The Stimulation of Glycolysis by Hypoxia in Activated Monocytes Is Mediated by AMP-activated Protein Kinase and Inducible 6-Phosphofructo-2-kinase*

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The activation of monocytes involves a stimulation of glycolysis, release of potent inflammatory mediators, and alterations in gene expression. All of these processes are known to be further increased under hypoxic conditions. The activated monocytes express inducible 6-phosphofructo-2-kinase (iPFK-2), which synthesizes fructose 2,6-bisphosphate, a stimulator of glycolysis. During ischemia, AMP-activated protein kinase (AMPK) activates the homologous heart 6-phosphofructo-2-kinase isoform by phosphorylating its Ser-466. Here, we studied the involvement of AMPK and iPFK-2 in the stimulation of glycolysis in activated monocytes under hypoxia. iPFK-2 was phosphorylated on the homologous serine (Ser-461) and activated by AMPK in vitro. The activation of human monocytes by lipopolysaccharide induced iPFK-2 expression and increased fructose 2,6-bisphosphate content and glycolysis. The incubation of activated monocytes with oligomycin, an inhibitor of oxidative phosphorylation, or under hypoxic conditions activated AMPK and further increased iPFK-2 activity, fructose 2,6-bisphosphate content, and glycolysis. In cultured human embryonic kidney 293 cells, the expression of a dominant-negative AMPK prevented both the activation and phosphorylation of co-transfected iPFK-2 by oligomycin. It is concluded that the stimulation of glycolysis by hypoxia in activated monocytes requires the phosphorylation and activation of iPFK-2 by AMPK.

Energy deprivation (e.g. hypoxia and inhibitors of oxidative phosphorylation such as oligomycin) leads to the activation of the AMP-activated protein kinase (AMPK)† via an increase in the AMP:ATP ratio (for review see Refs. 1 and 2). AMPK is a heterotrimeric protein composed of a catalytic (α) and two regulatory (β, γ) subunits (3, 4). It is considered as a “metabolic master switch” (5), which inactivates key targets that control anabolic pathways, thereby conserving ATP (1, 2). AMPK is also implicated in the stimulation of glucose uptake that occurs in contracting muscle (6, 7).

We showed previously that AMPK phosphorylates Ser-466 of heart 6-phosphofructo-2-kinase (PFK-2), leading to its activation (8). This phenomenon participates in the well known stimulation of glycolysis by ischemia in the heart. PFK-2/fructose-2,6-bisphosphatase is a bifunctional enzyme catalyzing the synthesis and degradation of fructose 2,6-bisphosphate (Fru-2,6-P₂), the most potent stimulator of 6-phosphofructo-1-kinase and hence glycolysis. Tissue-specific isozymes of PFK-2/fructose-2,6-bisphosphatase have been identified in mammals. They possess a conserved catalytic core flanked by variable N- and C-terminal regulatory domains, and they differ in tissue distribution and response to phosphorylation by protein kinases (for review see Refs. 9 and 10). Chesney et al. (11) characterized a PFK-2 isoform, which was induced by proinflammatory stimuli and was therefore termed inducible PFK-2 (iPFK-2). iPFK-2 is identical to the previously described placentomal isoform (12) and is homologous to heart PFK-2. These isozymes are characterized by their relative PFK-2/fructose-2,6-bisphosphatase activities. Under physiological conditions, their PFK-2 activity is >100-fold that of their fructose-2,6-bisphosphatase activity (10), indicating that they mainly act as a kinase. The C-terminal regulatory domain of iPFK-2 contains Ser-461, which lies within a favorable consensus for phosphorylation by AMPK (449KGPNLRRNVSPLAS367), similar to that surrounding Ser-466 of heart PFK-2 (456KSQTPVRMMRNSFTPLSS373). A synthetic peptide corresponding to the sequence surrounding Ser-461 in iPFK-2 was indeed shown to be phosphorylated by AMPK in vitro (8).

