High Dissociation Rate Constant of Ferrous-Dioxy Complex Linked to the Catalase-like Activity in Lactoperoxidase*

Semira Galijasevic†, Ghasan M. Saed‡, Michael P. Diamond‡, and Husam M. Abu-Soud§§

From the Departments of Obstetrics and Gynecology and Biochemistry and Molecular Biology, Wayne State University School of Medicine, Detroit, Michigan 48201

Heme reduction of ferric lactoperoxidase (LPO) into its ferrous form initially leads to the accumulation of the unstable form of LPO-Fe(II), which spontaneously converts to a more stable species, the two of which can be identified by Soret peaks at 440 and 434 nm, respectively. Our data demonstrate that both LPO-Fe(II) species are capable of binding O₂ at a similar rate to generate the ferrous-dioxy complex. Its formation with respect to O₂ was first order and monophasic and with rate constants of $k_{on} = 3.8 \times 10^4$ M⁻¹ s⁻¹ and $k_{off} = 11.2$ s⁻¹. The dissociation rate constant for the formation of LPO-Fe(II)-O₂ is relatively high, in contrast to hemoprotein model compounds. This high dissociation rate can be attributed to a combination of effects that include the positive trans effect of the proximal ligand, the heme pocket environment, and the geometry of the Fe-O₂ linkage. Our results have also shown that the decay of the LPO-Fe(II)-O₂ complex occurs by two sequential O₂-independent steps. The first step involves formation of a short-lived intermediate that can be characterized by its Soret absorption peak at 416 nm and may be attributed to the weakening of the Fe(II)-O₂ linkage with a rate constant of 0.5 s⁻¹. The second step is spontaneous conversion of this intermediate to generate the native enzyme and presumably superoxide as end products with a rate constant of 0.03 s⁻¹. A comprehensive kinetic model that links LPO-Fe(II)-O₂ complex formation to the LPO catalase-like activity, combined with the classic catalytic cycle, is presented here.

Hydrogen peroxide (H₂O₂) is freely diffusible through biological membranes, and its overproduction or inhalation is extremely destructive to cells and tissues (1, 2). Superoxide (O₂⁻) is mainly formed through the univalent reduction of molecular oxygen by the membrane-bound NADPH oxidase in phagocytic cells and endothelial cells (3). Most of these cells, however, the main source of O₂⁻ is from the mitochondria (3). Most of the O₂⁻ generated in vivo is utilized primarily to produce H₂O₂ nonenzymatically or by superoxide dismutate (4). Nitric oxide synthase and several oxidase enzymes, such as monoamine and amino acid oxidase, can also directly produce H₂O₂ (5, 6). Because H₂O₂ has both beneficial and harmful functions, its effect in a given biological setting requires precise control to regulate its action at tissues throughout the body. Therefore, understanding the circumstances that influence the rate of H₂O₂ synthesis and degradation is of critical importance for optimal biological function. Catalase and cytoplasmic glutathione peroxidase are the major H₂O₂ scavengers and protect cells from the toxic effects of H₂O₂ by catalyzing its decomposition into molecular oxygen and water (4, 7, 8). Recently, lactoperoxidase (LPO) has been identified as the major macromolecular consumer of H₂O₂ in animal airway secretions (9, 10). At this site, catalase displays very low levels of expression that are insufficient to protect the epithelium against pathogens (11, 13). In addition, LPO and other members of the mammalian peroxidase superfamily (e.g. eosinophil peroxidase and myeloperoxidase) are all implicated in NO scavenging and protein nitration, as well as production of cytotoxic substances that protect against microbial, fungal, and bacterial infections (14–22).

