The methanogenic archaean *Methanococcus maripaludis* can use ammonia, alanine, or dinitrogen as a nitrogen source for growth. The euryarchaeonal nitrogen repressor NrpR controls the expression of the *nif* (nitrogen fixation) operon, resulting in full repression with ammonia, intermediate repression with alanine, and derepression with dinitrogen. NrpR binds to two tandem operators in the *nif* promoter region, nifOR1 and nifOR2. Here we have undertaken both *in vivo* and *in vitro* approaches to study the way in which NrpR, nifOR1, nifOR2, and the effector 2-oxoglutarate (2OG) combine to regulate *nif* expression, leading to a comprehensive understanding of this archaeal regulatory system. We show that NrpR binds as a dimer to nifOR2, and cooperatively as two dimers to both operators. Cooperative binding occurs only with both operators present. nifOR1 has stronger binding and by itself can mediate the repression of *nif* transcription during growth on ammonia, unlike the weakly binding nifOR2. However, nifOR2 in combination with nifOR1 is critical for intermediate repression during growth on alanine. Accordingly, NrpR binds to both operators together with higher affinity than to nifOR1 alone. NrpR responds directly to 2OG, which weakens its binding to the operators. Hence, 2OG is an intracellular indicator of nitrogen deficiency and acts as an inducer of *nif* transcription via NrpR. This model is upheld by the recent finding (J. A. Dodsworth, personal communication) in our laboratory that 2OG levels in *M. maripaludis* vary with growth on different nitrogen sources.

Transcriptional regulation in the domain Archaea (1) is intriguing because, in many cases, homologs of bacterial regulators function in the context of the archaenal basal transcriptional apparatus, which resembles that of the Eukarya (2–5). Archaeal promoters consist of an AT-rich TATA box 24–26 bp upstream from the transcriptional initiation site and a purine-rich B recognition element immediately upstream of the TATA box. During transcription initiation, TATA-binding protein-recognition element, which determines the directionality of transcription (6). The complex containing these three factors is sufficient to initiate transcription in a cell-free system (7), although an additional factor, transcription factor E, increases transcription from some promoters (8, 9). Archaeal TATA-binding protein, transcription factors B and E, and the RNA polymerase are all homologs of the eukaryal transcription counterparts. However, homologs of bacterial transcriptional regulators are common in Archaea, and those that have been studied experimentally include the Lrp (10) homologs, which can function as either repressors or activators (11–14). Binding sites for these Lrp homologs can be upstream of the TATA box (15), overlapping it (12) or overlapping the transcriptional start site (16), indicating either activation or inhibition of different steps of the transcriptional initiation process. A few homologs of eukaryal transcriptional regulators as well as uniquely archaeal regulators are also known, and their regulatory actions have been investigated (9, 17–20). Histones and other non-sequence-specific DNA-binding proteins (21, 22) also have been found in some instances to play a role in the regulation of archaeal genes (23). Archaea thus possess a complex mix of transcriptional regulatory schemes.

Dinitrogen fixation occurs only in the domains Bacteria and Archaea (24). Nitrogen fixation has been demonstrated in various methanogens (24), and *nif* (nitrogen fixation) genes, which are organized into operons, have been detected (25–27). Nitrogen fixation is highly energy expensive and is regulated tightly both transcriptionally and post-translationally (28). The transcriptional regulation of *nif* genes in Bacteria involves diverse systems (28), whereas the *nif* regulation in those Archaea that have been studied is entirely different (see below)

Our laboratory has studied *nif* regulation as a model of transcriptional regulation in Archaea, using the species *Methanococcus maripaludis* (29, 30), in which a facile genetic system offers the unusual opportunity within Archaea to conduct *in vivo* as well as *in vitro* studies (31). *nif* expression in *M. maripaludis* is repressed by ammonia and derepressed when dinitrogen is the sole nitrogen source (32, 33). In addition, an intermediate level of expression occurs with alanine as a nitrogen source (34). Previously, we identified two tandem palindromes (nifOR1 and nifOR2) (see Fig. 1), both with the conserved sequence GGAA-N6-CCCT (N6 denotes six nucleotides), within the *nif* promoter region (33). Although both operators are highly similar to the consensus sequence, only nifOR2 is needed for repression during growth on ammonia. However, nifOR2 in combination with nifOR1 is required for intermediate repression during growth on alanine (34). Furthermore, an unknown factor present in the cell extract binds more effectively to both operators together than to nifOR1 alone. We demonstrated recently (18) that a novel regulator, NrpR, with homologs known only in the Euryarchaeota, is the repressor of *nif* expression.
In this study, we extended our investigation of the roles of the nitrogen operators and NrpR and report that 2-oxoglutarate (2OG) \(^1\) functions as an inducer. Using purified His-tagged NrpR for \textit{in vitro} binding studies, we show the primary role played by nifOR\(_1\), the importance of nifOR\(_2\) in mediating cooperative binding of NrpR to DNA, and the direct role of 2OG in affecting the binding affinity of NrpR to the operators. The binding properties of purified NrpR to the \textit{nif} operators at different concentrations of 2OG account for the regulatory effects observed \textit{in vivo}.

