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Genetic Characterization of Fibroblast Growth Factor-5 Gene in Rabbits

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Abstract: Fibroblast growth factor 5 (*FGF-5*) gene is a member of the fibroblast growth factor (FGF) family. The protein encoded by this gene has a variety of biological activities including the embryonic development and cell growth. This study aimed to characterize *FGF-5* gene and to detect the possible association between the polymorphism of this gene with body weight in local Egyptian rabbits. The DNA was extracted from blood samples of seventy rabbits, PCR was performed using specific primers for *FGF-5* exon 3 in rabbit and the PCR products were at 288-bp. These products were digested using *Taq*I endonuclease to detect the genetic polymorphism of this gene in rabbits. All tested animals are genotyping as TT due to the presence of fixed nucleotide T at position 58 in all amplified fragments which is responsible for the elimination of the restriction site T^CGA. The nucleotide sequence of *FGF-5* allele T in rabbits reared in Egypt was submitted to NCBI/Bankit/GenBank and has the accession number KP682502. To detect the possible association between body weight in rabbits and the single nucleotide polymorphism of *FGF-5* exon 3, the nucleotide sequence analysis of the whole amplified fragments was performed for 4 representative animals with different body weights and the sequences were aligned using ClustalW2. The result declared that all four sequences possess 100% identity between them without any SNP. In conclusion, due to the negative association between *FGF-5* exon 3 with body weight in rabbits reported in this study, we need further studies to find another molecular marker associated with body weight in rabbits for using it in marker assisted selection program (MAS) as a step toward the production improvement of this animal which is considered one of the meat sources in Egypt.

Key words: Rabbit · *FGF-5* · PCR · RFLP · SNPs

INTRODUCTION

Fibroblast growth factors (FGFs) are small polypeptide growth factors which share in common certain structural characteristics. Many FGFs contain signal peptides for secretion and are secreted into the extracellular environment. FGFs and the FGF signaling pathway appear to play significant roles not only in normal development and wound healing, but also in tumor development and progression [1]. FGFs are widely present in various tissues, thus far were identified 23 kinds of FGFs. One member of FGF family is *FGF-5* [2] which is considered a promising candidate gene for economically important quantitative traits. It plays a central role in the stimulation of cell growth and proliferation in multiple cell types [3]. The rabbit FGF-5 gene mapped on chromosome 15 [4] containing three exons [5] and its molecular weight is 34 kDa [6].

Rabbit has its importance as supplier of meat and it is widely accepted thought out the world for human consumption [7] and in Egypt, rabbits have become as a source of food. The adaptation of rabbit populations to climatic conditions may represents a genetic variability in their gene pool and this variability causes genetic differentiations among rabbit. The genetic diversity of reared and wild animals is declining and this warrants serious attention of the researchers and conservators to find out ways to conserve the diversity at the maximum level. The estimation of genetic variability of a species is an important criterion for its conservation and further genetic improvement [8].

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Genetic polymorphism can be identified by several techniques; one of the most commonly used methods is PCR-RFLP. It is a powerful method for identifying nucleotide sequence variation in amplified DNA and can detect single base substitutions in enzymatic restriction sites [9].

In this study, we aimed to identify the genetic characterization of *FGF-5* gene in domesticated rabbits reared in Egypt and to detect the genetic variation and single nucleotide polymorphism within *FGF-5* exon 3 in local Egyptian rabbits using PCR-RFLP and nucleotide sequence analysis techniques.

MATERIALS AND METHODS

Animals and Genomic DNA Extraction: The blood samples were collected from 70 local Egyptian rabbits. The animals were collected from the research station (in Sakha) which is belonged to Animal Production Research Institute. The weights of these animals were recorded every 2 weeks from week 4 to week 12. Genomic DNA was extracted from the whole blood according to the method described by Miller *et al*. [10] with minor modifications. Briefly, blood samples were mixed with cold 2x sucrose-triton and centrifuged at 5000 rpm for 15 min at 4°C. The nuclear pellet was suspended in lysis buffer, sodium dodecyl sulfate and proteinase K and incubated overnight in a shaking water bath at 37°C. Nucleic acids were extracted with saturated NaCl solution. The DNA was picked up and washed in 70% ethanol. The DNA was dissolved in 1x TE buffer. DNA concentration was determined, using Nano Drop1000 Thermo Scientific spectrophotometer and then diluted to the working concentration of 50ng/µl.

