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Molecular Characterization, Sequence Analysis and Tissue Expression of a Porcine Gene-COMT

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Abstract: The full-length cDNA sequences of one porcine gene, COMT, was amplified using the rapid amplification of cDNA ends (RACE) method based on one pig EST sequence which was highly homologous to the coding sequence of human COMT gene. Sequence prediction analysis revealed that the open reading frame of this gene encodes a protein of 270 amino acids that has high homology with the catechol-O-methyltransferase (COMT) of seven species: cattle (82%), horse (79%), human (77%), chimpanzee (77%), rhesus monkey (76%), mouse (76%) and rat (74%)—so that it can be defined as porcine COMT gene. This novel porcine gene was assigned to GeneID: 100155530. This gene is structured in four exons and three introns as revealed by computer-assisted analysis. The phylogenetic analysis revealed that the porcine COMT gene has a closer genetic relationship with the COMT gene of cattle. Tissue expression analysis indicated that the porcine COMT gene is generally and differentially expressed in detected tissues including spleen, muscle, skin, kidney, lung, liver, fat and heart. Our experiment is the first to establish the primary foundation for further research on the porcine COMT gene.
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Key words: pig; COMT; RACE; Tissue Expression Profile; Sequence Identification

INTRODUCTION

Catechol-O-methyltransferase (COMT) catalyzes the transfer of a methyl group from S-adenosylmethionine to catecholamines, including the neurotransmitters dopamine, epinephrine, and norepinephrine. This O-methylation results in one of the major degradative pathways of the catecholamine transmitters. In addition to its role in the metabolism of endogenous substances, COMT is important in the metabolism of catechol drugs used in the treatment of hypertension, asthma, and Parkinson disease. Recent research showed that a functional COMT polymorphism is associated with cognitive processing in the normal brain, older age, mild cognitive impairment and in various dementias(Brennan *et al.*, 2011; Valente *et al.*, 2011; Garcia-Garcia *et al.*, 2011; Ursini *et al.*, 2011; Nedić *et al.*, 2011; Müller *et al.*, 2010; Müller *et al.*, 2011; Dickerson *et al.*, 2011).

As mentioned above, COMT gene is an important gene. Until today, COMT gene has been reported in horse, human, chimpanzee, rhesus monkey, mouse and other animals. The pig COMT has not been reported.

In the present experiment, we will clone the full-length cDNA sequence of the porcine COMT gene, and further do necessary sequence analysis and tissue expression analysis. These will establish the primary foundation of understanding this porcine gene.

MATERIALS AND METHODS

Animals and Sample Preparation

One adult Yunnan local pig was slaughtered. Spleen, muscle, placenta, kidney, lung, liver, fat and heart samples were collected, frozen in liquid nitrogen and then stored at – 80 °C. The total RNA was extracted using the Total RNA Extraction Kit (Gibco, USA).These RNA samples were used to perform RACE PCR and tissue expression profile analysis.

5'- and 3'-RACE

5'- and 3'-RACE were performed to isolate the full-length cDNA for porcine COMT gene as the instructions of BD SMART™ RACE cDNA Amplification Kit (BD science, USA). For the porcine COMT gene, the Gene-Specific Primers (GSPs) were designed based on one pig EST sequence whose sequence is highly homologous to the coding sequence of human COMT gene: DN122053. The Gene-Specific Primers (GSPs) were: 5'-RACE GSP: 5'-GCAGCATTGTCAGGGTTAAGCTCGA-3', 3'-RACE GSP: 5'-GCTGACCATCGAGCTTAACCCTGAC-3'. RACE touchdown PCRs were carried out with 5 cycles of 94°C / 30 s and 72°C /3 min, followed by 5 cycles of 94°C / 30 s, 68°C / 30 s and 72°C / 3 min, finally with

30 cycles of 94°C / 30 s, 68 °C / 30 s, 72°C / 3 min to terminate reaction. The RACE PCR products were then cloned into pMD18-T vector (TaKaRa, Dalian, China) and sequenced bidirectionally with the commercial fluorometric method (SHENGGONG, Shanghai, China). At least five independent clones were sequenced for each PCR product.