**EXPERIMENTAL PROCEDURES**

\textbf{Media and Growth Conditions—} All \textit{M. maripaludis} strains were maintained in complex McCas medium (35) or minimal nitrogen-free medium described previously (36), with the addition of neomycin sulfate (1 mg/ml) or puromycin (2.5 \(\mu\)g/ml), as appropriate. NH\(_4\)Cl (10 mM), L-alanine (10 mM), or NH\(_4\)F (15 p.s.i. of 80% NH\(_3\), 20% CO\(_2\)) served as a nitrogen source. Mm706 (+pWLG40RepHis) (described below) was grown in a 12-liter fermenter (model MMF14-171816, New Brunswick Microferm) as follows. Anaerobic McCas medium (10 liters) (containing both neomycin and neomycin) was inoculated with 250 ml of fresh culture grown in modified 1-liter bottles (37) and sparged with 800 ml/min H\(_2\), 200 ml/min CO\(_2\), and 20 ml/min 1% H\(_2\)S in N\(_2\). Gases (except H\(_2\)S) were passed through a copper furnace set at 300 °C to scavenge trace amounts of O\(_2\). The impeller agitation rate was 200 rpm, and the temperature was 37 °C.

\textbf{Strain Construction—} To construct Mm706 (\textit{ΔnrpR}, neo) plasmid pTJL11R4 (18), in which the EcoRV-EcoRI portion of \textit{nrpR} had been replaced with a neomycin resistance cassette (38), was transformed into \textit{M. maripaludis} S2 (wild type) by the polyethylene glycol method (39). Replacement of genomic \textit{nrpR} by a homologous recombination was shown by Southern analysis, and the loss of NrpR DNA binding activity was confirmed by the gel shift assay. To construct C-terminal \textit{his}tagged \textit{nrpR}, the \textit{nrpR} gene was PCR amplified from pTJL11R4 (18), in which the EcoRV-EcoRI portion of \textit{nrpR} was fused to an archaeal histone promoter (41), allowing for constitutive expression in \textit{M. maripaludis}. This plasmid contained \textit{nrpR}-his, encoding NrpR with the amino acids alanine, and dinitrogen, respectively (Fig. 1). Mutagenesis of \textit{M. maripaludis} contained \textit{nrpR}-his fused to an archaeal histone promoter (41), allowing for constitutive expression in \textit{M. maripaludis}. This plasmid was sequenced to determine that no errors were introduced during PCR amplification. pWLG40RepHis was grown in a 12-liter fermenter (model MMF14-171816, New Brunswick Microferm) as follows. Anaerobic McCas medium (10 liters) (containing both neomycin and neomycin) was inoculated with 250 ml of fresh culture grown in modified 1-liter bottles (37) and sparged with 800 ml/min H\(_2\), 200 ml/min CO\(_2\), and 20 ml/min 1% H\(_2\)S in N\(_2\). Gases (except H\(_2\)S) were passed through a copper furnace set at 300 °C to scavenge trace amounts of O\(_2\). The impeller agitation rate was 200 rpm, and the temperature was 37 °C.

