Universität Basel

Publication

Myeloperoxidase targets oxidative host attacks to Salmonella and prevents collateral tissue damage

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 3765308
Author(s) Schürmann, Nura; Forrer, Pascal; Casse, Olivier; Li, Jiagui; Felmy, Boas; Burgener, Anne-Valérie; Ehrenfeuchter, Nikolaus; Hardt, Wolf-Dietrich; Recher, Mike; Hess, Christoph; Tschan-Plessl, Astrid; Khanna, Nina; Bumann, Dirk
Author(s) at UniBasel Bumann, Dirk ; Li, Jiagui ; Ehrenfeuchter, Nikolaus ; Schürmann, Nura ; Casse, Olivier ; Recher, Mike ; Khanna, Nina ;
Year 2017
Title Myeloperoxidase targets oxidative host attacks to Salmonella and prevents collateral tissue damage
Journal Nature Microbiology
Volume 2
Number 4
Pages / **Article-Number** 16268
Mesh terms Animals; Computer Simulation; Humans; Hydrogen Peroxide, metabolism; Hypochlorous Acid, metabolism; Kinetics; Mice; Neutrophils, immunology; Oxidation-Reduction; Oxidative Stress; Peroxidase, metabolism; Phagosomes, microbiology; Reactive Oxygen Species, metabolism; Respiratory Burst; Salmonella, pathogenicity
Host control of infections crucially depends on the capability to kill pathogens with reactive oxygen species (ROS). However, these toxic molecules can also readily damage host components and cause severe immunopathology. Here, we show that neutrophils use their most abundant granule protein, myeloperoxidase, to target ROS specifically to pathogens while minimizing collateral tissue damage. A computational model predicted that myeloperoxidase efficiently scavenges diffusible H2O2 at the surface of phagosomal Salmonella and converts it into highly reactive HOCl (bleach), which rapidly damages biomolecules within a radius of less than 0.1μm. Myeloperoxidase-deficient neutrophils were predicted to accumulate large quantities of H2O2 that still effectively kill Salmonella, but most H2O2 would leak from the phagosome. Salmonella stimulation of neutrophils from normal and myeloperoxidase-deficient human donors experimentally confirmed an inverse relationship between myeloperoxidase activity and extracellular H2O2 release. Myeloperoxidase-deficient mice infected with Salmonella had elevated hydrogen peroxide tissue levels and exacerbated oxidative damage of host lipids and DNA, despite almost normal Salmonella control. These data show that myeloperoxidase has a major function in mitigating collateral tissue damage during antimicrobial oxidative bursts, by converting diffusible long-lived H2O2 into highly reactive, microbicidal and locally confined HOCl at pathogen surfaces.
Publisher Nature Publishing Group
ISSN/ISBN 2058-5276
edoc-URL http://edoc.unibas.ch/54573/
Full Text on edoc Available;
Digital Object Identifier DOI 10.1038/nmicrobiol.2016.268
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/28112722
ISI-Number WOS:000398177800009
Document type (ISI) Journal Article