Quantitative real time PCR (qRT-PCR) for tissue expression profile analysis

qRT-PCR for evaluating the level of mRNA for COMT gene was performed on the ABI Prism 7300 Sequence Detection Systems (Applied Biosystems, Foster City, CA, USA). PCR reactions for each sample were carried out in 25μl reaction volume containing 1μl SYBR Green real-time PCR Master Mix, 100 ng cDNA template and 200 nM each primer. We selected the housekeeping gene beta-actin (DQ845171) as the internal control. The control gene primers used were: 5'- CGGGACATCAAGGAGAAGC -3' (forward primer 1) and 5'- TACTTGCGCTCTGGAGGC -3' (reverse primer1). The PCR product is 383-bp in length. The following COMT gene specific primers were used to perform the RT-PCR for tissue expression profile analysis: 5'-CTCCTTGGTCCTGGTGCT-3' (forward primer 2) and 5'-GGGATGATGTCCTGGGAT-3' (reverse primer2). The PCR product is 483-bp in length. Conditions for real-time PCR were: an initial denaturation at 95 °C for 3 min, 40 cycles of 95 °C for 15 s, 55℃ for 15 s , 72°C for 20 s. For each sample, reactions were set up in triplicate to ensure the reproducibility of the results. The gene relative expression levels were quantified relative to the expression of the reference gene, beta actin , by employing the $2^{-\Delta\Delta Ct}$ value model (Livak et al., 2001).

Sequence analysis

The cDNA sequence prediction was conducted using GenScan software (http://genes.mit.edu/GENSCAN.html). The protein prediction and analysis were performed using the Conserved Domain Architecture Retrieval Tool of BLAST at the National Center for Biotechnology Information (NCBI) server (http://www.ncbi.nlm.nih.gov/BLAST) and the ClustalW software (http://www.ebi.ac.uk/ clustalw).

RESULTS

RACE results for porcine COMT gene

For pig COMT gene, through 5'-RACE, one PCR product of 444 bp was obtained. The 3'-RACE product was 645 bp. These products were then cloned to T-vector and sequenced. Taken together, a 1056- bp cDNA complete sequence was finally obtained **(Fig.1)**.

