Published online before print September 7, 2016, doi: 10.4049/jimmunol.1601010

The Journal of Immunology September 7, 2016 1601010

Peroxiredoxin 1 Contributes to Host Defenses against *Mycobacterium tuberculosis*

Kazunori Matsumura*, Hiroki Iwai*, Masako Kato-Miyazawa*, Fumiko Kirikae*, Jizi Zhao*, Toru Yanagawa†, Tetsuro Ishii†, Tohru Miyoshi-Akiyama*, Keiji Funatogawa‡ and Teruo Kirikae*

Author Affiliations

1. *Department of Infectious Diseases, Research Institute, National Center for Global Health and Medicine, Shinjuku, Tokyo 162-8655, Japan;
2. †Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki 305-8575, Japan; and
3. ‡Department of Microbiology, Tochigi Prefectural Institute of Public Health and Environmental Science, Utsunomiya, Tochigi 329-1196, Japan

Address correspondence and reprint requests to Dr. Teruo Kirikae, Department of Infectious Diseases, Research Institute, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku, Tokyo 162-8655, Japan. E-mail address: tkirikae@ri.ncgm.go.jp

Abstract

Peroxiredoxin (PRDX)1 is an antioxidant that detoxifies hydrogen peroxide and peroxinitrite. Compared with wild-type (WT) mice, *Prdx1*-deficient (*Prdx1*$^{-/-}$) mice showed increased susceptibility to *Mycobacterium tuberculosis* and lower levels of IFN-γ and IFN-γ–producing CD4^{+} T cells in the lungs after *M. tuberculosis* infection. IL-12 production, c-Rel induction, and p38 MAPK activation levels were lower in *Prdx1*$^{-/-}$ than in WT bone marrow–derived macrophages (BMDMs). IFN-γ–activated *Prdx1*$^{-/-}$ BMDMs did

not kill *M. tubercuosis* effectively. NO production levels were lower, and arginase activity and arginase 1 (*Arg1*) expression levels were higher, in IFN-γ–activated *Prdx1*$^{-/-}$ than in WT BMDMs after *M. tuberculosis* infection. An arginase inhibitor, N^{ω}-hydroxy-nor-arginine, restored antimicrobial activity and NO production in IFN-γ–activated *Prdx1*$^{-/-}$ BMDMs after *M. tuberculosis* infection. These results suggest that PRDX1 contributes to host defenses against *M. tuberculosis*. PRDX1 positively regulates IL-12 production by inducing c-Rel and activating p38 MAPK, and it positively regulates NO production by suppressing *Arg1* expression in macrophages infected with *M. tuberculosis*.

Footnotes

- This work was supported by National Center for Global Health and Medicine Grants 21-A-105, 24-A-103, and 27-A-1102, Japan Society for the Promotion of Science Grant-in-Aid for Scientific Research 22590411, and by Japan Agency for Medical Research and Development Grant 16fk0108302h0003.

- The online version of this article contains supplemental material.

- Received June 10, 2016.
- Accepted August 16, 2016.