LPO is a hemoprotein enzyme that typically uses H₂O₂ with a combination of halides or pseudohalides to generate the corresponding hypohalous acid as a final end product (23–27). LPO also utilizes H₂O₂ in combination with various organic and inorganic substrates to generate free radicals and other reactive components as primary end products that ultimately lead to nitration or halogenation of tyrosine residues or nitration of thiol residues in proteins (12–17, 28–32). Organic and inorganic compounds may also serve as substrates enhancing the catalytic cycle of mammalian peroxidases by accelerating Compound II (LPO-Fe(IV)-O) formation and subsequent decay to the ground state, which is thought to be the rate-limiting step in the classic peroxidase cycle (12–17, 28–32). The enzyme has been identified as an antimicrobial agent in milk, saliva, and tears and is produced by goblet cells and submucosal glands that form airway mucus secretions (33, 34). A variety of evidence suggests that the peroxidase heme prosthetic group is involved in a wide range of important processes through its catalytic reactions that include binding, transport, and activation of oxygen, as well as deactivation of reactive oxygen compounds, oxidation/reduction reactions, and electron transport (17, 19, 35). In addition, the heme prosthetic group of LPO accommodates a large variety of molecules as ligands of the iron cation (17). Binding of these ligands to the peroxidase heme iron causes enzyme inhibition (17).

The presence of two different conformational states of the reduced form of LPO (LPO-Fe(II) state) has been reported in studies using a variety of spectroscopic techniques (36–38). However, functional differences between the two forms have not been reported until recently (39). For example, previous resonance Raman spectroscopy studies demonstrated that the

---

*This work was supported by National Institutes of Health Grant HL066367 (to H. M. A.-S.). The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

† To whom correspondence should be addressed: Wayne State University School of Medicine, Dept. of Obstetrics and Gynecology, The C.S. Mott Center for Human Growth and Development, 275 E. Hancock, Detroit, MI 48201. Tel.: 313-577-6178; Fax: 313-577-8554; E-mail: habusoud@med.wayne.edu.

†† The abbreviations used are: LPO, lactoperoxidase; NO, nitric oxide.
two LPO-Fe(II) species display no significant differences in the character of the Fe-N(histidine) bond, and both share the same state configuration (40). However, our recent diatomic binding studies have shown the existence of two spectroscopically and kinetically distinguishable LPO-Fe(II) species at equilibrium, one with the partially open heme pocket and one with the heme pocket relatively closed (39). We have also demonstrated that the presence of pathophysiologically relevant levels of peroxides and H2O2 serves as a catalytic sink for NO and reversibly inhibits Fe- and heme-dependent bronchodilation of preconstricted tracheal rings (14–16). Therefore, LPO and other members of the mammalian peroxidase superfamily display multiple functions in airway diseases.

Characterization of the LPO-Fe(II)-O2 complex, known as Compound III, generated by the addition of a slight excess of H2O2 relative to LPO native enzyme has been accomplished recently by employing techniques such as optical absorption and resonance Raman spectroscopy (37, 41–43). However, what role the LPO-Fe(II)-O2 complex plays during LPO catalysis is still unclear. In this study we examine the potential physiological relevance of the LPO-Fe(II)-O2 interaction. We utilize direct rapid kinetic methods to characterize O2 interactions with both forms of LPO-Fe(II). A modified comprehensive kinetic model is presented that describes LPO-Fe(II)-O2 accumulation, decay, and interaction with H2O2, as well as involvement in the catalase-like activity during steady state catalysis.

EXPERIMENTAL PROCEDURES

Materials—O2 gas was purchased from Matheson Gas Products, Inc., and used without further purification. All other reagents and materials were of the highest purity grades available and obtained either from Sigma or from Aldrich (Milwaukee, WI). Bovine LPO was obtained from Worthington Bio-Chemistry Corp. (Lakewood, NJ) and used without further purification. Purity was confirmed by demonstrating a RZ of >0.75 (A412/A280), as well as by SDS-PAGE analysis. LPO concentration was determined spectrophotometrically by utilizing an extinction coefficient of 112,000 M⁻¹ cm⁻¹ at 412 nm (44).

Optical Spectroscopy and Rapid Kinetic Measurements—Optical spectra were recorded on a Cary 100 UV-visible spectrophotometer at 25 °C. Anaerobic spectra were recorded using septum-sealed quartz cuvettes that were attached through quick-fit joints to an all-glass vacuum train system. LPO samples were made anaerobic by several cycles of evacuation and equilibrated with catalyst-deoxygenated N2. Separate buffer solutions were evacuated, gassed with N2, and anaerobically transferred either to the stopped-flow instrument or to anaerobic cuvettes using gas-tight syringes. Cuvettes were maintained under N2 positive pressure during spectral measurements.

