Nucleotide sequence of the cDNA encoding human tyrosinase-related protein

Tirza Cohen+, Rita M.Muller, Yashushi Tomita[1] and Shigeki Shibahara[2,*]
Friedrich Miescher-Institut, PO Box 2543, CH-4002 Basel, Switzerland and [1]Department of Dermatology and [2]Department of Applied Physiology, Tohoku University School of Medicine, Sendai 980, Japan

Submitted March 29, 1990 EMBL accession no. X51420

We have isolated a pigment cell-specific cDNA, pMT4, from B16 mouse melanoma cDNA library by differential hybridization (1) and initially considered that it codes for tyrosinase, an essential enzyme of melanin biosynthesis (1). However, the pMT4 was shown to map to the brown (*b*) locus (2) that determines the type of melanin produced, which is inconsistent with the assumption that tyrosinase is encoded at the *c* locus (3). Subsequently, the protein encoded by pMT4 was shown to possess no tyrosinase activity in transient expression assays (4) and tentatively termed tyrosinase-related protein (TRP) (2), since mouse TRP shares 40% amino acid homology with the sequence of mouse tyrosinase (4).Here we present the nucleotide and deduced amino acid sequence of the cDNA coding for human TRP, a homologue to mouse *b* locus gene product. Two cDNA clones were isolated from a cDNA library of S7 human melanoma cells (5), constructed in the Okayama-Berg vector (6), by using the mouse TRP cDNA, pMT4, as a hybridization probe. The assigned reading frame codes for a polypeptide of 527 amino acids with a molecular weight of 60,000, including a putative signal peptide of 24 amino acids (indicated by negative numbers). Human TRP is shorter than mouse TRP by ten amino acids at the carboxy terminus and the degree of sequence homology is about 93%.

```
AATTCTAAGAGAAGTTCATCAGAGACATCCTTCAGGATTGTGAGCTGGATTTTCCTCTAC 60

GTGCTTCAGTCTTCTCTACACAAAGAGCTGCAAACCAGGTCTTTGTTTTGCACTCTTATT 120

TCAAGCAGAATGAGTGCTCCTAAACTCCTCTCTCTGGGCTGTATCTTCTTCCCCTTGCTA 180
         MetSerAlaProLysLeuLeuSerLeuGlyCysIlePhePheProLeuLeu
                     -20                           -10
CTTTTTCAGCAGGCCCGGGCTCAATTCCCAAGACAGTGTGCCACTGTTGAGGCTTTGAGA 240
LeuPheGlnGlnAlaArgAlaGlnPheProArgGlnCysAlaThrValGluAlaLeuArg
                    -1  1                         10
AGTGGTATGTGTTGCCCAGACCTGTCCCCTGTGTCTGGGCCTGGGACAGACCGCTGTGGC 300
SerGlyMetCysCysProAspLeuSerProValSerGlyProGlyThrAspArgCysGly
                   20                            30
TCATCATCAGGGAGGGGCAGATGTGAGGCAGTGACTGCAGACTCCCGGCCCCACAGCCCT 360
SerSerSerGlyArgGlyArgCysGluAlaValThrAlaAspSerArgProHisSerPro
                   40                            50
CAGTATCCCCATGATGGCAGAGATGATCGGGAGGTCTGGCCCTTGCGCTTCTTCAATAGG 420
GlnTyrProHisAspGlyArgAspAspArgGluValTrpProLeuArgPhePheAsnArg
                   60                            70
ACATGTCACTGCAACGGCAATTTCTCAGGACACAACTGTGGGACGTGCCGTCCTGGCTGG 480
ThrCysHisCysAsnGlyAsnPheSerGlyHisAsnCysGlyThrCysArgProGlyTrp
                   80                            90
AGAGGAGCTGCCTGTGACCAGAGGGTTCTCATAGTCAGGAGAAATCTTCTGGACTTAAGT 540
ArgGlyAlaAlaCysAspGlnArgValLeuIleValArgArgAsnLeuLeuAspLeuSer
                  100                           110
AAAGAAGAAAAGAACCACTTTGTCCGGGCCCTGGATATGGCAAAGCGCACAACTCACCCT 600
LysGluGluLysAsnHisPheValArgAlaLeuAspMetAlaLysArgThrThrHisPro
