The yeast PDR5 gene encodes an efflux pump that confers multidrug resistance. Expression of PDR5 is positively regulated by the transcription factors Pdr1p and Pdr3p that recognize the same pleiotropic drug resistance elements (PDREs) in the PDR5 promoter. Pdr1p and Pdr3p belong to the Gal4p family of zinc cluster proteins. The function of Rdr1p is mediated through PDREs by inserting this DNA element in front of a minimal promoter. Activity of this reporter was increased in a Abdrl strain. Moreover, mutations known to reduce binding of Pdr1/Pdr3p abolished the induction observed in the Abdrl strain. Thus, we have identified a transcriptional repressor involved in the control of multidrug resistance.

Multidrug resistance is a widespread phenomenon that allows organisms ranging from bacteria to humans to defend themselves against a variety of toxic compounds. Drug resistance is mediated through membrane-bound transporters that act as drug efflux pumps. This process has been extensively studied in the yeast Saccharomyces cerevisiae. Two major classes of multidrug transporters have been identified: the major facilitator superfamily (MFS)1 and the ABC (ATP binding cassette) family of transporters (2–4). ABC transporters act in an ATP-dependent manner, and their overexpression leads to increased drug resistance. Members of the family of ABC transporters include Pdr5p, Sqq2p, and Yor1p (2).

The transcriptional activators Pdr1p and Pdr3p control the expression of many ABC transporters (3, 4). These activators belong to a family of transcriptional regulators called zinc cluster or binuclear cluster proteins (5–7). Members of this family contain six highly conserved cysteines that coordinate binding to two zinc atoms to allow proper folding of the DNA binding domain. The cysteine-rich region (or zinc finger) is usually followed by a short linker sequence that bridges the zinc finger to a dimerization domain (6). This domain is involved in recognition of specific DNA sequences through interaction of the zinc finger with DNA (for references see Ref. 8). Pdr1p and Pdr3p both recognize CGG triplets oriented in opposite directions (CGCGG) to form an inverted repeat (9). This motif is found in the target genes of Pdr1p and Pdr3p (10–17).

For example, three binding sites called PDREs (pleiotropic drug response elements) for Pdr1p and Pdr3p have been mapped in the PDR5 promoter (10, 12). Thus, Pdr1p and Pdr3p recognize the same DNA sequences in target promoters for activation of transcription. In addition, the PDR3 promoter also contains two PDREs and is positively regulated by its own gene product and by Pdr1p (18).

Deletion of PDR1 or PDR3 results in increased sensitivity to drugs while a double knockout is hypersensitive to drugs. Moreover, increased drug resistance is primarily caused by mutations in PDR1 and PDR3. These mutations are hyperactive transcription factors (19, 20) resulting in increased expression of target genes (such as PDR5, SNQ2, YOR1) and, hence, increased drug resistance. Whole-genome analysis of gene expression with hyperactive forms of Pdr1p and Pdr3p (or a chimeric Pdr1p activator) has allowed the identification of additional targets for these transcriptional activators (21, 22). These targets comprise genes encoding MFS and permeases (e.g. YOR949C) as well as genes involved in lipid and cell wall metabolism.

The yeast genome contains 55 genes encoding putative zinc cluster proteins (for a complete list see Akache et al. (7) and Ref. 23). Many of these genes are uncharacterized and their function unknown. To better understand the role of these genes, we have performed a phenotypic analysis of 33 members of the family of zinc cluster proteins (7). For example, deletion of YOR380W results in inhibition of growth on non-fermentable carbon sources and hypersensitivity to calcifluor white, a compound that has high affinity to chitin, a cell wall component (7).

However, the function and the target genes of YOR380W are unknown. To identify target genes of YOR380W, we have performed whole-genome analysis of gene expression with DNA microarrays. Our results show that a very limited number of genes have their expression altered by deletion of YOR380W. Strikingly, all the affected genes are up-regulated in the deletion strain, and they predominantly encode membrane proteins, including ABC transporters such as Pdr5p. Moreover, deletion of YOR380W results in increased resistance to cycloheximide. These data suggest that YOR380W is a transcrip-
Rdr1p Is a Repressor of PDR5 Expression