All kinetic measurements were performed with a temperature-controlled stopped-flow apparatus (Hi-Tech Scientific, model SF-61) equipped for anaerobic work. Addition of a slight excess of dithionite to an anaerobic solution of LPO-Fe(II) (initially caused rapid buildup of an unstable species as a function of O2 concentration for both the stable and unstable forms of LPO-Fe(II) was monitored at wavelengths determined based on the spectral changes that occur upon O2 binding to the LPO-Fe(II). Experiments were carried out at 10 °C and initiated by rapidly mixing equal volumes of the unstable form of LPO-Fe(II) (1.45 μM) (obtained immediately after reduction) with buffer solution supplemented with increasing concentrations of O2. In parallel, a similar study was repeated when a solution of the stable form of LPO-Fe(II) was rapidly mixed with a buffer solution supplemented with increasing concentrations of O2. To determine the apparent rate constants for generation of the LPO-Fe(II)-O2 complex, the time course of absorbance changes was fit to single (Y = 1 - e⁻kt) or double exponential (Y = Ae⁻kt + Be⁻kt + C) functions using a non-linear least-squares method provided by the instrument manufacturer. Signal-to-noise ratios were improved by averaging 7–10 individual traces for each experiment.

Solution Preparation—The molecular oxygen concentration was determined using an Apollo 4000 device (World Precision Instruments, Sarasota, FL) equipped with an O2-selective electrode. The various solutions were made by mixing different volumes of O2-saturated buffer with anaerobic buffer solutions. The O2-saturated buffer was made by bubbling O2 gas through the solution for 1 h in a septum-tipped flask. Utilizing the O2-selective electrode, the estimated ratio of the current (nA) measurement of the O2 sensor for O2-saturated and air-equilibrated buffers is ~4.8. Using an estimated concentration of air-equilibrated buffer (21% O2) of ~250 μM (45), we calculated that the O2 concentration of O2-saturated buffer is ~1.2 μM. These values, with the corresponding correction for temperature, were used to calculate the final O2 concentrations of all the various O2 solutions used in this study. The current for 0% oxygen concentration of the O2 sensor was adjusted prior to each measurement by adding several mg of dithionite, a strong reducing agent, per 20 ml of buffer. All the oxygen solutions were then immediately transferred to the stopped-flow apparatus that were surrounded by a thermostated anaerobic water jacket to maintain a constant temperature of 10 °C.

RESULTS

Initial Rapid Spectroscopic Characterization of O2 Binding to Ferrous LPO—To determine the role of the LPO-Fe(II)-O2 complex in catalytic activity, as well as to further our understanding of the potential role of LPO in catalase-like function, the direct reaction between LPO-Fe(II) and O2 was carried out using rapid kinetic measurements. Addition of a slight molar excess of dithionite to LPO-Fe(III) has been shown previously to cause immediate LPO heme iron reduction, as judged by a shift in the Soret absorption peak from 412 to 444 nm, and the appearance of additional absorbance peaks in the visible range at 561 and 595 nm. This intermediate is unstable and converted over a short period of time to a more stable form of LPO-Fe(II) that can be characterized based on the Soret absorbance spectrum centered at 434 nm (39). The absorption spectrum was obtained as a function of time by rapidly mixing a solution of the stable and unstable forms of LPO-Fe(II) with an equal volume of air-saturated buffer (−250 μM O2) as shown in Fig. 1. In both cases, the formation of the LPO-Fe(II)-O2 intermediate was essentially the same and completed within 0.5 s after mixing. This intermediate has an absorption peak centered at 426 nm and additional visible peaks at 549 and 588 nm (Fig. 1, A and B, respectively). In both cases, the spectral changes as a function of time indicate that the reactions involve a simple one-step mechanism in which both generate a six-coordinate ferrous-dioxy complex, Compound III.