\textbf{RESULTS}

\textbf{nifOR\(_2\) Is Critical for Intermediate Repression during Growth on Alanine—} Previously (33), a series of \textit{nif} promoter-\textit{lacZ} fusions were used to study the roles of nifOR\(_1\) and nifOR\(_2\) (Fig. 1) in \textit{nif} repression. In addition to the wild type promoter region, mutant promoter regions were made in which the sequence of each operator was altered while preserving its palindromic nature. Only nifOR\(_1\) is required for repression by ammonia, but nifOR\(_1\) and nifOR\(_2\) are both required for repression by alanine (34). Here we also tested the effect of altering the distance between nifOR\(_1\) and nifOR\(_2\). Fusions of wild type and mutant \textit{nif} promoter regions with \textit{lacZ} were introduced into \textit{M. maripaludis}, and \textit{β}-galactosidase assays were performed with cultures grown on the three nitrogen sources. As expected, the wild type \textit{nif} promoter region resulted in low, intermediate, and high levels of expression with ammonia, alanine, and dinitrogen, respectively (Fig. 1). Maturation of

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\(^1\) The abbreviations used are: 2OG, 2-oxoglutarate; BSA, bovine serum albumin; WT, wild type; nifOR, operator in \textit{nif} promoter region.
nifOR\textsubscript{1} (ct1ag1) abolished all repression, confirming the role of nifOR\textsubscript{1} as the "primary" operator. Mutagenesis of nifOR\textsubscript{2} (ct2ag2) removed repression by alanine only.

We tested an additional mutant (33) in which the spacing between nifOR\textsubscript{1} and nifOR\textsubscript{2} was decreased by 6 bp (ct4a) (Fig. 1). Repression occurred with ammonia but not with alanine (Fig. 1). Hence, both the sequence of nifOR\textsubscript{1} and its distance from nifOR\textsubscript{2} are important for the intermediate level of repression that normally occurs with alanine. Changing the distance between the two operators could destroy the ability of the repressor to bind to both operators at the same time. In the wild type nif promoter region, nifOR\textsubscript{1} and nifOR\textsubscript{2} were centered 3.1 helical turns apart and were thus on the same face of the DNA (in phase), whereas in the mutant, the two operators were centered 2.6 helical turns apart.

His-tagged NrpR Regulates nif Expression Like Wild Type NrpR in Vivo—In preparation for the purification of the nitrogen repressor NrpR, we constructed a gene encoding a C-terminal His-tagged NrpR (NrpR-His) and tested its activity in vivo. We transformed the replicative plasmid pWLG40RepHis containing constitutively expressed npr\textsubscript{R}-his into M. maripaludis strain Mm706, in which the internal portion of the nrf promoter region, nifOR\textsubscript{1} and nifOR\textsubscript{2} were centered 3.1 helical turns apart and were thus on the same face of the DNA (in phase), whereas in the mutant, the two operators were centered 2.6 helical turns apart.

NrpR-His Binds to WT nif and Single Operator Mutant Promoters with Different Affinities in vitro—We purified NrpR-His to >95% purity. We used gel mobility shift analysis to determine the ability of NrpR-His to bind to wild type and mutant forms of the DNA corresponding to the portion of the nrf promoter region that contains the nif operators (Fig. 1, nucleotides −13 to +73). NrpR-His (0.4 nm) bound to DNA containing both operators (Fig. 2A, WT nif) or nifOR\textsubscript{1} alone (Fig. 2A, ct1ag1) but not to DNA containing nifOR\textsubscript{2} alone (Fig. 2A, ct2ag2) or to DNA lacking both operators (Fig. 2A, dm). NrpR-His also bound to DNA in which both operators were present, but the distance between the operators was decreased by 6 bp (Fig. 2A, ct4a).

Increasing concentrations of NrpR-His resulted in increased binding, and except for the weakly binding construct ct1ag1, binding increased up to the point at which unbound DNA was nearly depleted (Fig. 2, B and C). Equilibrium dissociation constants (K\textsubscript{d}) estimated from the binding curves (Fig. 2C) were WT nif, 0.3 nm, ct2ag2 and ct4a, both 0.2 nm, and ct1ag1, >7 nm. These results showed that nifOR\textsubscript{1} is essential for significant binding, in agreement with the requirement for nifOR\textsubscript{1} for repression to occur in vivo. NrpR-His, despite its similarity in sequence to nifOR\textsubscript{1}, has much weaker binding that must result from the nucleotides flanking the conserved portions of the operator.

