

Nucleotide sequence of an intronless gene for a human arylamine N-acetyltransferase related to polymorphic drug acetylation

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A genetic polymorphism of liver arylamine N-acetyltransferase (NAT; EC 2.3.1.5) activity in man causes interindividual variation in the response to a variety of amine drugs and potential carcinogens (1). We screened a human λ EMBL3 genomic library, constructed using DNA from a heterozygous rapid acetylator, using a cDNA specific for rabbit liver NAT (2). Below is shown the complete nucleotide sequence of a 1891 bp EcoRI fragment from one of the positive clones which contains an open reading frame with the potential to encode a human NAT. The gene contains no introns and shows 82% and 61% homology in the coding region to cDNAs for rabbit (2) and chicken (3) liver NAT, respectively. The fragment was expressed using the SV40-based vector p91023(B) in COS-1 cells to produce a protein with enzyme activity characteristic of a genetically polymorphic human NAT (4).

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GAATTCAGTGTCTCCCTGTGACCCCACTAACCCCTCTTTTGTTCACCAGGCCTTACCACAATCTAACAGACTGCATTTTATCC 90
ATTTATTCAGTTTCCTATTTGTGGTCCCTTCAACTCCCATTAATAATAATTTTGGAGGCAAGCAAGTACTGAGAACATAGGAAACAC 186
ATCAAGAGTATTCGTAAACTATTTCTGAATCAATCAGTGAATGAATGAATTAATCAATATATTTTGGATGAGGAGCTTTGTGTAG 270
GTACAGCTAAATGGGAAATCAAGTGGGTGATGTACCATGAATACCATATACTCTACTGTATAATTTCTCTGCTTATATCAAACTGTT 360
ATAAGCTATTAATAATGATACCAATTTGGAATCTCTTTTACTCATCACAAGAACCACCAAAACAGTGTGTATACATTTGGCTCCTT 450
ATTTAATCTGGATTTCCAACCTCTCATGCTTAAAGACGGAAGATACAATAACTTTCTTACAGGGTCTGAGACTACTAAGAGAACT 540
TATGCATGTAAGAGGATTCATGTCAGTGAATACTAACAAAGAAATTAATGACAGACTTATAACCATTTGTGTTTTTACGATTTA 630
AAATACGTTATACCCTATAAATTAGTCAACAGGAGAAATCAATGCTAAAGATGATATGTTTTATGTTTGTGTTTCTGCTTAGGGGAT 720
CATGGACATTTAAGCATATTTTGAAGAATTTGGCTATAAGAACTTAGGAACAAATTTGGACTTGGAAACATTAAGTACATTTCTGAGCA 810
M D I E A Y F E R I G Y K N S R N K L D L E T L T D I L E H
CCAGATCCGGGCTGTCCCTTTGAGAACCTTAACATGCATTTGGGCAAGCCATGGAGTGGCTTAGAGCTATTTTATGATCAATTTGT 900
Q I R A V P F F E N L N H C G Q A H E L G L E A I F D H I V
AAGAAGAAACCGGGTGGGTGGTCTCCAGGTCATCAACTCTGTACTGGGCTTGACCAATCGGTTTTGAGACCACAAATGTTAGG 990
R R N R G W C L Q V N Q L L Y W A L T T I G F Q T T H L G.
AGGGTATTTTACATCCCTCCAGTTAACAAATACAGCACTGGCATGGTTCACTTCTCTGTCAGGGTACCATTTGATCCAGGAATTACAT 1080
G Y F Y I P F F E N L N H C G Q A H E L G L E A I F D H I V
TGTGATGCTGGTCTGGAAGCTCTCCAGATGTGGCAGCCTTAGAATTAATTTCTGGGAAGGATCAGCCTCAGGTGCCTTGATTTT 1170
V D A G S G S S S Q R W Q P L E L I S G R D Q F Q V P C I F
CTGCTGACAGAGAGAGAGGATCTGGTACCTGGACCAATCAGGAGAGCAGATATATTACAAACAAGAAATTTCTAATTTCTCATCT 1260
C L T E E R G I W Y L D Q I R R E Q Y I T N K E F L N S H L
CTGCGAAAGAGAAACACCAAAAAATATACTTATTACGCTTGAACCTTGAACAATTTGAAGATTTTGAAGTCTATGAATACATACCTGCA 1350
L P K K K E Q K I Y L P T L E F R T I E D F E S R N T Y L Q
GACGCTCCCAACATCTTCAATTAACAACCATCATTGTTCCTTGCAGACCCAGAGGGGTTTACGTTTGGGGCTTCATCTCTCAC 1440
T S P T S S F I T T S F C S L Q T P E G V Y C L V G F I L T
CTATAGAAAATTCATATAAAGACAATACAGATCTGGTCCAGTTAAACCTCTCAGTGGAGAGGGTTGAAGAGTGTGAAAAATAT 1530
Y R K P N Y R K D N T D L V E F R T L T E E V E E V L K N I
ATTTAAGATTTCTTGGGGAGAAATCTCGTGCCCAAACTGGTATGGATCCCTTACTATTAGAATAAGGAAACAAAATAAACCCCTGTG 1620
F K I S L G R N L V P K P G D G S L T I
TATGTATCACCCACTCAGTAATCACTTATGTCATCAGATATCTCTCCTACCCCTCAGTATTTTGAAGAAATCTTAAACATC 1710
AAATTTCTACATCAATAAATGTGAGCATTATTAATAAACAATAACTTTTAAAGAAACATAAGGACACATTTTCAATTAATAAAAAA 1800
TAAAGGCATTTTAAAGGATGGCTGTGATATCTTGGGAAGCAGAGTATTCTATGCTAGAAAACATTTAATATTGATTTATTTGTGAAATTC 1890
    
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