                  120                           130
TTATTTGTCATTGCCACCAGGAGATCAGAAGAAATACTGGGGCCAGATGGCAACACGCCA 660
LeuPheValIleAlaThrArgArgSerGluGluIleLeuGlyProAspGlyAsnThrPro
                  140                           150
CAATTTGAGAACATTTCCATTTATAACTACTTTGTTTGGACACACTATTACTCAGTCAAA 720
GlnPheGluAsnIleSerIleTyrAsnTyrPheValTrpThrHisTyrTyrSerValLys
                  160                           170
AAGACTTTCCTTGGGGTAGGACAGGAAAGCTTTGGTGAAGTGGATTTCTCTCATGAGGGA 780
LysThrPheLeuGlyValGlyGlnGluSerPheGlyGluValAspPheSerHisGluGly
                  180                           190
CCAGCTTTTCTCACATGGCACAGGTACCACCTCCTGCGTCTCGAGAAAGACATGCAGGAA 840
ProAlaPheLeuThrTrpHisArgTyrHisLeuLeuArgLeuGluLysAspMetGlnGlu
                  200                           210
ATGTTGCAAGAGCCTTCTTTCTCCCTTCCTTACTGGAATTTTGCAACGGGGAAAAATGTC 900
MetLeuGlnGluProSerPheSerLeuProTyrTrpAsnPheAlaThrGlyLysAsnVal
                  220                           230
TGTGATATCTGCACGGATGACTTGATGGGATCCAGAAGCAACTTTGATTCCACTCTAATA 960
CysAspIleCysThrAspAspLeuMetGlySerArgSerAsnPheAspSerThrLeuIle
                  240                           250
AGCCCAAACTCTGTCTTTTCTCAATGGCGAGTGGTCTGTGACTCCTTGGAAGATTATGAT 1020
SerProAsnSerValPheSerGlnTrpArgValValCysAspSerLeuGluAspTyrAsp
                  260                           270
ACCCTGGGAACACTTTGTAACAGCACCGAGGATGGGCCAATTAGGAGAAATCCAGCTGGA 1080
ThrLeuGlyThrLeuCysAsnSerThrGluAspGlyProIleArgArgAsnProAlaGly
                  280                           290
AATGTGGCCAGACCAATGGTGCAACGTCTTCCTGAACCACAGGATGTCGCTCAGTGCTTG 1140
AsnValAlaArgProMetValGlnArgLeuProGluProGlnAspValAlaGlnCysLeu
                  300                           310
GAAGTTGGTTTATTTGACACGCCTCCTTTTTATTCCAACTCTACAAACAGTTTCCGAAAC 1200
GluValGlyLeuPheAspThrProProPheTyrSerAsnSerThrAsnSerPheArgAsn
                  320                           330
ACAGTGGAAGGTTACAGTGACCCCACGGGAAAGTATGACCCTGCTGTTCGAAGTCTTCAC 1260
ThrValGluGlyTyrSerAspProThrGlyLysTyrAspProAlaValArgSerLeuHis
                  340                           350

AATTTGGCTCATCTATTCCTGAATGGAACAGGGGGACAAACCCATTTGTCTCCAAATGAT 1320
AsnLeuAlaHisLeuPheLeuAsnGlyThrGlyGlyGlnThrHisLeuSerProAsnAsp
                  360                           370
CCTATTTTTGTCCTCCTGCACACCTTCACAGATGCAGTCTTTGATGAATGGCTGAGGAGA 1380
ProIlePheValLeuLeuHisThrPheThrAspAlaValPheAspGluTrpLeuArgArg
                  380                           390
TACAATGCTGATATATCCACATTTCCATTGGAAAATGCCCCTATTGGACATAATAGACAA 1440
TyrAsnAlaAspIleSerThrPheProLeuGluAsnAlaProIleGlyHisAsnArgGln
                  400                           410
TACAACATGGTGCCATTCTGGCCCCCAGTCACCAACACAGAAATGTTTGTTACTGCTCCA 1500
TyrAsnMetValProPheTrpProProValThrAsnThrGluMetPheValThrAlaPro
                  420                           430
GACAACCTGGGATACACTTATGAAATTCAATGGCCAAGTCGGGAGTTTAGTGTACCTGAG 1560
AspAsnLeuGlyTyrThrTyrGluIleGlnTrpProSerArgGluPheSerValProGlu
                  440                           450
ATAATTGCCATAGCAGTAGTTGGCGCTTTGTTACTGGTTGCACTCATTTTTGGGACTGCT 1620
IleIleAlaIleAlaValValGlyAlaLeuLeuLeuValAlaLeuIlePheGlyThrAla
                  460                           470
TCTTATCTGATTCGTGCCAGACGCAGTATGGATGAAGCTAACCAGCCTCTCCTCACTGAT 1680
SerTyrLeuIleArgAlaArgArgSerMetAspGluAlaAsnGlnProLeuLeuThrAsp
                  480                           490
```