NrpR-His Binds to Single Operators as a Dimer and Cooperatively to Two Operators as a Dimer Pair—NrpR-His binding to nifOR\textsubscript{1} (ct2ag2) or nifOR\textsubscript{2} (ct1ag1) alone or to the deletion construct ct4a produced a single shifted band, always of the same mobility (Fig. 2, A and B, band A). NrpR-His binding to both operators together (WT nif) produced a band of the same mobility at low concentrations of NrpR-His (Fig. 2, A and B, band B) but also produced a slower migrating band (Fig. 2, A and B, band B) at higher concentrations of NrpR-His. We hypothesized that band A was a NrpR-His dimer bound to a single operator, whereas band B was two NrpR dimers, one bound to each operator. To test this hypothesis, we determined the binding stoichiometries of NrpR-His to wild type and mutant nif operator DNAs by generating Ferguson plots (43), a method in which the R\textsubscript{F} values of unknown protein complexes at different acrylamide concentrations are compared against those of native molecular mass standards to derive their native molecular masses. Unbound NrpR-His was 160,000 Da, NrpR-His bound to WT nif operator DNA was 329,000 Da, NrpR-His-clt2ag2 was 185,000 Da, and NrpR-His-ct4a was 178,000 Da (Fig. 3). Subtracting the molecular masses of unbound DNA determined from the same acrylamide gel concentrations (WT nif was 47,000 Da, ct2ag2 was 49,000 Da, and ct4a was 38,000 Da) and dividing by the molecular mass of the NrpR-His monomer (60,811 Da) indicated that 2.6 monomers were present in free NrpR-His, 4.6 monomers were bound to WT nif; 2.2 monomers were bound to ct2ag2, and 2.3 monomers were bound to ct4a. We concluded that bands A and B (Fig. 2, A and B) contained a dimer and a dimer pair of NrpR-His, respectively. Because NrpR-His barely bound nifOR\textsubscript{2} alone even at high concentrations, we concluded that interactions between two NrpR-His dimers formed a pair that bound cooperatively to the two operators. Cooperative binding of dimer pairs to ct4a may not be possible because the spacing between the two operators is unfavorable or because the two operators are not on the same face of the helix, as seen in analogous bacterial and λ repression systems (44, 45).
We found previously (18) that NrpR binding activity was similar in cell extracts of ammonia-, alanine-, and dinitrogen-grown cultures. This observation suggested that some additional factor must modulate NrpR binding to operator DNA \textit{in vivo}. Gel mobility assays showed that 2OG (5 mM) markedly inhibited the binding of NrpR-His to WT \textit{nif} DNA (Fig. 4A). Alanine, glutamine, or glutamate had no effect. Increasing the concentrations of 2OG had increasing effects (Fig. 4B), and estimates of \( K_d \) (Fig. 4C) showed that increasing 2OG decreased the binding affinity of NrpR-His over a range of less than 0.1 mM to 1.6 mM 2OG (Fig. 4D). 2OG may act as an inducer in concert with NrpR to regulate \textit{nif} expression.

NrpR-His Has Higher Binding Affinity to WT \textit{nif} than Mutant Operator DNAs in the Presence of 2OG—Because NrpR-His binds cooperatively to \textit{nifOR}_1 and \textit{nifOR}_2 together (as described above), one would expect higher affinities for WT \textit{nif} than for ct2ag2 or ct4a. Although this was not observed in the absence of 2OG (Fig. 2C), it was the case in the presence of a moderate concentration of 2OG. Thus, the presence of as little as 0.1 mM 2OG was sufficient to render the affinities for the double and single operator configurations different by 5-fold (Fig. 2C). The situation in the absence of 2OG may correspond to ammonia-grown cells, in which cellular 2OG levels may be very low and marked repression occurs similarly with both operators, \textit{nifOR}_1 alone, or \textit{nifOR}_1 with \textit{nifOR}_2 at an altered distance. The situation with concentrations of 0.1 mM 2OG (or higher) may correspond to alanine-grown cells, in which both operators appropriately spaced are required for repression. In dinitrogen-grown cells, 2OG levels are likely so high that NrpR cannot bind even to both operators together.