**TABLE I**

| Strains used in this study |
|---------------------------|
| Strain                  | Genotype               | Reference |
| FY73  MA20 ura3–52 his3-D200 | 24                     |
| FZP  MA20 ura3–52 HIS1                   | 7                     |
| KHS1 MA20 ura3–52 his3-D200 pdr5Δ::G418    | This study          |
| KHS2 MA20 ura3–52 HIS1 pdr5Δ::G418          | This study          |

**Materials and Methods**

**Strains and Media**—S. cerevisiae strains used in this study are derived from FY73 (24) and are listed below in Table I. Deletion of the *PDR5* open reading frame (ORF) was performed using the PCR method of Baudin et al. (25) using oligos with 45 nucleotides of homology to the target gene at their 5'- and 14 nucleotides complementary to the KanMX (G418) selection marker. Plasmid pFA6 (26) was used as a template for PCR with the oligonucleotides CTGAATTCATATTCCTTTGCGGGTACTGCTTTCCGATTTTA to amplify chromosomal DNA. PCR products were verified by DNA sequencing. A low copy version of the reporter was constructed using the oligos ATCGAGTCGAGGAAGATAAGTCTCCGGC GAAAGACATTTTACACCATCGGAGACATTTCCTCTTTT. The construction was verified by generating a plasmid containing a PDR5-LacZ-1P cassette. The reporter was used to generate promoters upstream of the ATG codon. Promoter sequences were verified by DNA sequencing.

**Localization of PDR15**—A reporter containing a Pdr1p/Pdr3p binding site (or mutants) was amplified from strains FY73 and FZP, respectively. Deletions were verified by Southern blot analysis using a probe located upstream of the ATG of the *PDR5* ORF. Yeast extract/peptone/dextrose medium (YPD) and synthetic dextrose medium (SD) were prepared according to Ref. 37.

**Microarray Analysis**—Yeast cells (strains FY73 and FZP, Table I) were grown in rich medium (YPD) (27), to an *A*$_{600}$ of 0.8–1.0, and total RNA was isolated by the hot phenol procedure (28). RNA was further purified with Qiagen columns according to the manufacturer's protocol except that RNA was eluted for 15 min. cDNA labeling and hybridization were performed exactly as described previously (29, 30). Custom-made yeast whole-genome microarrays (~6200 yeast ORFs) were obtained from the Microarray Center at the Ontario Cancer Institute (Toronto, Canada). Scanning and quantification were performed exactly as described previously (29, 30). The function of this (putative) ORF is unknown.

**RESULTS**

To identify genes regulated by Rdr1p, RNA was isolated from wild-type strain FY73 (24) and a strain carrying a deletion of the putative DNA binding domain of *RDR1* (7). We then performed a whole-genome analysis of gene expression using DNA microarrays. Data were obtained on about 6000 genes and are an average of two independent experiments performed with duplicate genomes. First, we did not observe any gene whose expression was decreased more than 1.5-fold in the deletion strain (data not shown). Thus, these data strongly suggest that Rdr1p is not a transcriptional activator under the conditions tested (rich medium). On the contrary, this study revealed that five genes were overexpressed more than 2-fold in the deletion strain (Table II). Interestingly, four of these genes encode membrane-associated transporters. The strongest induction (6.3-fold) was observed with *PDR5*. Two other genes (*PDR15* and *PDR16*) also involved in drug resistance were up-regulated in the absence of the zinc cluster protein encoded by *RDR1*. Expression of ORF *YOR049C* was up-regulated by a factor of 4 (Table II). The function of this (putative) ORF is unknown. However, the sequence of the ORF predicts a protein of 354 amino acids with a high probability of possessing seven transmembrane domains (data not shown). Finally, *PHO84*, a member of the MFS family and encoding a high affinity inorganic phosphate/H+ symporter was up-regulated in absence of Rdr1p. Thus, our results suggest that Rdr1p is a transcriptional repressor.

To confirm the microarray results, we performed Northern blot analysis of RNA isolated from wild-type and *∆drd1* strains (Fig. 5B). *PDR5* mRNA level was increased about five times in the deletion strain in close agreement with the microarray analysis. Similarly, deletion of the *RDR1* gene resulted in a modest increase of *PDR16* mRNA (about 2-fold), again in agreement with the results generated with microarrays. Equal loading and transfer of RNA isolated for wild-type and knockout strains was shown by the similar signals obtained with an actin.
Rdr1p Is a Repressor of PDR5 Expression

Fig. 1. Northern blot analysis of selected genes. Wild-type strain (FY73) and Δrdr1 strains (FZP) were grown in rich medium and RNA isolated. 20 μg of total RNA were loaded per lane for Northern blot analysis (see "Material and Methods"). Probes are indicated on the right of the autoradiograms, and the strains are at the top.