The subsequent change in the absorption spectra was a result of the decay of this intermediate to ground state, which occurs through the generation of a transient intermediate whose spectrum was characterized by absorbance peaks at 416, 548, and 586 nm (Fig. 2A). This spectrum differs from that of either LPO Compound I or LPO Compound II, whose Soret absorption peaks centered at 410 and 430 nm, respectively, but is similar to that of oxymyoglobin and nitric oxide synthase ferrous-dioxy complex (46–49), indicating that this is another oxygenated LPO intermediate. The spectral time line in Fig. 1 is much different from that found in Fig. 2. Fig. 1A shows spectra collected at 3.4, 7.1, 22.1, 35.6, 40.1, and 44.6 s of initiating the reaction, whereas Fig. 1B shows spectra collected at 55, 56, 57, 60, 69, and 224 s of initiating the reaction. Fig. 2A shows spectra collected at 3.4, 7.1, 22.1, 35.6, 40.1, and 44.6 s of initiating the reaction, whereas Fig. 2B shows spectra collected at 55, 56, 57, 60, 69, and 224 s of initiating the reaction.

Kinetic Analysis of O2 Binding to Ferrous LPO—We further examined the kinetics of formation of the transient intermediate species as a function of O2 concentration for both the unstable and stable forms of LPO-Fe(II) by monitoring the change in absorbance at 416 and 424 nm, respectively. Experiments were performed under pseudo-first order conditions by rapid mixing of equal volumes of LPO-Fe(II) (2 μM) with buffer solutions supplemented with different O2 concentrations. The pseudo-first order rate constants for both stable and unstable forms

Downloaded from http://www.jbc.org/ by guest on July 22, 2018
of LPO were identical and obtained by a fit of the data to one exponential function equation. The second order rate constants for the reaction of LPO-Fe(II) with O2 were obtained by a fit of the pseudo-order rates, determined as a function of the oxygen concentration, to one exponential function. The plot of the pseudo-first order rate constant for the initial Fe(II)-O2 complex formation was linear with a positive intercept, indicating that the reaction is reversible and proceeds through a simple one-step mechanism with 
\[ k_{on} = 3.8 \times 10^4 \text{ M}^{-1} \text{s}^{-1} \] and 
\[ k_{off} = 11.2 \text{ s}^{-1} \] (Fig. 3). The decay of the LPO-Fe(II)-O2 complex was monitored by following the absorbance changes at 460 nm. These decreases in absorbance were successfully fitted to a double exponential function with observed rates of 0.5 and 0.03 s\(^{-1}\). The subsequent conversion of this intermediate into the kinetically and spectroscopically distinct intermediate occurred via mechanisms independent of O2 concentration (Fig. 4).

**DISCUSSION**

The present studies support the notion that the formation of the LPO-Fe(II)-O2 complex during steady state catalysis is a fundamental feature of the kinetic reactions of LPO. Its formation and decay operate to accelerate the removal of the unwanted H2O2 from the LPO milieu. This is specifically important in the human airway where catalase, a major H2O2 scavenger, exists in very low levels (50), thus leaving LPO to serve as the major H2O2 scavenger at this site.

One of the most remarkable findings of the present study is the low affinity of LPO-Fe(II) toward O2 and the instability of this complex in contrast to related hemoprotein model compounds (46–49, 51–54). The LPO-Fe(II)-O2 complex is relatively unstable and subsequently decays through a two-step irreversible O2-independent process. Under such circumstances, practically all the LPO-Fe(II)-O2 sample is converted to another oxygenated LPO species that may be formed by the influences of the positively charged heme pocket, in which weakening of the Fe–O2 bond allows the Fe to move out of the plane of the porphyrin ring toward the proximal histidine. This transient species can be characterized by its Soret absorbance...
interacts with high dissociation rate in LPO-Fe(II)-O2 including the positive LPO-Fe(II) heme pocket, both LPO-Fe(II) forms display similar constrained and able to bind small ligands at low rates (reaction 6). The two lines present in the figure indicate that the complex decay under this condition was biphasic, and each step follows an irreversible O2-independent mechanism. Experimental conditions were as described in Fig. 3.

peak at 416 nm prior to its decay to the ground state. These observations are consistent with structural data of hemoprotein model compounds, in which changes in the position of the heme iron lead to a fundamental alteration in their UV-visible spectra (51–54).