iPFK-2 is constitutively expressed in several human cancer cell lines. This isoform has also been shown to be induced in monocytes activated by lipopolysaccharide (LPS) (11), a component of the outer membrane of Gram-negative bacteria, which triggers and mimics an inflammatory response. The response of monocytes to LPS includes the production of cytokines and chemokines, the release of arachidonic acid metabolites, and the generation of reactive oxygen species and nitrogen monoxide (13–15). Monocyte activation consumes energy, which triggers and mimics an inflammatory response. The response of monocytes to LPS includes the production of cytokines and chemokines, the release of arachidonic acid metabolites, and the generation of reactive oxygen species and nitrogen monoxide (13–15). Monocyte activation consumes energy, which triggers and mimics an inflammatory response. The response of monocytes to LPS includes the production of cytokines and chemokines, the release of arachidonic acid metabolites, and the generation of reactive oxygen species and nitrogen monoxide (13–15). Monocyte activation consumes energy, which triggers and mimics an inflammatory response. The response of monocytes to LPS includes the production of cytokines and chemokines, the release of arachidonic acid metabolites, and the generation of reactive oxygen species and nitrogen monoxide (13–15).
sequently by LPS and hypoxia are still unknown. We tested whether this synergism results from the phosphorylation and activation of iPFK-2 by AMPK in hypoxia.

EXPERIMENTAL PROCEDURES

Materials—The construct encoding recombinant polyhistidine-tagged iPFK-2 (21) was a generous gift of R. Bartrons (Barcelona, Spain). Recombinant iPFK-2 was purified (22) from human embryonic kidney (HEK)-293 cells transfected with this construct. Liver AMPK was purified as described previously (23). Wild-type and dominant-negative iAMPK constructs were described previously (24). Rabbit polyclonal anti-phospho-S466 (8) and anti-iPFK-2 (11) antibodies were raised against synthetic peptides. These peptides and the SAMS peptide (25) were synthesized by V. Stroobant (Ludwig Institute for Cancer Research, Brussels, Belgium).

In Vitro Studies—For the measurement of kinetic properties, purified iPFK-2 and heart PFK-2 were incubated with 1 mM MgATP and AMPK at 30 °C (26), and aliquots were taken for PFK-2 assay (27). For determination of phosphorylation, iPFK-2 was incubated with 0.1 mM Mg\(^{2+}\)-\[^{32}P\]ATP (1000 cpm/pmol) and AMPK. Aliquots were taken and analyzed as described previously (26). The amount of purified enzymes used in each experiment is given in the figure legends.

Cell Culture—Peripheral blood mononuclear cells were isolated by centrifugation of human whole blood through a density gradient of Ficoll-Paque (Amersham Biosciences) and cultured in Petri dishes (10-cm diameter, 10 \(\times\) 10\(^6\) monocytes/dish) in RPMI 1640 medium with 10\% (v/v) fetal calf serum (11). After 2 h of culture, the medium and nonadherent cells were removed by aspiration, and the remaining adherent monocytes were incubated without (resting) or with (activated) 1 \(\mu\)g/ml LPS (Escherichia coli 0111:B4, Sigma). The percentage of monocytes in the cultures was determined by fluorescence-activated cell sorter analysis for CD14 expression (28). The cells were incubated under the conditions and the periods of time indicated in the figure legends. Following incubation, the medium was aspirated, and the cells were immediately lysed in 0.8 ml of ice-cold lysis buffer (8) for enzyme assays or in 0.5 ml of 50 mM NaOH for Fru-2,6-P\(_2\) determination. Total RNA was isolated with the High Pure RNA isolation kit (Roche Molecular Biochemicals). HEK-293 cells were cultured in Dulbecco’s modified Eagle Medium supplemented with 10\% (v/v) fetal calf serum (11). After 2 h of culture, aliquots were taken and analyzed as described previously (26). The amount of purified enzymes used in each experiment is given in the figure legends.

**RESULTS**

Phosphorylation and Activation of iPFK-2 by AMPK in Vitro—Purified iPFK-2 was phosphorylated by AMPK with a stoichiometry close to 0.7 mol of phosphate incorporated/mol of enzyme subunit, indicating phosphorylation at one site. The rate and the extent of phosphorylation were stimulated by AMP (Fig. 1A), and phosphorylation correlated with PFK-2 activation (Fig. 1B). The treatment with AMPK led to a 2.5-fold increase in \(V_{\text{max}}\) of PFK-2 with no significant change in \(K_{\text{m}}\) for fructose 6-phosphate or MgATP (Table I). These changes in kinetic properties resemble those seen after the phosphorylation of heart PFK-2 by AMPK (Table I) (8). The similarity among the sequences surrounding Ser-461 of iPFK-2 and Ser-466 of heart PFK-2 led us to use the antibody raised against the phosphorylated Ser-466 of heart PFK-2 (anti-p\(S_466\)) to study the phosphorylation of Ser-461 in iPFK2. Immunoblotting with this antibody showed that AMPK phosphorylated Ser-461 of iPFK-2 (Fig. 2).

