

2 Pirin is an iron-dependent redox regulator of NF- κ B.

Liu F, Rehmani I, Esaki S, Fu R, Chen L, de Serrano V, Liu A
Proc Natl Acad Sci U S A. 2013 Jun 11; 110(24):9722-7

Alerts for similar articles

Save to MyF1000/Follow Export

Recommendations:

24 Jun 2013

Recommended



Bruce Demple

F1000 Structural Biology

Stony Brook University, Stony Brook, NY,
USA.

Follow

Interesting Hypothesis, New Finding

DOI: 10.3410/f.718013939.793478597

This paper uses biochemical and structural analysis to probe the role of the non-heme iron in mammalian pirin protein, a binding partner for the important regulator nuclear factor (NF) κ B. In contrast to iron-containing bacterial proteins that bind DNA directly (e.g. SoxR and PerR), pirin acts indirectly through its association with NF κ B. Reversible conversion between Fe(II) and Fe(III) in pirin generates a shape change that the authors propose is transmitted to NF κ B, and they demonstrate that the DNA binding in vitro is affected dramatically. It remains to be seen whether the same redox regulation occurs in cells.

Disclosures

None declared

Add Comment

No comments yet.

Comments:

Abstract:

Pirin is a nuclear nonheme Fe protein of unknown function present in all human tissues. Here we describe that pirin may act as a redox sensor for the nuclear factor κ B (NF- κ B) transcription factor, a critical mediator of intracellular signaling that has been linked to cellular responses to proinflammatory signals and controls the expression of a vast array of genes involved in immune and stress responses. Pirin's regulatory effect was tested with several metals and at different oxidations states, and our spectroscopic results show that only the ferric form of pirin substantially facilitates binding of NF- κ B proteins to target κ B genes, a finding that suggests that pirin performs a redox-sensing role in NF- κ B regulation. The molecular mechanism of such a metal identity- and redox state-dependent regulation is revealed by our structural studies of pirin. The ferrous and ferric pirin proteins differ only by one electron, yet they have distinct conformations. The Fe center is shown to play an allosteric role on an R-shaped surface area that has two distinct conformations based on the identity and the formal redox state of the metal. We show that the R-shaped area composes the interface for pirin-NF- κ B binding that is responsible for modulation of NF- κ B's DNA-binding properties. The nonheme Fe protein pirin is proposed to serve as a reversible functional switch that enables NF- κ B to respond to changes in the redox levels of the cell nucleus.

DOI: 10.1073/pnas.1221743110

PMID: 23716661

Abstract courtesy of PubMed: A service of the National Library of Medicine and the National Institutes of Health.

Library Resources	Article Recommendations	Articles (beta access only)	Articles	Posters
The F1000.com website uses cookies. By continuing to browse the site, you are agreeing to our user agreement.			Advisory Panel	Upcoming meetings
F1000 Specialists	F1000Prime Faculty	About/Contact	Blog	For Depositors
F1000 Updates	Blog		Submit	For Societies
About/Contact	Subscribe		Author Guidelines	Register
	About		Register	About/Contact
	Contact		About/Contact	

© 2000-2013 Faculty of 1000 Ltd. ISSN 2051-9796 | [Legal](#) | [Partner of HINARI](#) • [CrossRef](#) • [ORCID](#)