Table II

| Systematic name | Gene  | Gene product                                                                 | Expression (Δrdr1/WT) |
|-----------------|-------|-------------------------------------------------------------------------------|-----------------------|
| YOR153W        | PDR5  | Drug-efflux pump involved in resistance to multiple drugs, member of the ABC   | 6.3                   |
|                 |       | family (ATP-binding cassette (ABC) superfamily                               |                       |
| YOR049C        | PDR5  | Putative 7-transmembrane protein                                              | 4.0                   |
| YML123C        | PHO84 | High affinity inorganic phosphate/H22 symporter, member of the phosphate/H22 | 2.5                   |
|                 |       | symporter (PHS) family of the major facilitator superfamily (MFS)             |                       |
| YNL231C        | PDR16 | Phosphatidylinositol transfer protein, involved in regulation of phospholipase | 2.2                   |
|                 |       | D (Spo14p) activity, involved in lipid biosynthesis and multidrug resistance  |                       |
| YDR406W        | PDR15 | Putative multidrug resistance transporter. Member of ATP-binding cassette      | 2.0                   |
|                 |       | (ABC) superfamily                                                             |                       |

Fig. 2. Resistance to cycloheximide is increased by deletion of RDR1 and is mediated through PDR5. Wild-type strain FY73 or strains carrying a deletion of RDR1 (strain FZP), PDR5 (strain KH51), or both genes (strain KH52) were grown overnight in YPD. Cells were spun down, resuspended in water, and serially diluted (left to right: 1.25 × 10^4, 2.5 × 10^3, 5 × 10^2, and 1 × 10^1 cells). Cells were then spotted on YPD plates either with (upper panel) or without (lower panel) 0.2 μg/ml cycloheximide. Gene deletions are indicated on the right. WT, wild-type strain.
Rdr1p negatively regulates the PDR5 promoter.

The PDR5 promoter has been shown to contain three sites that are recognized by the transcriptional activators Pdr1p and Pdr3p (12). The sites contain CGG triplets oriented in opposite direction (CCGGCG) forming an inverted repeat (9). All genes (except PHO84) identified with the microarray analysis (Table II) contain DNA sequences that match the consensus Pdr1p/Pdr3p binding site in their promoters (Table III). Thus, Rdr1p may exert its repressive effect by acting on Pdr1p/Pdr3p recognition sites. To test this possibility, we inserted oligonucleotides corresponding to a Pdr1p/Pdr3p binding site (site number three in Ref. 12) in front of a minimal CYC1 promoter driving lacZ transcription. Insertion of a PDRE in front of a minimal CYC1 promoter greatly increased promoter activity when compared with the minimal promoter (Fig. 4, lanes 1 and 3). Strikingly, activity of the PDRE3-CYC1 reporter was increased about 8-fold when assayed in a Δrdr1 strain (Fig. 4, lanes 3 and 4) whereas the activity of a reporter lacking the PDRE remained at basal levels (Fig. 4, lanes 1 and 2). These results strongly suggest that the effect of Rdr1p on PDR5 transcription is mediated by the Pdr1p/Pdr3p binding site. We then assayed the activity of reporters that contain mutations in the PDRE that reduce binding of Pdr1p and Pdr3p. The mutations are located in either of the CGG triplets that are crucial for binding of Pdr3p (9). As expected, the activity of the mutant was reduced when tested in a wild-type background (Fig. 4, lanes 5 and 7). Mutations in either CGG triplet abolished the induction observed in a Δrdr1 strain (Fig. 4, lanes 5–8). Thus, this mutant analysis further suggests that the negative effect of Rdr1p on PDR5 expression is mediated by PDREs. Rdr1p and Pdr1p/Pdr3p appear to function on highly related DNA sequences.

