The phagosome and redox control of antigen processing

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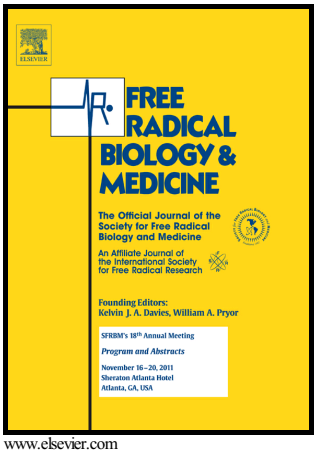

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The phagosome and redox control of antigen processing.

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Abstract

In addition to debris clearance and antimicrobial function, versatile organelles known as phagosomes play an essential role in the processing of exogenous antigen in antigen presenting cells. While there has been much attention on human leukocyte antigen haplotypes in the determination of antigenic peptide repertoires, the lumenal biochemistries within phagosomes and endosomes are emerging as equally-important determinants of peptide epitope composition and immunodominance. Recently, the lumenal redox microenvironment within these degradative compartments has been shown to impact two key antigenic processing chemistries: proteolysis by lysosomal cysteine proteases and disulfide reduction of protein antigens. Through manipulation of the balance between oxidative and reductive capacities in the phagosome—principally by modulating NADPH oxidase (NOX2) and γ-interferon-inducible lysosomal thiol reductase (GILT) activities—studies have demonstrated changes to antigen processing patterns leading to modified repertoires of antigenic peptides available for presentation, and subsequently, altered disease progression in T cell-driven autoimmunity. This review focuses on the mechanisms and consequences of redox-mediated phagosomal antigen processing, and the potential downstream implications to tolerance and autoimmunity.

Keywords

Redox; Phagosome; ROS; MHC; Antigen processing; Antigen presentation; NADPH oxidase; GILT; Autoimmunity; Tolerance; Proteolysis; Disulfide reduction; Cathepsins

Abbreviations

APC; antigen presenting cell, CGD; chronic granulomatous disease, DC; dendritic cell, FcγR; Fc gamma receptor, GILT; γ-interferon-inducible lysosomal thiol reductase, GPI; glucose-6-phosphate isomerase, HEL; hen egg lysozyme, IFN-γ; interferon-gamma, Ig; immunoglobulin, IL; interleukin, LPS; lipopolysaccharide, MHC; major histocompatibility complex, MOG; myelin oligodendrocyte glycoprotein, MS; multiple sclerosis, NADPH; nicotinamide adenine dinucleotide phosphate, NOX2; NADPH oxidase 2, OVA; ovalbumin, Phox;