**DISCUSSION**

The results presented here lead to a model for an inducer-controlled binding of the repressor NrpR to \textit{nif} operator DNA that accounts for the regulatory effects observed \textit{in vivo} (Fig. 5). The wild type configuration of the \textit{nif} promoter region, containing both operators \textit{nifOR}_1 and \textit{nifOR}_2 appropriately spaced, cooperatively binds a NrpR dimer pair with high affinity. This binding results in repression during growth on ammonia, in which cellular 2OG levels are low, and repression during growth on alanine, in which both operators appropriately spaced are required for repression. Altering the secondary operator \textit{nifOR}_2 alone, or \textit{nifOR}_2 with \textit{nifOR}_1 at an altered distance. The situation with concentrations of 0.1 mM 2OG (or higher) may correspond to alanine-grown cells, in which both operators appropriately spaced are required for repression. In dinitrogen-grown cells, 2OG levels are likely so high that NrpR cannot bind even to both operators together.
it with respect to nifOR1 removes the ability of NrpR dimer pairs to bind cooperatively, so only a single dimer binds to nifOR1 at a lower affinity compared with cooperative binding to both operators together. As a result, repression occurs only during growth on ammonia in which 2OG levels are low, whereas during growth on alanine, 2OG levels are sufficient to disrupt the relatively weak binding of the NrpR dimer to the nifOR1. Our laboratory has shown recently that cellular 2OG levels indeed vary in M. maripaludis with nitrogen conditions. Although absolute intracellular metabolite levels are difficult to measure accurately, the relative levels differed by 10-fold, with approximate levels of 0.08 mM in ammonia-grown cells and 0.8 mM in dinitrogen-grown cells. These values correspond roughly to the 10-fold range of 2OG concentrations (0.1–1.6 mM) over which the $K_d$ for NrpR binding to the nif operators varies (Fig. 4D).

2OG and glutamine are both signals of nitrogen status and together signal nitrogen sufficiency (high glutamine, low 2OG) or nitrogen deficiency (low glutamine, high 2OG). In E. coli, 2OG interacts directly with PII nitrogen sensor proteins, whereas glutamine controls their covalent modification (28). PII in turn regulates nitrogen assimilation functions at several levels, including transcription by interaction with the NtrB-NtrC two component regulators (47). In other instances, 2OG alone seems to signal nitrogen status. In Azotobacter vinelandii, 2OG binds to NifA, releasing it from its inactive NifA-NifL complex, and in cyanobacteria, 2OG binds directly to the transcriptional regulator NtcA, in both cases activating nif transcription (48–50). Our laboratory has shown recently in cell extracts of M. maripaludis that 2OG reverses the negative effect that the PII homologs NifI1 and NifI2 (30, 51) have on nitrogenase activity. NrpR provides another instance in which 2OG affects a nitrogen regulator.

This work has led to an unusual level of understanding of an archaeal regulatory system (3) because the roles of a repressor, an inducer, and two operators are now known in vitro and in vivo. The system invites comparison with well studied bacterial repression systems such as LacI (52, 53) and CI (46). Like NrpR with nif regulation, each of these systems uses auxiliary operators, but they differ as well. In the LacI system, two auxiliary operators are 92 and 401 bp from the primary operator. LacI is a tetramer, and DNA looping evidently allows it to bind simultaneously to the primary operator and one of the auxiliary operators. In contrast, CI is a dimer, two of which interact to bind cooperatively to two operators, which are centered only 24 bp apart (46). The protein-DNA binding system in NrpR appears to be more similar to CI, in which the repressor is a dimer and the operators are centered 31 bp apart. On the other hand, the mechanism that modulates binding is more like LacI, in which an inducing ligand decreases binding affinity, rather than CI, in which the cellular concentration of the intact repressor itself determines the amount bound. (It is interesting to note, however, that an auxiliary operator is not always

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*Fig. 4.* 2OG inhibits binding of NrpR to operator DNA. A, gel shift of NrpR-His (0.4 nM) binding to WT nif (0.02 nM) in the absence (No NrpR) or presence of potential effectors (5 mM). B, effect of increasing 2OG concentration (0, 0.001, 0.003, 0.009, 0.03, 0.08, 0.2, 0.7, and 2 mM). C, binding versus NrpR-His concentration at various 2OG concentrations (mM). D, $K_d$ versus 2OG concentration using data from C.

*Fig. 5.* Model for repressor-operator binding resulting in the regulation of nif transcription in M. maripaludis. The wedge represents intracellular 2OG concentration, which varies with growth on three different nitrogen sources. Ovals represent NrpR monomers. Underlines represent wild type (straight) and altered or repositioned (squiggly) operator sequences.
necessary for full repression by NrpR because a single operator, which may have high affinity for NrpR, appears sufficient in the case of glnA (34). In any case, even though NrpR is a regulator known only in the Euryarchaeota, its basic mechanism appears analogous to bacterial repression, and NrpR presumably occludes the binding or action of some components of the archaeal transcription initiation machinery.