DISCUSSION

This study focused on a member of the Gal4p family of transcriptional regulators, RDR1 (YOR380W). Our previous work has shown that deletion of RDR1 results in absence of growth on non-fermentable carbon sources and sensitivity to calcofluor white, a phenotype associated with cell wall defects (42, 43). To gain insights into the role of RDR1, we have performed a whole-genome analysis of gene expression with RNA isolated from wild-type and cells lacking Rdr1p. No genes had their expression decreased by a factor of 1.5-fold or more in the Δrdr1 strain suggesting that Rdr1p is not a transcriptional activator. On the other hand, five genes had RNA levels increased by at least 2-fold in the deletion strain (Table II). Most of these genes encode membrane proteins.

Microarray data were confirmed by Northern blot analysis for PDR5 and PDR16 (Fig. 1). Furthermore, deletion of RDR1 results in increased resistance to cycloheximide (Fig. 2), a phenotype expected from the increased expression of the ABC transporter Pdr5p (39–41). Even though removal of Rdr1p results in increased expression of multidrug resistance genes other than PDR5, genetic analysis showed that the major target of Rdr1p is PDR5 with regard to cycloheximide resistance (Fig. 2). The effect of Rdr1p is likely to be at the transcriptional level, because a PDR5-lacZ reporter mimicked the activity observed for the endogenous gene. For example, increased activity of the PDR5 promoter was observed with both integrated and episomal lacZ reporters when assayed in a strain deleted of RDR1 (Fig. 3). This effect was specific, because no increase in reporter activity was observed with a SNQ2 reporter when tested in a Δrdr1 background.

Consensus target DNA sequences for Pdr1p/Pdr3p are found in all (but one) promoters of genes identified in our analysis (Table III). Therefore, we focused on this DNA element. A reporter consisting of a minimal CYC1 promoter under the control of a single PDRE shows increased activity in absence of Rdr1p (Fig. 4). Thus, the DNA sequences involved in activation by Pdr1p/Pdr3p and repression by Rdr1p are the same or overlap. Moreover, PDRE mutants with decreased binding to Pdr1p (9) and presumably Pdr3p do not show increased activity in the absence of Rdr1p. In summary, our studies strongly suggest that Rdr1p acts through Pdr1p/Pdr3p binding sites. However, many genes (11, 13–17) (like SNQ2) that have been shown to contain PDREs and to be regulated by Pdr1p/Pdr3p are not affected by removal of Rdr1p. Thus, the effect of Rdr1p appears to be mediated by a subset of the target genes of
Pdr1p/Pdr3p. We have shown that the zinc cluster proteins Leu3p and Uga3p both recognize CGG triplets oriented in opposite directions (an everted repeat) and spaced by 4 bp (CCGN₄CGG) (44). However, target genes of Leu3p and Uga3p are completely different. Discrimination of these highly related DNA sequences is achieved by nucleotides located between the CGG triplets (44). Thus, nucleotides outside the PDRE core sequence (CCGNCGG) may allow targeting of Rdr1p to a subset of the Pdr1p/Pdr3p-responsive genes.

What is the mechanism of action of Rdr1p? It is possible that Rdr1p binds directly to PDREs found in promoters of target genes resulting in decreased activity. For example, Rdr1p could compete with Pdr1p and Pdr3p for binding to PDREs. A related model would involve the formation of heterodimers between Rdr1p and Pdr1p or Pdr3p. Such heterodimers would be impaired for activation of the PDR5 gene. In support of this model, zinc cluster proteins Oaf1 and Pp2p, involved in activation of peroxisomal genes, have been shown to bind to DNA as heterodimers (45). Ada3p, a subunit of the SAGA complex involved in chromatin remodeling, represses activity of Pdr1p (46). Thus, the action of Rdr1p may be mediated by Ada3p. Another possibility is that the effect of Rdr1p is indirect. Rdr1p may control the level of a transcription factor involved in activation of PDR5 gene expression. A number of hyperactive alleles of PDR1 and PDR3 have been isolated (19, 20). One may speculate that these mutations relieve the inhibitory effect of Rdr1p. However, activation of a PDR5 reporter by some Pdr1p mutants is increased more than 80-fold as compared with wild-type Pdr1p (19) whereas the maximal effect achieved by removing Rdr1p is only 10-fold. Thus, inactivation of Rdr1p is unlikely to account in full for the hyperactivity of the Pdr1p/Pdr3p mutants.