**AMPK Is Activated by Oligomycin and Hypoxia in Resting Monocytes**—To activate AMPK, resting monocytes were incubated under hypoxic conditions or with two known activators of AMPK, namely 5-aminooimidazole-4-carboxamide riboside (0.5 mM), a precursor of the AMP analog ZMP or oligomycin (1 \(\mu\)M), an inhibitor of oxidative phosphorylation. Basal AMPK activity was low and similar to that measured in normoxic perfused hearts or cells in culture (8) and remained unchanged over the incubation period (Fig. 3). By contrast, AMPK activity progressively increased during incubation with oligomycin or hypoxia to reach maximal values between 10 and 20 min before decreas-
Purified iPFK-2 or heart PFK-2 (0.1 mg/ml) was incubated with (w/) or without (w/o) AMPK (0.6 unit/ml) with 0.2 mM AMP and 1 mM MgATP in a final volume of 100 μl at 30°C for 30 min. Aliquots (10 μl) were taken for the measurement of PFK-2 activity. PFK-2 was measured at pH 7.1 in the presence of 5 mM MgATP and concentrations of fructose 6-phosphate up to 10 times the $K_m$ in the presence of 1 mM fructose 6-phosphate and concentrations of MgATP up to 10 times the $K_m$. The results are the means ± S.E. for three different experiments.

### Table I. Effects of AMPK on the kinetic properties of iPFK-2 and heart PFK-2

|          | iPFK-2 w/o AMPK | iPFK-2 w/ AMPK | heart PFK-2 w/o AMPK | heart PFK-2 w/ AMPK |
|----------|-----------------|----------------|-----------------------|---------------------|
| $V_{max}$ (milliunits/mg protein) | 10 ± 1          | 25 ± 2"        | 50 ± 4                | 125 ± 10"           |
| $K_m$ for fructose 6-phosphate (μM) | 53 ± 2          | 50 ± 4          | 57 ± 3                | 46 ± 1              |
| $K_m$ for MgATP (μM) | 650 ± 32        | 582 ± 37        | 930 ± 12              | 745 ± 5             |

*p < 0.01 in comparison with sample incubated without AMPK.

**Fig. 2.** Immunoblot of inducible and heart PFK-2 phosphorylated by AMPK with the anti-pS466 antibody. Purified PFK-2 (0.15 mg/ml) was incubated with AMPK (0.6 unit/ml), AMP (0.2 mM), and 1 mM MgATP in a final volume of 20 μl at 30°C. After 30 min, samples were removed for SDS-PAGE and immunoblotted with the anti-pS466 antibody.

**Fig. 3.** Time-dependent activation of AMPK by hypoxia or oligomycin in resting monocytes. Resting monocytes were submitted to hypoxia (a), hypoxia (95% N2, 5% CO2) (b), 1 μM oligomycin (c), or 0.5 mM 5-aminoimidazole-4-carboxamide riboside (d). The values are the means ± S.E. for at least three different preparations.

**Fig. 4.** Time-dependent induction of IL-1β and iPFK-2 by LPS in monocytes. A, reverse transcription-PCR analysis of IL-1β, iPFK-2, and β-actin mRNAs obtained from resting or LPS-activated monocytes. The effects of oligomycin (1 μM, 15 min) on iPFK-2 and IL-1β mRNA was analyzed in monocytes cultured for 6 h. B, immunoblot analysis with anti-iPFK-2 antibody on 10 μg of protein from extracts of resting or LPS-activated monocytes. The effect of oligomycin (1 μM, 15 min) was also verified.

The effect of hypoxia was also investigated and compared with that of oligomycin. Resting monocytes or monocytes activated by LPS for 6 h, an incubation period sufficient to induce iPFK-2, were submitted to hypoxia or oligomycin. In resting and LPS-activated monocytes, this hypoxic episode resulted in AMPK activation, which was less pronounced as seen with oligomycin (Fig. 6A). Hypoxia also activated PFK-2 but only in LPS-activated cells (Fig. 6B). The hypoxia-induced activation of PFK-2 was less than that observed with oligomycin and paralleled AMPK activation (Fig. 6).