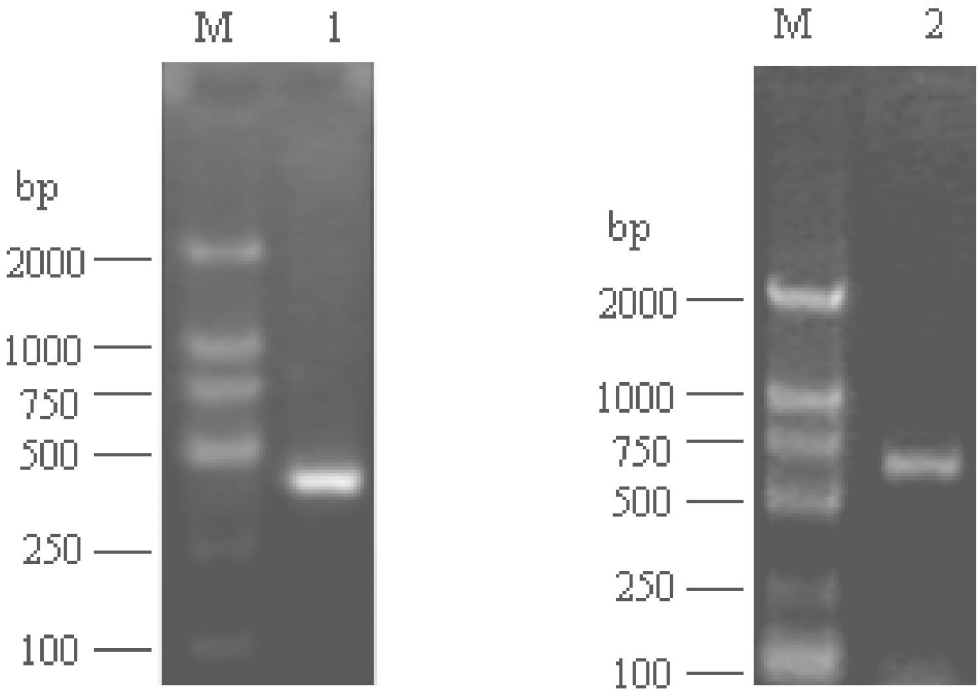


Fig. 1 RACE results for pig COMT gene. M, DL2000 DNA markers 1, 5'-RACE product for pig COMT gene; 2, 3'-RACE product for pig COMT gene

Sequence analysis

The nucleotide sequence analysis using the BLAST software at NCBI server (http://www.ncbi.nlm.nih.gov/BLAST) revealed that this gene was not homologous to any of the known porcine genes and it was then deposited into the GenBank database (Accession number: GU373691). The sequence prediction was carried out using the GenScan software. An open reading frame encoding 270 amino acids was found in the 1056-bp cDNA sequence. Further BLAST analysis of this protein revealed that this protein has high homology with the motile sperm domain containing 1 (COMT) of seven species: cattle (accession number: NP_001095787; 82%), horse (accession number: NP_001075303; 79%), human (accession number: AAA68929; 77%), chimpanzee (accession number: XP_003317142; 77%), rhesus monkey (accession number: XP_001105683; 76%), mouse (accession number: O88587; 76%) and rat (accession number: NP_036663; 74%). The complete cDNA sequence of this gene and the encoded amino acids were shown in Fig. 2.

```
GCACAAGATGCTAGAGGCCCTGCCCCTGCTGCTGGCAGTCTGCTCCTTGGTCCTGGTGCTGCTGACA
        M  L  E  A  L  P  L  L  L  A  V  C  S  L  V  L  V  L  L  T
CTGTTGTGGCTGCTGCCACACTCGAAGTGCTCTCTCATCTTCATTGCCTGGGAAGAGTTTATCCTG
 L  L  W  L  L  P  H  S  K  C  S  L  I  F  I  A  W  E  E  F  I  L
CTTCCCGTCAGGAACCTCCTCATGGGCAGCAGCAAGGAACAGCGCATTCTGCAATATGTGCTGCAG