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REFERENCES

1. Woese, C. R., Kandler, O., and Wheelis, M. L. (1990) Proc. Natl. Acad. Sci. U. S. A. 87, 4576–4579
2. Bell, S. D., Magill, C. P., and Jackson, S. P. (2001) Biochem. Soc. Trans. 29, 392–395
3. Ouhammouch, M. (2004) Curr. Opin. Genet. Dev. 14, 133–138
4. Soppa, J. (2001) Adv. Appl. Microbiol. 50, 171–217
5. Thomm, M. (1996) FEBS Microbiol. Rev. 18, 159–171
6. Bell, S. D., Kosa, P. L., Sigler, P. B., and Jackson, S. P. (1999) Proc. Natl. Acad. Sci. U. S. A. 96, 13692–13697
7. Bell, S. D., and Jackson, S. P. (1998) Trends Microbiol. 6, 222–228
8. Hanaszka, B. L., Darcy, T. J., and Reeve, J. A. (2001) J. Bacteriol. 183, 1813–1818
9. Bell, S. D., Brinkman, A. B., van der Oost, J., and Jackson, S. P. (2001) EMBO Rep. 2, 133–138
10. Calvo, J. M., and Matthews, R. G. (1994) Microbiol. Rev. 58, 466–490
11. Bell, S. D., Kosa, P. L., Sigler, P. B., and Jackson, S. P. (1999) Proc. Natl. Acad. Sci. U. S. A. 96, 13692–13697
12. Bell, S. D., and Jackson, S. P. (1998) Trends Microbiol. 6, 222–228
13. Ouhammouch, M., Dewhurst, R. E., Hausner, W., Thomm, M., and Boos, W. (2003) J. Bacteriol. 181, 2929–2935
14. Bell, S. D., and Jackson, S. P. (1998) Trends Microbiol. 6, 222–228
15. Ouhammouch, M., Dewhurst, R. E., Hausner, W., Thomm, M., and Boos, W. (2003) J. Bacteriol. 181, 2929–2935
16. Bell, S. D., Brinkman, A. B., van der Oost, J., and Jackson, S. P. (2001) EMBO Rep. 2, 133–138
17. Kruger, K., Hermann, T., Armbruster, V., and Pfeifer, F. (1998) J. Mol. Biol. 279, 761–771
18. Bell, S. D., and Jackson, S. P. (2000) J. Biol. Chem. 275, 31624–31629
19. Ouhammouch, M., and Geiduschek, E. P. (2001) EMBO J. 20, 146–156
20. Brinkman, A. B., Bell, S. D., Brinkman, A. B., van der Oost, J., and Jackson, S. P. (2002) J. Biol. Chem. 277, 29537–29549
21. Ouhammouch, M., Dewhurst, R. E., Hausner, W., Thomm, M., and Geiduschek, E. P. (2003) Proc. Natl. Acad. Sci. U. S. A. 100, 5097–5102
22. Brinkman, A. B., Dahlke, I., Tuintinga, J. E., Lammers, T., Dumay, V., de Heus, E., Lebbink, J. H., Thomm, M., and van der Oost, J. (2000) J. Biol. Chem. 275, 38160–38169
23. Kruger, K., Hermann, T., Armbruster, V., and Pfeifer, F. (1998) J. Mol. Biol. 279, 761–771
24. Lie, T. J., and Leigh, J. A. (2003) Mol. Microbiol. 47, 235–246
25. Lee, S. J., Engelmann, A., Hefracher, R., Qiu, Q., Vieker, G., Heebeln, C., Thomm, M., and Boos, W. (2003) J. Biol. Chem. 278, 983–990
26. Vieker, G., Engelmann, A., Heebeln, C., and Thomm, M. (2003) J. Biol. Chem. 278, 18–26
27. White, M. F., and Bell, S. D. (2002) Trends Genet. 18, 621–626
28. Reeve, J. A. (2003) Mol. Microbiol. 48, 587–598
29. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
30. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
31. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
32. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
33. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
34. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
35. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
36. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
37. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
38. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
39. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
40. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
41. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
42. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
43. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
44. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
45. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
46. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
47. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
48. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
49. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
50. Heinicke, I., Muller, J., Pittelkow, M., and Klein, A. (2004) Mol. Genet. Genomics
Regulation of *nif* Expression in *Methanococcus maripaludis*: ROLES OF THE EURYARCHAEAL REPRESSOR NrpR, 2-OXOGLUTARATE, AND TWO OPERATORS

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