Oligomycin Stimulates PFK-1 Flux in Activated Monocytes—To evaluate the effect of oligomycin on glycolysis, the rate of detritiation of [3-3H]glucose, an estimation of the flux through PFK-1 (29), was measured. The detritiation of [3-3H]glucose was measured in monocytes activated by LPS for up to 12h, incubated with or without oligomycin (Fig. 5D). A stimulation of glucose detritiation was observed in LPS-activated monocytes compared with resting monocytes. Moreover, oligomycin further increased the flux through PFK-1 in LPS-activated monocytes but not in resting monocytes. A comparison of Fig. 5, A, B, and D, indicates that the increase in
glycolytic flux is remarkably correlated with the increase in Fru-2,6-P2 content and PFK-2 activity.

*iPFK-2 Activation by Oligomycin Is Prevented by a Dominant-negative Mutant of AMPK*—To test the involvement of AMPK in the activation of iPFK-2 by oligomycin, the effect of a dominant-negative mutant of AMPK (\textsuperscript{\textalpha}DN AMPK) was investigated in HEK-293 cells. These cells are known to be transfected with high efficiency and have been used previously to study the effect of AMPK on the heart PFK-2 activation (8). The transfection of HEK-293 cells with the iPFK-2 construct resulted in a 5–10-fold increase in total PFK-2 content (7 ± 1 microunits/mg protein in untransfected cells to 67 ± 15 microunits/mg protein in cells transfected with 5 μg of iPFK-2 DNA, \(n = 6\)). Incubation with oligomycin for 15 min activated both endogenous AMPK (4-fold) and transfected iPFK-2 (2-fold) in a time-dependent manner (Fig. 7, A and B) but had no effect on endogenous PFK-2 (Fig. 7B). In addition, immunoblotting with the anti-pS466 antibody revealed a time-dependent phosphorylation of iPFK-2 (Fig. 7C). We previously demonstrated the dominant-negative character of the \(\textsuperscript{\textalpha}DN AMPK construct by verifying that its transfection abolished the oligomycin-induced activation of both endogenous (Fig. 7A) (8) and transfected wild-type AMPK in HEK-293 cells (8). We investigated the effect of this dominant-negative AMPK on the activation of iPFK-2 by oligomycin. The co-expression of \(\textsuperscript{\textalpha}DN AMPK abolished both the phosphorylation (Fig. 7D) and activation of iPFK-2 (Fig. 7B), demonstrating that AMPK mediates the oligomycin-induced activation of iPFK-2 in intact cells.

**DISCUSSION**
The results presented here suggest that AMPK and iPFK-2 are implicated in the stimulation of glycolysis by hypoxia in LPS-activated monocytes. The incubation of resting monocytes with LPS induced the expression of iPFK-2, a PFK-2 isoform

![Figure 5](http://www.jbc.org/)

**Fig. 5.** **Effect of oligomycin on AMPK and PFK-2 activity, Fru-2,6-P2 content, and glycolysis in resting and LPS-activated monocytes.** Resting monocytes (squares) or LPS-activated monocytes (circles) were incubated for the indicated periods of time. At the indicated time, monocytes were incubated without (open symbols) or with (filled symbols) 1 μmol oligomycin. After 15-min incubation with oligomycin, the cells were lysed for measurement of PFK-2 activity (A), Fru-2,6-P2 content (B), and AMPK activity (C). D, after 5-min incubation with oligomycin, radioactive glucose was added, and the cells were further incubated for 15 min for measurement of glucose degritiation. The values are the means ± S.E. for 3–5 different preparations. *, significant effect \((p < 0.01)\) of LPS; #, significant effect \((p < 0.05)\) of oligomycin in LPS-activated cells.