Even though our microarray analysis points to a very limited number of affected genes, removal of Rdr1p results in an interesting phenotype, an increased resistance to cycloheximide. Previous studies (3, 4) have identified Pdr1p and Pdr3p as positive regulators of PDR5, and our laboratory has recently discovered an additional transcriptional activator of PDR5.2 This study shows that PDR5 is also negatively regulated by Rdr1p. Thus, the regulation of the PDR5 gene expression appears to be more complex than initially anticipated. Further studies will be required to better understand the mechanism of action of RDR1, but the results presented here raise the possibility that similar transcriptional repressors would be present in pathogenic yeasts such as Candida albicans.

Acknowledgments—We thank Dr. Deming Xu (Best Microarray Center, University of Toronto) for microarray analysis. We are grateful to Dr. Martine Raymond (Institut de Recherches Cliniques de Montréal) for critical reading of the manuscript as well as very helpful advice and material. We thank Dr. Geoffrey Hendy for comments on the manuscript. We also thank Dvs. J. J. Lebrun, H. Zingg, and S. Laporte for advice.

REFERENCES
1. Goffeau, A., Park, J., Paulsen, I. T., Jonniaux, J. L., Dinh, T., Mordant, P., and Saier, M. H. (1997) Yeast 13, 43–54.
2. Decottignies, A., and Goffeau, A. (1997) Nature Genet. 15, 137–145.
3. Bauer, B. E., Wolffer, H., and Kuchler, K. (1999) Biochim. Biophys. Acta 1461, 217–236.
4. Koloszkowska, A., and Goffeau, A. (1999) Drug Res. Updates 2, 403–414.
5. Todd, R. B., and Andrianopoulos, A. (1997) Fungal Gen. Biol. 21, 388–405.
6. Schierling, P., and Helmsberg, S. (1996) Nucleic Acids Res. 24, 4599–4607.
7. Akache, B., Wu, K., and Turcotte, B. (2001) Nucleic Acids Res. 29, 2181–2190.
8. Schwabe, J. W., and Rhodes, D. (1997) Nat. Struct. Biol. 4, 680–683.
9. Hellauer, K., Rochon, M.-H., and Turcotte, B. (1996) Mol. Cell. Biol. 16, 6096–6102.
10. Kitzmann, D. J., Hallett, A., and Dwyer-Rowley, W. S. (1994) Mol. Cell. Biol. 14, 4653–4661.
11. Kitzmann, D. J., Hallett, T. C., Voet, M., Wysock, W., Golin, J., Volckaert, G., and Dwyer-Rowley, W. S. (1995) Mol. Cell. Biol. 15, 6878–6883.
12. Kitzmann, D. J., Hallett, T. C., Mahe, Y., and Dwyer-Rowley, W. S. (1996) J. Biol. Chem. 271, 23049–23054.
13. Mahe, Y., Parle-McDermott, A., Nourani, A., Delahodde, A., Lamprecht, A., and Kuchler, K. (1996) Mol. Microbiol. 20, 109–117.
14. Wolffer, H., Mahe, Y., Parle-McDermott, A., Delahodde, A., and Kuchler, K. (1997) FEBS Letters 418, 269–274.
15. Nourani, A., Wesolowski-Louvel, M., Delaveau, T., Jacq, C., and Delahodde, A. (1997) Mol. Cell. Biol. 17, 5453–5460.
16. Hallstrom, T. C., and Dwyer-Rowley, W. S. (1998) J. Biol. Chem. 273, 2098–2104.

2 B. Akache and B. Turcotte, unpublished results.
17676  

Rdr1p Is a Repressor of PDR5 Expression  

17. Hallstrom, T. C., Lambert, L., Schorling, S., Balzi, E., Goffeau, A., and Moye-Rowley, W. S. (2001) J. Biol. Chem. 276, 23674–23680

18. Delahodde, A., Delaveau, T., and Jacq, C. (1995) Mol. Cell. Biol. 15, 4043–4050

19. Carvajal, E., van den Hazel, H. B., Cybulski-Kolaczkowska, A., Balzi, E., and Goffeau, A. (1997) Mol. Gen. Genet. 256, 406–415

20. Nourani, A., Papajova, D., Delahodde, A., Jacq, C., and Subik, J. (1997) Mol. Gen. Genet. 256, 397–405

21. DeRisi, J., van den Hazel, B., Marc, P., Balzi, E., Brown, P., Jacq, C., and Goffeau, A. (2000) FEBS Lett. 470, 156–160

22. Devaux, F., Marc, P., Bouchoux, C., Delaveau, T., Hikkel, I., Potier, M. C., and Jacq, C. (2001) EMBO Rep. 2, 493–498