 L  P  V  R  N  L  L  M  G  S  S  K  E  Q  R  I  L  Q  Y  V  L  Q
CACGCAGTGGCGGGGGACCCAGAGAGCGTGCTGGACACCATCGACACCTACTCCTCTCAGAAGGAG
 H  A  V  A  G  D  P  E  S  V  L  D  T  I  D  T  Y  S  S  Q  K  E
TGGGCCATGCACGTGGGCAGAAAGAAAGGCCAGATCGTGGACACTGTGGTGCAGGAGCAGCGTCCT
 W  A  M  H  V  G  R  K  K  G  Q  I  V  D  T  V  V  Q  E  Q  R  P
TCTGTGCTGCTGGAGCTGGGGGCTTACTGTGGCTACTCGGCTGTGCGCATGGCCCGCCTGCTGCTG
 S  V  L  L  E  L  G  A  Y  C  G  Y  S  A  V  R  M  A  R  L  L  L
CCCAGCGCCCGGCTGCTGACCATCGAGCTTAACCCTGACAATGCTGCCATCGCCCAGCAGGTGGTG
 P  S  A  R  L  L  T  I  E  L  N  P  D  N  A  A  I  A  Q  Q  V  V
GACTTCGCAGGCCTGCAGGACAGGGTGACCGTTGTCGTCGGGGCATCCCAGGACATCATCCCTCAG
 D  F  A  G  L  Q  D  R  V  T  V  V  V  G  A  S  Q  D  I  I  P  Q
CTGAAGAAGAAATATGATGTGGATACGCTGGACATGGTCTTTCTTGACCACTGGAAGGACCGGTAC
 L  K  K  K  Y  D  V  D  T  L  D  M  V  F  L  D  H  W  K  D  R  Y
CTGCCAGACACGCTCCTGCTAGAGGAATGTGGCCTGCTGCGGAAGGGAACGGTGTTGCTGGCCGAC
 L  P  D  T  L  L  L  E  E  C  G  L  L  R  K  G  T  V  L  L  A  D
AACGTCATCTGCCCGGGGGCCCCAGATTTCCTGGCACACGTGCGAGGGTGCGGCCGCTTCGAGTGT
 N  V  I  C  P  G  A  P  D  F  L  A  H  V  R  G  C  G  R  F  E  C
ACACACTTTAGCTCATACCTGGAGTACTCGCAGATGGTGGATGGCCTGGAGAAGGCTGTCTACAAG
 T  H  F  S  S  Y  L  E  Y  S  Q  M  V  D  G  L  E  K  A  V  Y  K
GGCCCAGGCAGCCCTGCACAGCCTTGACGGCCTGCCCTGTGCCAGCTCCCTCTCCAACCCTGGTTCTG
 G  P  G  S  P  A  Q  P  *
GAGGGTGCAGTGAACCCACTTCTGCCAACTTCGCTTCTGCTAGTATCTATCTGTCTGTCTTCCATGCAG
CCCCCTTGAGGCCAGTGAGGCCCAGGCCTGCCCACACGGGTCCGCCCCAAGTGCAACCAGCTCACCT
TGCAAAATCACCCCAATAAATCTGGAAAGTATCTGCCTATAAAAAAAAAAAAAAAAAAAA
```