A modified working kinetic model that incorporates our current results is shown in Fig. 5. In this model, LPO reacts rapidly and reversibly with H2O2 generating a ferryl ·cation radical, Compound I (reaction 1). LPO Compound I is capable of oxidizing co-substrates such as SCN− through a single 2e− transition generating LPO-Fe(III) and the corresponding hypohalous acid (reaction 2) (23–27). Compound I may also oxidize an array of substrates through two sequential one-e− steps forming a long-lived intermediate, Compound II, and LPO-Fe(III) (reactions 3 and 4), respectively (28–31, 55). O2− interacts with the LPO-Fe(III) heme iron to generate LPO-Fe(II)-O2 (reaction 5). Formation of Fe(II)-O2 complexes through this route is reversible, is relatively fast, and occurs via a one- or two-step mechanism (56, 57). The presence of superoxide dismutase completely inhibited Compound III formation, but the presence of catalase had no significant effect on this process (57). In the presence of a slight excess of H2O2, Compound II is readily converted to Compound III (reaction 6).

LPO heme reduction causes immediate buildup of a transient intermediate that displays a relatively open, unrestricted pocket (reaction 7), which converts with time to one that is constrained and able to bind small ligands at low rates (reaction 8) (39, 58, 59). Despite the remarkable alteration in the LPO-Fe(II) heme pocket, both LPO-Fe(II) forms display similar affinity toward O2 and generate low spin six-coordinated ferrous-dioxy complex that can be characterized by the Soret absorbance peak at 424 nm and two resolved absorbance peaks centered at 549 and 588 nm (reactions 9 and 10) (42, 60). The O2 dissociation constant of LPO-Fe(II)-O2 binding is significantly high compared with other hemoproteins (reactions 11 and 12) (47, 51, 54). Three major factors can account for the high dissociation rate in LPO-Fe(II)-O2 including the positive trans effect contributed by the proximal ligand, the heme pocket environment, and the geometry of Fe-O2 linkage. Indeed, previous resonance Raman spectroscopy studies demonstrated that the ν(Fe-O2) frequency for LPO was considerably lower than those reported for related and relevant hemoprotein model compounds (37, 61, 62). Collapse or narrowing in the heme cavity radius and/or the orientation of the O2 bond may increase the interaction between the O=O and the positively charged l-arginine that is localized above the heme iron on the distal side of LPO. Therefore, the electron density on the antibonding π* orbital of the O=O bond is pulled up by the influence of a positively charged residue localized on the distal side above the heme moiety (62, 63). Weakening the Fe=O2 linkage might allow the ligand trans to O2 to pull the iron out of the plane away from the O2. This course of action is associated with the generation of a new oxygenated LPO species that can be identified by its Soret absorbance peak centered at 416 nm (reaction 13) similar to oxyhemoglobin and nitric oxide synthases (46, 47–49). The later intermediate is unstable, and its formation and autooxidation to ground state, which involves electron transfer to O2 as a primary step to form superoxide (reaction 14), occurs in an oxygen-independent fashion. Our rapid kinetic measurements demonstrated that the rate for O2 dissociation is relatively high and leads to the formation of LPO-Fe(II) (reactions 11 and 12). LPO-Fe(II) is not a dead end product as judged by its ability to utilize H2O2 in the production of Compound II (reaction 15).

In regards to the biological relevance of our findings, patients with asthma and chronic obstructive pulmonary disease display higher levels of H2O2 in their breath condensates compared with normal subjects (9, 64, 65). LPO and other mammalian peroxidases are also present at high levels in the airways of asthmatic subjects. Although LPO functions to maintain sterility of the airway in the setting of constant exposure to inhaled debris and potential pathogens, it may also serve to scavenge the excess H2O2 and protect the airway epithelium from H2O2 toxicity. Related studies by Huwiler et al. (41) have demonstrated that oxygen is released by LPO in the presence of a slight excess of peroxidase. Kohler et al. (66) have also shown that the stoichiometry of O2 release to the consumption of H2O2 was 1:2, typical of catalase activity. It is important to note that this ratio is applied when high or low H2O2 concentrations have been used (41). Several kinetic mechanisms have been proposed to provide a mechanistic explanation for these experimental findings and to explain the buildup of the LPO ferrous-dioxy complex during steady state catalysis (43, 66). Our modified working kinetic model shown in Fig. 5 indicates the formation of LPO-Fe-O2 complex intermediate in the catalytic mechanism of the enzyme. As such, it might represent an alternative pathway, whose biological function is to accelerate the removal of H2O2 from the LPO milieu by having catalase-like activity.