23. Angus-Hill, M. L., Schlichter, A., Roberts, D., Erdjument-Bromage, H., Tempst, P., and Cairns, B. R. (2001) Mol. Cell 7, 741–751

24. Winston, F., Dollard, C., and Ricupero-Hovasse, S. L. (1995) Yeast 11, 53–55

25. Baudin, A., Ozier-Kalogeropoulos, O., Denouel, A., Lacroute, F., and Cullin, C. (1993) Nucleic Acids Res. 21, 3329–3330

26. Wach, A., Brachat, A., Pohlmann, R., and Philippen, P. (1994) Yeast 10, 1793–1808

27. Sherman, F. (1991) Methods Enzymol. 194, 3–21

28. Kohrer, K., and Domdey, H. (1991) Methods Enzymol. 194, 398–405

29. Hemming, S. A., Jansma, D. B., MacGregor, P. F., Friesen, J. D., and Edwards, A. M. (2000) J. Biol. Chem. 275, 35506–35511

30. Hellauer, K., Sirard, E., and Turcotte, B. (2001) J. Biol. Chem. 276, 13877–13902

31. Traven, A., Wong, J. M. S., Xu, D., Septa, M., and Ingles, C. J. (2001) J. Biol. Chem. 276, 4020–4027

32. Philippen, P., Stotz, A., and Scherf, C. (1991) Methods Enzymol. 194, 169–182

33. Ausubel, F. M., Brent, R., Kingston, R. E., Moore, D. D., Seidman, J. G., Smith, J. A., and Struhl, K. (1989) Current Protocols in Molecular Biology, pp. 2.9.1–2.9.11 and 4.9.1–4.9.14, Greene Publishing Associates and Wiley-Interscience, New York

34. Alarco, A. M., Balan, I., Talibi, D., Mainville, N., and Raymond, M. (1997) J. Biol. Chem. 272, 19304–19313

35. Sikorski, R. S., and Hieter, P. (1989) Genetics 122, 19–27

36. Forsburg, S. L., and Guarente, L. (1988) Mol. Cell. Biol. 8, 647–654

37. Sherman, F., Fink, G. R., and Hicks, J. B. (1986) Methods in Yeast Genetics, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY

38. Guarente, L. (1983) Methods Enzymol. 101, 181–191

39. Leppert, G., McDevitt, R., Falco, S. C., Van Dyk, T. K., Ficke, M. B., and Golin, J. (1990) Genetics 125, 13–20

40. Meyers, S., Schauer, W., Balzi, E., Wagner, M., Goffeau, A., and Golin, J. (1992)Curr. Genet. 21, 431–436

41. Hirata, D., Yano, K., Miyahara, K., and Miyakawa, T. (1994) Curr. Genet. 26, 285–294

42. Hampshey, W. (1997) Yeast 13, 1099–1133

43. Lussier, M., White, A. M., Sheraton, J., di Paolo, T., Treadwell, J., Southard, S. B., Horstein, C. I., Chen-Weiner, J., Ram, A. P., Kaptrey, J. C., Roemer, T. W., Vo, D. H., Bondoc, D. C., Hall, J., Zhong, W. W., Sdicu, A. M., Davies, J., Kli, F. M., Robbins, P. W., and Bussey, H. (1997) Genetics 147, 435–450

44. Noel, J., and Turcotte, B. (1998) J. Biol. Chem. 273, 17463–17468

45. Rotteinstein, H., Kal, A. J., Hamilton, B., Ruis, H., and Tabak, H. F. (1997) Eur. J. Biochem. 247, 776–783

46. Martens, J. A., Geneza, J., Saleh, A., and Brandl, C. J. (1996) J. Biol. Chem. 271, 15884–15890
Zinc Cluster Protein Rdr1p Is a Transcriptional Repressor of the PDR5 Gene Encoding a Multidrug Transporter
Karen Hellauer, Bassel Akache, Sarah MacPherson, Edith Sirard and Bernard Turcotte

J. Biol. Chem. 2002, 277:17671-17676.
doi: 10.1074/jbc.M201637200 originally published online March 6, 2002

Access the most updated version of this article at doi: 10.1074/jbc.M201637200

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 44 references, 19 of which can be accessed free at http://www.jbc.org/content/277/20/17671.full.html#ref-list-1