Fig. 2 The complete cDNA sequence and encoded amino acids of COMT (GenBank accession number: GU373691) . ATG, start codon; TGA, stop codon.

* indicates the stop codon.

```
Pig                 MLEALPLLLAVCSLVLVLLTLLWLLP--HSKCSLIFIAWEEFILLPVRNLLMGSSKEQRI
Cattle              MLEAPPLLLVAGGVGLALLALRWLATTDLQFFGRAFIVWNEFIMKPIRNLLMGSSKEQRI
Horse               MLEPTPMLLAAFSLGLALLPLLFFLR----RWGWLLIGWNECILQPIHNLLMGDSKEQRI
Human               MPEAPPLLLAAVLLGLVLLVVLLLLLR-HWGWGLSLIGWNEFILQPIHNLLMGDTKEQRI
Chimpanzee          MLEAPPLLLAAVLLGLVLLVVLLLLLR-HWGWGLCLIGWNEFVLQPIHNLLMGDTKEQRI
Rhesus monkey       MLEAPPLLLAAVFLGLVLVVLLLILR--RWGWGLCLICWNEFVLQPIRNLLMGDTKEQRI
Mouse               ------MLLAAVSLGLLLLAFLLLLR--HLGWGLVAIGWFEFVQQPVHNLLMGGTKEQRI
Rat                 ------MPLAAVSLGLLLLALLLLLR--HLGWGLVTIFWFEYVLQPVHNLIMGDTKEQRI
                          : *.  : * *: . :          .   * * * :  *::**:**.:*****

Pig                 LQYVLQHAVAGDPESVLDTIDTYSSQKEWAMHVGRKKGQIVDTVVQEQRPSVLLELGAYC
Cattle              LQHVLQHAVAGDPQSVVAAIDSYSLEKEWAMHVGEKKGQIVDRVLREQQPSVLLELGAYC
Horse               LRHVLQHAVAGDPQSVLETIDAYCSQKEWAMNVGDKKGQFLDAVVQEQQPSVLLELGAYC
Human               LNHVLQHAEPGNAQSVLEAIDTYCEQKEWAMNVGDKKGKIVDAVIQEHQPSVLLELGAYC
Chimpanzee          LNHVLQHAEPGNAQSVLEAIDTYCEQKEWAMNVGDKKGKIVDAVIQEHQPSVLLELGAYC
Rhesus monkey       LHHVLQHAEPGNAQSVVEAIDTYCQQKEWAMNVGDKKGKIVDAVIQEHQPSMLLELGAYC
Mouse               LRHVQQHAKPGDPQSVLEAIDTYCSEKEWAMNVGDAKGQIMDAVIREYRPSLVLELGAYC
Rat                 LRYVQQNAKPGDPQSVLEAIDTYCTQKEWAMNVGDAKGQIMDAVIREYSPSLVLELGAYC
                    *.:* *:*  .*:..:**:  :**:*.  :*****:**  **:::* *::*  **::*******

Pig                 GYSAVRMARLLLPSARLLTIELNPDNAAIAQQVVDFAGLQDRVTVVVGASQDIIPQLKKK
Cattle              GYSAVRMARLLLPGARLLTIEFNPDYAAITQRMVEFAGLQDKVTVVLGASQDIIPQLKKK
Horse               GYSAVRMARLLPPGARLLTIEINPDYAAITQRMLDFAGLQDRVTVVLGASQDIIPQLKKK
Human               GYSAVRMARLLSPGARLITIEINPDCAAITQRMVDFAGMKDKVTLVVGASQDIIPQLKKK
Chimpanzee          GYSAVRMARLLSPGARLITIEINPDCAAITQRMVDFAGVKDKVTLVVGASQDIIPQLKKK
Rhesus monkey       GYSAVRMARLLSPGARLLTIEINPDYAAITQRMVDFAGMQDKVTVVVGASQDIIPQLKKK
Mouse               GYSAVRMARLLPPGARLLTMEINPDYAAITQQMLDFAGLQDKVSILIGAPQDLIPQLKKK
Rat                 GYSAVRMARLLQPGARLLTMEMNPDYAAITQQMLNFAGLQDKVTILNGASQDLIPQLKKK
                    ************ *.***:*:*:*** ***:*::::***::*:*::: **.**:*******

Pig                 YDVDTLDMVFLDHWKDRYLPDTLLLEECGLLRKGTVLLADNVICPGAPDFLAHVRGCGRF
Cattle              YDVDTLDMVFLDHWKDRYLPDMLLLEECGLLREGTVLLADNVIYPGAPDFLEYVRGNSRF
Horse               YDVDTLDVVFLDHWKDRYLPDTLLLEECGLLRKGTVLLADNVIVPGAPDFLAHVRGSGRF
Human               YDVDTLDMVFLDHWKDRYLPDTLLLEECGLLRKGTVLLADNVICPGAPDFLAHVRGSSCF
Chimpanzee          YDVDTLDMVFLDHWKDRYLPDTLLLEECGLLRKGTVLLADNVICPGAPDFLAHVRGSSCF
Rhesus monkey       YDVDTLDMVFLDHWKDRYLPDTLLLEECGLLRKGTVLLADNVICPGAPDFLAHVRRSNRF
Mouse               YDVDTLDMVFLDHWKDRYLPDTLLLEECGLLRKGTVLLADNVIVPGTPDFLAYVRGSSSF
Rat                 YDVDTLDMVFLDHWKDRYLPDTLLLEKCGLLRKGTVLLADNVIVPGTPDFLAYVRGSSSF
                    ********:************** *****:*****:********** **:*****  :**   . *

Pig                 ECTHFSSYLEYS-QMVDGLEKAVYKGPGSPAQP-
Cattle              ECSHFSSYLEYS-KVVDGLEKVVYKGLSGPARP-
Horse               ECTHFSSYLEYSLWVVDGVEKAVYLGPGSPAQP-
Human               ECTHYQSFLEYR-EVVDGLEKAIYKGPGSEAGP-
Chimpanzee          ECTHYQSFLEYR-EVVDGLEKAIYKGPGSEAGP-
Rhesus monkey       ECTHYQSFLEYR-KVVDGLEKAIYKGPGSEAQP-
Mouse               ECTHYSSYLEYM-KVVDGLEKAVYQGPGSSPVKS
Rat                 ECTHYSSYLEYM-KVVDGLEKAIYQGPSSPDKS-
                    **:*:.*:***    :***:**.:* * ..
```