REFERENCES

1. Shibahara,S., Tomita,Y., Sakakura,T., Nager,C., Chaudhuri,B. and Muller,R. (1986) *Nucl. Acids Res.* **14**, 2413–2427.
2. Jackson,I.J. (1987) *Proc. Natl. Acad. Sci. USA* **85**, 4392–4396.
3. Coleman,D.L. (1962) *Arch. Biochem. Biophys.* **69**, 562–568.
4. Muller,G., Ruppert,S., Schmid,E. and Schutz,G. (1988) *EMBO J.* **7**, 2723–2730.
5. Bruggen,J., Macher,E. and Sorg,C. (1981) *Cancer Immunol. Immunother.* **10**, 121–127.
6. Okayama,H. and Berg,P. (1982) *Mol. Cell. Biol.* **2**, 161–170.

* To whom correspondence should be addressed

+Present address: Department of Human Genetics, Hadassah Hospital, POB 12000, 91120 Jerusalem, Israel

```
CAGTATCAATGCTATGCTGAAGAAAGAATATGAAAAACTCCAGAATCCTAATCAGTCTGT 1740
GlnTyrGlnCysTyrAlaGluGluArgIleEnd
                  500
GGTCTAACAAATGCCCTACTCTCTTATGCATTAGTATCACAAAACCACCTGGTTGAATAT 1800

AATAGATTGAGTTATTAACTGTATTTTCTTTCACTTTATTACCTTCTTTCTAATACAAGC 1860

ATATGTTAGCATTAAAGTTCTAGGCATACTTTTCAAAGCTGGGAAGACCCTTTCAGAATC 1920

TTTTCAATGGGTTTTAATTTTCAGTTCTATTTAAAATGGTGAATGACACTAAACTCCATG 1980

ATATTTAAGGATAGTGTGAAGATCTTTGGCATGATTTAAAGGTTGAGTATGTGAAGATAT 2040

AAGTGAACTACCATGCTTTGTTTACGTGTAAAGGAAAATAATGTTTGATAGTAAATGTCC 2100

ACTTAAAATACATGAATGGGCATTTCTAAAATGTTAAAACATAAACACATTTCCATTCAT 2160

GGATATTTGTCAACAGATTTAAAGAAAACCACAGTTATTAATTAAAGAAAATTAATTATG 2220

TGTAGTTATAAACCAATGAAATTTTGATTAACCTTTTCAAATTAATGTTCCAGTTTGAAG 2280

ACCAATCAAATATATTATTTAGTCAACATATACTATTTAGTCTCAGGTTCAAGGCTACAA 2340

CAAAAATCACCATCTTTGTCAAACTTTGGAGAGGGAAAATCTTCACTTTCTTAAGCAACA 2400

ATGGATATTGCCTGTGTTTGCCACTGTGTTTCCCTGCCTCTCAATTCGCTGAAAAAGGAA 2460

CTACCTATCCTTACATTTCACCTACTAATGTCTCTTCTAACATCTTAGAGGTCCATGGAG 2520

AAGGCATATGGAGAACATGTTTTATACTGCTCTATAAATAGTATTCCAATCACTGTGCTT 2580

AATTTAAATAGCATTATCTTATCATTTATCAGCCTTTTATGTATTTTCCAAGTAAAATAT 2640

TAACATATTATTTCATTGGTCTTCTTTTTTATCTGGTTCTATATGAATGCTATTTTTTCC 2700

CTTCTCTTCTAACATGAAATATATTTTCTCTTTTTGATCTTGTGCTATGAAACAATCTTA 2760

CCAAAGAACTGTATAAGGTGGTCATAAGTGAATATTTTAATTAAAATTGGTAAAAATAAA 2820

AAAAAAAAAAATAAAAT 2837
```