![Figure 6](http://www.jbc.org/)

**Fig. 6.** **Activation of AMPK and PFK-2 by hypoxia in monocytes.** Resting monocytes or monocytes activated by LPS for 6 h were incubated under normoxic conditions (open bars) or submitted to a 15-min incubation under hypoxic condition (95% \(N_2\), 5% \(O_2\)) or with 1 μmol oligomycin (filled bars) as indicated. After this incubation, the cells were lysed for measurement of AMPK (A) and PFK-2 (B) activity. The values are the means ± S.E. for four different preparations. *, significant effect \((p < 0.01)\) of hypoxia or oligomycin compared with normoxic control; #, significant effect \((p < 0.05)\) of oligomycin compared with hypoxia.
transfected with iPFK-2. Therefore, during hypoxia, AMPK phosphorylation and activation of iPFK-2 were completely allowed the same time course. Finally, the oligomycin-induced AMPK phosphorylation and activation of iPFK-2 in HEK-293 cells. HEK-293 cells under hypoxia activated AMPK and PFK-2, increased Fru-2,6-P₂ concentration, and (iii) a peptide containing the sequence resembling heart PFK-2, and (ii) phosphorylation of iPFK-2 could be detected close to 1, (ii) phosphorylation of iPFK-2 could be detected at the same site, namely Ser-461 in iPFK-2. This finding is further supported by the fact that (i) stoichiometry of phosphorylation was supposed to be 1, and the concentration of Fru-2,6-P₂ was ~2 pmol/mg protein, a concentration that was 10 times lower than that measured in H36.12j cells. Furthermore, we found that the concentration of cyclic AMP in resting monocytes (4 pmol/g cells) was 10-fold lower than in H36.12j cells and remained unchanged in LPS-activated monocytes. In these activated monocytes, which express iPFK-2, hypoxia increased Fru-2,6-P₂ concentrations to maximal values similar to those observed in normoxic H36.12j cells. Therefore, the conclusions drawn from the study of the response of H36.12j macrophages to hypoxia are probably not applicable to normal human monocytes.

Few studies have shown striking effects of hypoxia on monocytes in the absence of additional stimuli. Likewise, in our experiments, hypoxia alone had no significant effect on glycolysis but increased glycolytic flux after LPS activation. The fact that monocyte responses to hypoxia are enhanced by stimulants such as LPS and interferon-γ (32–34) reflects the important role of these stimuli in coordinating monocyte activity. We postulate that LPS primes monocytes to respond to hypoxia, which inevitably occurs in and around diseased tissues. The subsequently expressed iPFK-2 could thus be activated by AMPK under hypoxic conditions, thereby furnishing ATP to boost the inflammatory response.

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REFERENCES
1. Hardie, D. G., and Carling, D. (1997) Eur. J. Biochem. 246, 259–273
2. Hardie, D. G., and Hawley, S. A. (2001) Bioessays 23, 112–119
3. Stapleton, D., Mitchellill, K. I., Gao, G., Widmer, J., Michell, B. J., Teh, T., House, C. M., Fernandez, C. S., Cox, T., Witters, L. A., and Kemp, B. E. (1996) J. Biol. Chem. 271, 611–614
4. Woods, A., Cheung, P. C. F., Smith, F. C., Davison, M. D., Scott, J., Beri, R. K., and Carling, D. (1996) J. Biol. Chem. 271, 10282–10290
5. Hardie, D. G., Carling, D., and Carlson, M. (1998) Annu. Rev. Biochem. 67, 821–855
6. Kurth-Kraczek, E. J., Hirshman, M. F., Goodyear, L. J., and Winder, W. W. (1999) Diabetes 48, 1667–1671
7. Russell, A. R., Bergeron, R., Shulman, G. I., and Young, L. H. (1999) Am. J. Physiol. 271, H643–H649
8. Marsin, A.-S., Bertrand, L., Rider, M. H., Deprez, J., Beauloye, C., Vincent, M. F., Van den Berghe, G., Carling, D., and Hue, L. (2000) Curr. Biol. 10, 1247–1255
9. Hue, L., and Rider, M. H. (1987) Biochem. J. 245, 313–324
10. Okar, D. A., Manzano, A., Navarro-Sabate, A., Riera, L., Bartrons, R., and Lange, A. J. (2001) Trends Biochem. Sci. 26, 30–35