Fig. 3 The alignment of the protein encoded by COMT gene from pig and other seven kinds of COMT from cattle, horse, human, chimpanzee, rhesus monkey, mouse and rat.

From the sequencing and structural results described, this gene can be defined as the porcine COMT gene. This novel porcine gene was assigned to GeneID: 100155530. Based on the results of the alignment of thirty different species of COMT, a phylogenetic tree was constructed using the ClustalW software (http://www.ebi.ac.uk/clustalw), as shown in Fig.5. The phylogenetic tree analysis revealed that the pig COMTgene has a closer genetic relationship with the cattle COMT gene than with those of horse, human, chimpanzee, rhesus monkey, mouse and rat.

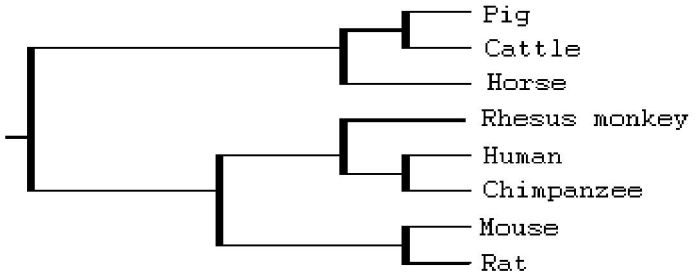


Fig.4 The phylogenetic tree for eight kinds of COMT genes

To obtain the genomic DNA of COMT gene, the publicly available pig genome database at the NCBI Pig Genome Resources (http://www.ncbi.nlm.nih.gov/projects/genome/guide/pig/) was screened using the open reading frame (ORF) cDNA sequence of COMT gene as a seed. A bacterial artificial chromosome (BAC) clone (Sus scrofa chromosome 14 clone CH242-153A5, GenBank accession no. CT737290) which encompasses entire COMT gene was identified by BLASTGen analysis. The pig COMT gene (nucleotides 137,451-141,637 in the Sus scrofa chromosome 14 clone CH242-153A5) is 4,187 bp in length and consists of four exons. All exon–intron splice junction sequences conform to the GT–AG rule (Fig.5).

