Myeloperoxidase (MPO) produces hypochlorous acid (HOCl)

Nüsse, O., Shamovsky, V.
Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 83

This document contains 1 reaction (see Table of Contents)
Myeloperoxidase (MPO) produces hypochlorous acid (HOCl)

**Stable identifier:** R-HSA-6789126

**Type:** transition

**Compartments:** phagocytic vesicle lumen

Phagosomal myeloperoxidase (MPO) is an important heme enzyme released by activated leukocytes (Klebanoff SJ & Rosen H 1978; Austin GE et al. 1994; Klebanoff S 2013). MPO protein has little bactericidal effect per se, but the enzyme-generated products are chemical oxidants that have potent antibacterial, antiviral, and antifungal properties (Pattison DI et al. 2012). Ferric MPO enzyme cycles through redox intermediates that undergo a complex array of reactions. Initial oxidation of the resting iron (III) form of the enzyme by hydrogen peroxide gives rise to a primary catalytic complex, known as Compound I (Winterbourn CC et al 2006; Davies MJ 2011; Pattison DI et al. 2012). Compound I can then undergo either two electron reduction with halide or pseudo-halide ions to form hypohalous acids (HOX where X = Cl, Br, SCN) or undergo two successive one-electron reductions, via Compound II, with consequent radical formation (the peroxidase cycle) (Winterbourn CC et al 2006; Davies MJ 2011). Due to the high reduction potentials of the Compound I and II, MPO can oxidize a variety of substrates. Chloride ion is one of the physiological substrate of MPO. Cl- undergoes a two-electron oxidation to form hypochlorous acid (HOCl) (Winterbourn CC et al 2006; Davies MJ 2001; Pattison DI et al. 2012). Studies using specific probes or biomarkers such as 3-chlorotyrosine showed that MPO reacts with H2O2 and chloride present in the phagosome to produce HOCl, and that the HOCl reacts with ingested bacteria (Jiang Q et al. 1997; Palazzolo AM et al. 2005; Kenmoku S et al. 2007; Chapman AL et al. 2002; Albrett AM et al. 2018; Degrossoli A et al. 2018). Furthermore, rapid killing of numerous organisms by isolated neutrophils has been shown to require MPO (Klebanoff SJ et al. 2013; Green JN et al. 2017). HOCl reacts readily with a range of biological molecules to form potently microbicidal products such as chloramines (Green JN et al. 2017). HOCl reacts with ROS forming toxic hydroxyl radical and singlet oxygen, however the specific role of HOCl in the microbial killing remains unclear. Modelling studies indicated that phagosomal proteins could scavenge much of the HOCl before it reaches the microbe thus limiting its ability to kill (Winterbourn CC et al. 2006).
Literature references


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Author/Editor</th>
<th>Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018-10-23</td>
<td>Authored, Edited</td>
<td>Shamovsky, V.</td>
</tr>
<tr>
<td>2018-11-07</td>
<td>Reviewed</td>
<td>Nüsse, O.</td>
</tr>
</tbody>
</table>