We have shown that the high off-rate observed for the O2 complex with LPO may be a key feature that drives decomposition of the enzyme-O2 complex and promotes generation of ligand-free LPO-Fe(II) (koff = 11 s−1). In a similar action, at higher levels of H2O2, LPO-Fe(II) can bind H2O2 generating Compound II, thereby closing the catalase-like cycle (18). The removal of LPO-Fe(II) from the equilibrium mixture of Fe-O2, Fe(II), and O2 causes the reaction to shift from the bound to unbound form enhancing the overall rates of catalysis. Alternatively, Compound III may decay to ground state (koff = 0.5 s−1) through another oxygenated intermediate that can be characterized by its absorption peak at 416 nm and again engage in the LPO catalytic cycle. The value is ~20-fold smaller than the rate constant for the dissociation rate constant of LPO-Fe(II)-O2. In an air-saturated solution, formation of the LPO-Fe(II)-O2 complex occurred at rates that were 40–100× faster than complex decay. Under such circumstances, practically all the LPO-Fe(II) sample exists in its Fe(II)-O2 form prior to decay. Therefore, accumulation of the LPO-Fe(II)-O2 during steady state catalysis of LPO requires continuous production of LPO-Fe(II)-O2 complex, which can be achieved in the presence of a high H2O2 concentration. Under these circumstances, the degree of LPO-Fe(II)-O2 accumulation and stability depends in part on the H2O2 concentration used and the rate of the conversion of Compound II to Compound III.
which is the rate-limiting step in the reaction.

The apparent ability of H$_2$O$_2$ to stabilize the LPO-Fe(II)-O$_2$ complex is unprecedented, and it may be governed by a mechanism that accelerates the regeneration of the LPO-Fe-O$_2$ complex. Such a reaction that involves the decay of Compound III to either LPO-Fe(II) or LPO-Fe(III), and both react with H$_2$O$_2$ to generate Compound II directly or through the formation of Compound I, respectively, which in turn reacted with H$_2$O$_2$ and converts to Compound III. When a low H$_2$O$_2$ concentration was used, the conversion of Compound II to Compound III declined. Thus the decay of the LPO-Fe(II)-O$_2$ complex occurs faster than its formation, and as a replacement for Compound III, Compound II accumulated during steady state catalysis. The ability of LPO to generate superoxide, a ligand for LPO-Fe(III) and a substrate for both Compounds I and II during H$_2$O$_2$ consumption, might thus also contribute to the increased overall transit time of the accumulation and stability of LPO-Fe(II)-O$_2$. In addition, a two-step mechanism has been observed previously for H$_2$O$_2$ consumption during steady state catalysis (18, 42). The transformation that is apparent from our kinetic analysis may represent a switch in subcycles in which the first step is limited by the rate of formation of Compound I when the reaction is initiated by the mixing of native LPO and H$_2$O$_2$. In this case the second step of H$_2$O$_2$ consumption is the turnover of LPO catalase-like catalysis. Thus, the variation in the binding affinity of LPO-Fe(III), LPO-Fe(II), and LPO Compound II toward H$_2$O$_2$ accounts for the inflection point in the H$_2$O$_2$ consumption rate. Therefore, the overall catalytic activity of LPO is determined by three major factors: 1) the concentration of H$_2$O$_2$, 2) the stability of Compound III formed during steady state catalysis, and 3) the affinity of LPO-Fe(II) and Compound II toward H$_2$O$_2$.