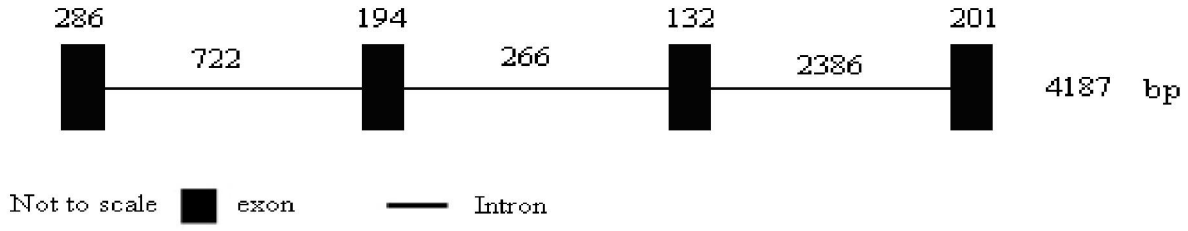
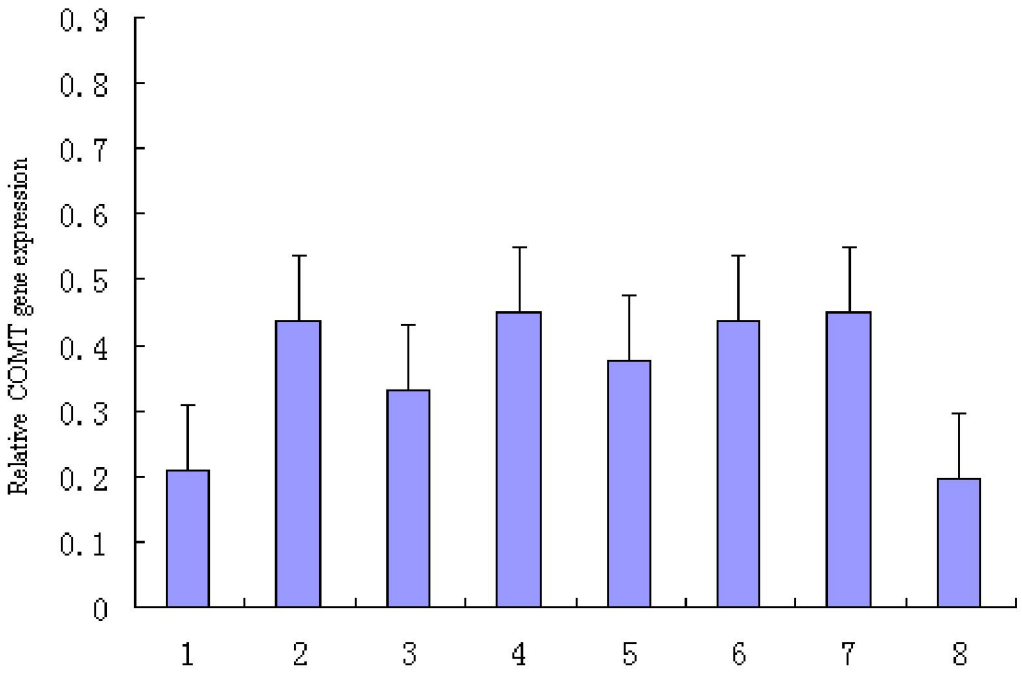


Fig. 5 The genomic sequence organization representing the ORF of the swine COMT gene.

Tissue Expression Profile

The qRT-PCR analysis of the tissue expression profile was carried out using the tissue cDNAs of one adult pig as the templates. The tissue expression analysis indicated that the porcine COMT gene is generally and differentially expressed in detected tissues including spleen, muscle, placenta, kidney, lung, liver, fat and heart.



1, skin; 2, kidney; 3, spleen; 4, heart; 5, fat; 6, muscle; 7, liver; 8, lung;

Fig.6 Tissue expression profile analysis of the porcine COMT gene

DISCUSSION

In the current study, we firstly get the full length of porcine COMT gene cDNA by using 5'- and 3'-RACE. With the development of modern bioinformatics and specific pig NCBI EST database was established along with different convenient analysis tools make researchers much easier to find the useful ESTs which was highly homologous to the coding sequence of human genes. Based on these pig EST sequences, we can obtain the complete coding sequences of some novel porcine genes through the some modern experimental methods such as rapid amplification of cDNA ends (RACE) method. From the clone and sequence analysis of porcine COMT gene, it could be seen that this is an effective method to isolate some novel porcine genes.

Through sequence analysis, we found that the encoding protein of the porcine COMT gene is highly homologous with COMT proteins of human, mouse and other mammals. This implied that the COMTgenes were highly conserved in some mammals and the pig COMTgene will have similar functions as the COMT genes of human, mouse and other mammals. We also found that the pig COMT protein does not show complete identity to human, mouse or other mammals. This implied that the porcine COMT gene will have some differences in functions to those of human, mouse or other mammals. From phylogenetic analysis we found that porcine COMT gene has a closer genetic relationship with the COMT gene of cattle, this implied that we can use cattle as a model organism to study the pig COMTgene.

