

Sequence of a cDNA coding for human glutathione peroxidase confirms TGA encodes active site selenocysteine

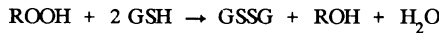
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Submitted May 26, 1987

Accession no. Y00369

Selenium dependent glutathione peroxidase (1) is a nuclear encoded cytosolic and mitochondrial enzyme which maintains the integrity of DNA and lipids as well as reducing levels of endogenous hydrogen peroxide as follows:



where ROOH represents peroxidized DNA (2), lipid hydroperoxides, membrane-associated phospholipid hydroperoxides or hydrogen peroxide. We have isolated a cDNA coding the human enzyme from a kidney library in λ gt10 by cross-hybridization with a bovine cDNA (3); 24 of 5300 clones hybridized with the probe. The active site selenocysteine residue (-CH₂SeH) at position 47 (i.e. SeC) is encoded by the nonsense codon, TGA, as is similarly observed in the mouse gene (4). Interestingly evidence suggests that the selenium atom is incorporated cotranslationally (5) rather than via a posttranslational modification step. This clone possesses 5 bp of the 5'-untranslated region, the 603 bp coding region, 223 bp of the 3'-untranslated region and a canonical polyadenylation signal, AATAAA, upstream of the polyA tract. The amino acid sequence reveals the protein possesses approximately 87% and 85% homology with preprocessed bovine (3) and mouse enzymes, respectively.

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      1                               10                               20
Met Cys Ala Ala Arg Leu Ala Ala Ala Ala Ala Gln Ser Val Tyr Ala Phe Ser Ala Arg Pro Leu Ala Gly Gly Glu Pro Val
GCGCC ATG TGT GCT GCT CGG CTA GCG GCG GCG GCG GCG CAG TCG GTG TAT GCC TTC TCG GCG GCG CGG CTG GCC GGC GGG GAG CCT GTG 89

30                               40                               50
Ser Leu Gly Ser Leu Arg Gly Lys Val Leu Leu Ile Glu Asn Val Ala Ser Leu [SeC] Gly Thr Thr Val Arg Asp Tyr Thr Gln Met Asn
AGC CTG GGC TCC CTG OGG GGC AAG GTA CTA CTT ATC GAG AAT CTC TCA GCG GCG TCC CTC [TGA] GGC ACC ACG GTC CGG GAC TAC ACC CAG ATG AAC 179

60                               70                               80
Glu Leu Gln Arg Arg Leu Gly Pro Arg Gly Leu Val Leu Gly Phe Pro Cys Asn Gln Phe Gly His Gln Glu Asn Ala Lys Asn Glu
GAG CTG CAG OGG GCG CTC GGA CCC CGG GGC CTG GTG CTC GGC TTC CCG TGC AAC CAG TTT GGG CAT CAG GAG AAC GCC AAG AAC GAA 269

90                               100                              110
Glu Ile Gln Asn Ser Leu Lys Tyr Val Arg Pro Gly Gly Phe Glu Pro Asn Phe Met Leu Phe Glu Lys Cys Glu Val Asn Gly Ala
GAG ATT CAG AAT TCC CTC AAG TAC CTC GCG CCT GGT GCT GGG TTC GAG CCC AAC TTC ATG CTC TTC CAG AAG TGC GAG GTG AAC GGT GCG 359

120                              130                              140
Gly Ala His Pro Leu Phe Ala Phe Leu Arg Glu Ala Leu Pro Ala Pro Ser Asp Asp Ala Thr Ala Leu Met Thr Asp Pro Lys Leu Ile
GGG GGC CAC CCT CTC TTC GCC TTC CTG OGG GAG GCC CTG CCA GCT CCC AGC GAC GAC GCC ACC GGG CTT ATG ACC GAC CCC AAG CTC ATC 449

150                              160                              170
Thr Trp Ser Pro Val Cys Arg Asn Asp Val Ala Trp Asn Phe Glu Lys Phe Leu Val Gly Pro Asp Gly Val Pro Leu Arg Arg Tyr Ser
ACC TGG TCT CGG GTG TGT GGC AAC GAT GTT GCC TGG AAC TTT GAG AAG TTC CTG GTG GGC CCT GAC GGT GTG CCC CTA GCG AGG TAC AGC 539

180                              190                              200 201
Arg Arg Phe Gln Thr Ile Asp Ile Glu Pro Asp Ile Glu Ala Leu Leu Ser Gln Gly Pro Ser Cys Ala AM
CGC CGC TTC CAG ACC ATT GAC ATC GAG CCT GAC ATC GAA GCC CTG CTG TCT CAA GGG CCC AGC TGT GGC TAC GGGCCCCCTCCTACCCGGCTGCT 635
TGGCAGTTGCGAGTCTGCTCTCGGGGGGTTTTTCATCTATGAGGGTGTTCCTCTAAACTACGAGGGAGGAACCTGATCTTACAGAAAATACCCACTGAGATGGGTGTGCTGCC 755
TGTTGATCCCGACTCTCTGCCACAGCAAGGOGAGTTTTCCCACTAATAAAGTCCGGGTGTGAGCAAAAAAAAAAAAAA 832
    
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Translated Mol. Weight = 21964.60

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