REFERENCES
1. Halliwell, B., and Gutteridge, J. M. C. (1989) in Free Radicals in Biology and Medicine (Halliwell, B., and Gutteridge, J. M. C., eds) pp. 1–20, Clarendon Press, Oxford
2. Schallerreuter, K. U., Moore, J., Wood, J. M., Beazley, W. D., Gaze, D. C., Tolin, D. J., Marshall, H. S., Panzke, A., Panzig, E., and Hibberts, N. A. (1999) J. Investig. Dermatol. Symp. Proc. 4, 91–96
3. Boveris, A., and Chance, B. (1973) Biochem. J. 134, 707–716
4. McCord, J. M. (1969) J. Biol. Chem. 244, 6049–6055
5. Rosen, G. M., Tsai, P., Weaver, J., Porausuphatana, S., Roman, L. J., Starkov, A. A., Fiskum, G., and Pou, S. (2002) J. Biol. Chem. 277, 40275–40280
6. Chance, B., Sies, H., and Boveris, A. (1979) Physiol. Rev. 59, 527–605
7. Yamamoto, Y., and Takahashi, K. (1995) Arch. Biochem. Biophys. 305, 541–545
8. Esoworthy, R. S., Chu, F. F., Geiger, P., Grisotti, A. W., and Doroshow, J. H. (1990) Arch. Biochem. Biophys. 307, 29–34
9. El-Chemaly, S., Salathe, M., Baier, S., Conner, G. E., and Forteza, R. (2003) Am. J. Respir. Crit. Care Med. 167, 425–430
10. Gerson, C., Sabater, J., Scuri, M., Torbati, A., Coffey, R., Abraham, J. W., Laurodo, I., Forteza, R., Wanner, A., Salathe, M., Abraham, W. M., and Conner, G. E. (2000) Am. J. Respir. Cell Mol. Biol. 23, 665–671
11. Conner, G. E., Salathe, M., and Forteza, R. (2002) Am. J. Respir. Crit. Care Med. 166, 557–561
12. Salathe, M., Holderby, M., Forteza, R., Abraham, W. M., Wanner, A., and Conner, G. E. (1997) Am. J. Respir. Cell Mol. Biol. 17, 97–105
13. Thomas, D. L., Milligan, T. W., Joyner, R. E., and Jeffers, K. E. (1984) Infect. Immun. 62, 529–533
15. Abu-Soud, H. M., and Hazen, S. L. (2000) J. Biol. Chem. 275, 5425–5430
16. Abu-Soud, H. M., Khasawneh, M. Y., Sohn, J. T., Murray, P., Haxhiu, M. A., Fiskum, G., and Pou, S. (2002) Am. J. Respir. Crit. Care Med. 166, 557–561
17. Kettle, A. J., and Winterbourn, C. C. (1997) Redox Rep. 2, 3–15
18. Ghiaudi, E., and Laurenti, E. (2003) Eur. J. Biochem. 270, 4403–4412
19. Ortiz de Montellano, P. R. (1992) Annu. Rev. Pharmacol. Toxicol. 32, 89–107
20. Eiserich, J. P., Hristova, M., Cross, C. E., Jones, A. D., Freeman, B. A., Halliwell, B., and van der Vliet, A. (1998) Nature 391, 393–397
21. Wu, W., Chen, Y., and Hazen, S. L. (1999) J. Biol. Chem. 274, 25933–25944
22. Nauseef, W. M. (1998) Biochemistry 37, 6355–6364
23. Weiss, S. J., Test, S. T., Eckmann, C. M., Roos, D., and Regiani, S. (1986) Science 234, 200–203
24. Abu-Soud, H. M., and Klebanoff, S. J. (1998) J. Immunol. 162, 1949–1953
25. Weiss, S. J., Test, S. T., Eckmann, C. M., Ross, D., and Regiani, S. (1986) Science 234, 200–203
26. Mayeno, A. N., Curran, A. J., Roberts, R. L., and Foote, C. S. (1989) J. Biol. Chem. 264, 5660–5665
27. Klebanoff, S. J., Walterszeder, A. M., and Rosen, H. (1984) Methods Enzymol. 105, 399–403
28. Furtmuller, P. G., Burner, U., Regelesberger, G., and Ohlinger, C. (2000) Biochemistry 39, 15578–15584
29. Abu-Soud, H. M., and Hazen, L. H. (2000) Free Radic. Biol. Med. 28, 1717–1725
30. Marquez, L. A., Dunford, H. B., and Van Wart, H. (1990) J. Biol. Chem. 265, 399–403
High Dissociation Rate Constant of Ferrous-Dioxy Complex Linked to the Catalase-like Activity in Lactoperoxidase
Semira Galijasevic, Ghassan M. Saed, Michael P. Diamond and Husam M. Abu-Soud

J. Biol. Chem. 2004, 279:39465-39470.
doi: 10.1074/jbc.M406003200 originally published online July 17, 2004

Access the most updated version of this article at doi: 10.1074/jbc.M406003200

Alerts:
• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 61 references, 17 of which can be accessed free at http://www.jbc.org/content/279/38/39465.full.html#ref-list-1