From the tissue distribution analysis in our experiment it can be seen that the porcine COMT gene was obviously differentially expressed in some tissues. As we did not study functions at protein levels yet, there might be many possible reasons for differential expression of porcine COMT gene. The suitable explanation for this under current conditions is that at the same time those biological activities related to the mRNA expression of porcine COMT gene were presented diversely in different tissues.

CONCLUSION

In conclusion, we first isolated the porcine COMT gene and performed necessary sequence analysis and tissue transcription profile analysis. This established the primary foundation for further insight into this novel porcine gene.

Acknowledgments

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REFERENCES

[1]. Brennan PA, Hammen C, Sylvers P, Bor W, Najman J, Lind P, Montgomery G, Smith AK.Interactions between the COMT Val108/158Met polymorphism and maternal prenatal smoking predict aggressive behavior outcomes. Biol Psychol. 2011 Apr; 87(1):99-105.

[2]. Dickerson F, Stallings C, Sullens A, Origoni A, Leister F, Krivogorsky B, Yolken R.Association between cognitive functioning, exposure to Herpes Simplex Virus type 1, and the COMT Val158Met genetic polymorphism in adults without a psychiatric disorder.Brain Behav Immun. 2008 Oct;22(7):1103-7.

[3]. Garcia-Garcia M, Barceló F, Clemente IC, Escera C.COMT and ANKK1 gene-gene interaction modulates contextual updating of mental representations. Neuroimage. 2011 Jun 1;56(3):1641-7.

[4]. Liu, Y.G. and S.Z. Gao, 2009a. A novel porcine gene, MMP7, differentially expressed in muscles from black-boned pig and local common pig. J. Appl. Genet., 50:253-256.

[5]. Liu, Y.G. and S.Z. Gao, 2009b. Molecular Cloning, Sequence Identification and Tissue Expression Profile of Three Novel Pig (Ovis aries) Genes - BCKDHA, NAGA and HEXA. Biol. Res., 42：69-77

[6]. Liu, Y.G., 2009. A novel HADHA gene differentially expressed in muscle and other tissues from black-boned vs. ordinary pig. Anim. Sci. Pap. Rep., 27:127-137

[7]. Müller T, Woitalla D, Muhlack S.Inhibition of catechol-O-methyltransferase modifies acute homocysteine rise during repeated levodopa application in patients with Parkinson's disease.Naunyn Schmiedebergs Arch Pharmacol. 2011 Jun;383(6):627-33.

[8]. Müller T. Catechol-O-methyltransferase enzyme: cofactor S-adenosyl-L-methionine and related mechanisms.Int Rev Neurobiol. 2010;95: 49-71.

[9]. Nedić G, Borovecki F, Klepac N, Mubrin Z, Hajnsek S, Nikolac M, Muck-Seler D, Pivac N. Association study of a functional

catechol-o-methyltransferase polymorphism and cognitive function in patients with dementia. Coll Antropol. 2011 Jan;35 Suppl 1:79-84.

[10]. Ursini G, Bollati V, Fazio L, Porcelli A, Iacovelli L, Catalani A, Sinibaldi L, Gelao B, Romano R, Rampino A, Taurisano P, Mancini M, Di Giorgio A, Popolizio T, Baccarelli A, De Blasi A, Blasi G, Bertolino A. Stress-related methylation of the catechol-O-methyltransferase Val 158 allele predicts human prefrontal cognition and activity. J Neurosci. 2011 May 4;31(18):6692-8.

[11]. Valente NL, Vallada H, Cordeiro Q, Bressan RA, Andreoli SB, Mari JJ, Mello MF. Catechol-O-methyltransferase (COMT) val158met polymorphism as a risk factor for PTSD after urban violence. J Mol Neurosci. 2011 Mar;43(3):516-23.

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