substrate degradation is PA700. Hence, PA700 is believed to facilitate substrate degradation in order to mediate the majority of the biological effects of the proteasome [4-8].

By covalent ligation with ubiquitin, proteins are selected for destruction in this pathway. Ubiquitin-Like (UBLs) Proteins, including as ubiquitin, Small Ubiquitin-Like Modifier (SUMO), and NEDD8, are used in ubiquitination to tag the target protein. An isopeptide bond is formed between the C terminus of ubiquitin and one or more lysine side chains in the target proteins during ubiquitination, a posttranslational modification of proteins in which the modifier is a polypeptide. The activating enzyme E1, the conjugating enzyme E2, and the ubiquitin ligase E3 are the three enzymes that mediate the three consecutive phases of protein modification by ubiquitin. Ubiquitination is reversible, and proteins that have undergone it can be deubiquitinated through proteolysis by particular deubiquitinating enzymes. However, the current understanding of UPS strongly implies that protein ubiquitination appears to be necessary but not essential. Ubiquitin molecules can form polyubiquitin chains that are attached to target proteins, which are typically identified and destroyed by the proteasome [9,10].

Correspondence to: Heran Jastrab, Department of Microbiology, New York University School of Medicine, New York, USA, E-mail: heranj@med.nyu.edu

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