FIG. 7. α1DN AMPK prevents the oligomycin-induced phosphorylation and activation of iPFK-2 in HEK-293 cells. HEK-293 cells were co-transfected with 5 μg of iPFK-2 DNA and 5 μg of α1DN AMPK DNA (A) or α1 wild-type AMPK DNA as control (B). Cells were incubated with 0.5 μM oligomycin. At the indicated times, cells were lysed for measurement of AMPK (A) and PFK-2 (B) activity. The triangles indicate endogenous PFK-2 activity in nontransfected cells. The values are the means ± S.E. for four different preparations. C, immunoblot of phosphorylated iPFK-2 (anti-pS466 antibody) on samples taken at the indicated times from cells transfected with iPFK-2 and α1 wild-type AMPK NT; untransfected cells. D, immunoblot of phosphorylated iPFK-2 (anti-pS466 antibody) on samples taken from cells transfected with iPFK-2 and α1DN AMPK as indicated and incubated with oligomycin for 10 min.
11. Chesney, J., Mitchell, R., Benigni, F., Bacher, M., Spiegel, L., Al-Abed, Y., Han J. H., Metz, C., and Bucala, R. (1999) Proc. Natl. Acad. Sci. U. S. A. 96, 3047–3052
12. Sakai, A., Kato, M., Fukasawa, M., Ishiguro, M., Furuya, E., and Sakakibara, R. (1996) J. Biochem. 119, 506–511
13. Bone, R. C. (1991) Ann. Intern. Med. 115, 457–469
14. Glauser, M. P., Zanetti, G., Baumgartner, J.-D., and Cohen, J. (1991) Lancet 338, 732–736
15. Suzuki, T., Hashimoto, S.-I., Toyoda, N., Nagai, S., Yamazaki, N., Deng, H.-Y., Sakai, J., Yamashita, T., Nukiwa, T., and Matsushima, K. (2000) Blood 96, 2584–2591
16. Lang, C. H., Bagby, G. J., Fong, B. C., and Spitzer, J. J. (1985) Am. J. Physiol. 248, R471–R478
17. Orlinska, U., and Newton, R. C. (1993) J. Cell. Physiol. 157, 201–208
18. Guida, E., and Stewart, A. (1998) Cell. Physiol. Biochem. 8, 75–88
19. Remenoyder, J. P., and Majno, G. (1968) Am. J. Pathol. 53, 301–316
20. Hunt, T. K., Knighton, D. R., Thackral, K. K., Goodson, W. H., and Andrews, W. S. (1983) Surgery 96, 48–54
21. Manzano, A., Rosa, J. L., Ventura, F., Perez, J. X., Nadal, M., Estivill, X., Ambrosio, S., Gil, J., and Bartrons, R. (1998) Cytogenet. Cell Genet. 82, 214–217
22. Bertrand, L., Alessi, D. R., Deprez, J., Deak, M., Viaene, M., Rider, M. H., and Hue, L. H. (1999) J. Biol. Chem. 274, 30927–30933
23. Carling, D., and Hardie, D. G. (1989) Biochim. Biophys. Acta 1012, 81–86
24. Stein, S. C., Woods, A., Jones, N. A., Davison, M. D., and Carling, D. (2000) Biochem. J. 345, 437–443
25. Davies, S. P., Carling, D., and Hardie, D. G. (1989) Eur. J. Biochem. 186, 123–128
26. Deprez, J., Vertommen, D., Alessi, D. R., Hue, L., and Rider, M. H. (1997) J. Biol. Chem. 272, 17269–17275
27. Crepin, K. M., Vertommen, D., Dem, G., Hue, L., and Rider, M. H. (1993) J. Biol. Chem. 268, 15277–15284
28. Van Schaftingen, E., Lederer, B., Bartrons, R., and Hers, H. G. (1982) Eur. J. Biochem. 129, 191–195
29. Hue, L., and Hers, H. G. (1974) Biochem. Biophys. Res. Commun. 58, 352–339
30. Bontemps, F., Hue, L., and Hers, H. G. (1978) Biochem. J. 174, 603–611
31. Kawaguchi, T., Veech, R. L., and Uyeda, K. (2001) J. Biol. Chem. 276, 28551–28561
32. West, M. A., Li, M. H., Seatter, S. C., and Bubrick, M. P. (1994) J. Trauma 37, 82–90
33. Hempel, S. L., Monick, M. M., and Hunninghake, G. W. (1996) Am. J. Respir. Cell Mol. Biol. 14, 170–176
34. Metinko, A. P., Kunkel, S. L., Standiford, T. J., and Strieter, R. M. (1992) J. Clin. Invest. 90, 791–798
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