Polymerase Chain Reaction (PCR): A PCR cocktail consisted of 1.0 mM upper and lower primers specific for rabbit *FGF-5* gene, 0.2 mMdNTPs, 10 mMTris (pH 9), 50 mMKCl, 1.5 mM$MgCl_2$, 0.01 % gelatin (w/v), 0.1 % Triton X-100 and 1.25 units of Taq polymerase. The cocktail was aliquot into PCR tubes with 100 ng of rabbit DNA. The reaction was run at 94°C for 5min, 30 cycles of 94°C for 1min, 58°C for 30s, 72°C for 45s and a final extension at 72°C for 5min. The PCR products were electrophoresed on 2% agarose gel stained with ethidium bromide to test the amplification success. The primers used in this study were designed on the basis of DNA sequence of the rabbit *FGF-5* gene [11].

F: CCT ATG CCT CAG CAA TAC ATA GAA CT
R: ATC CAA AGC GAA ACT TGA GTC TG

Restriction Fragment Length Polymorphism (RFLP): Ten µl of PCR product of *FGF-5* exon 3 were digested with 1µl of *Taq*I FastDigest restriction enzymes for 15 min at 37°C. The restriction fragments were subjected to electrophoresis in 2% agarose/ethidium bromide gel in 1x TBE buffer (0.09 M Tris-boric acid and 0.002 M EDTA). Gels were visualized under UV light and documented in FX Molecular Imager apparatus (BIO-RAD).

Sequence Analysis: The amplified fragments of *FGF-5* gene for 4 animals; two of them with the highest body weight and the other two with the lowest body weight; were purified and sequenced by Macrogen Incorporation (Seoul, Korea). Sequence analysis and alignment were carried out using ClustalW2. The nucleotide sequences of the rabbit *FGF-5* gene were submitted to GenBank (NCBI, BankIt).

RESULTS AND DISCUSSION

The protein encoded by fibroblast growth factor 5 (*FGF-5*) gene is a member of the fibroblast growth factor (FGF) family. FGF family members possess broad mitogenic and cell survival activities and are involved in a variety of biological processes, including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion [12]. This gene was identified as an oncogene, which confers transforming potential when transfected into mammalian cells. Targeted disruption of the homolog of this gene in mouse resulted in the phenotype of abnormally long hair, which suggested a function as an inhibitor of hair elongation [13].

The disruption of *FGF-5* expression in mammals increases the length of the anagen (growth) phase of the hair cycle, resulting in a phenotype of extremely long hair. This has been shown in many species, including cats [14], dogs [15], mice [2], rabbits [16], camels, sheep and goats [17], elephants and mammoths [18].

Due to the absence of any molecular information about *FGF-5* gene in rabbits reared in Egypt, we aimed in this study to detect the genetic polymorphism in exon 3 of this gene using RFLP technique and to examine its association with body weight in rabbit. We used in this study 70 local Egyptian rabbits. The weights of tested

Table 1: Range and means of body weights for tested rabbits

	Body weight	
Age	Range	Mean±SD
4 weeks	0.280-0.935	0.521±0.173
6 weeks	0.475-1.325	0.776±0.206
8 weeks	0.705-1.715	1.052±0.224
10 weeks	1.000-1.990	1.342±0.216
12 weeks	1.29-2.445	1.648±0.233

animals were recorded every 2 weeks from week 4 to week 12 and the ranges as well as means of body weights were showed in Table 1.

The primers used in this study amplified 288-bp fragments from exon 3 of *FGF-5* gene in rabbits (Fig. 1).

These amplified fragments were digested with *Taq*I restriction enzymes. Depending on the presence or absence of the restriction site T^CGA at position 57^58, we can differentiate between 3 different genotypes; TT with one undigested fragment at 288-bp, CC with two digested fragments at 231- and 57-bp and CT with 3 digested fragments at 288-, 231- and 57-bp. All tested rabbits are genotyping as TT where all amplified fragments remained as intact fragments after treating with *Taq*I endonuclease (Figs. 2 and 3) due to the presence of fixed nucleotide T at position 58 in all amplified fragments (Fig. 4) which is responsible for the elimination of the restriction site T^CGA. The nucleotide sequence of *FGF-5* allele T in rabbits reared in Egypt was submitted to nucleotide sequences database NCBI/Bankit/GenBank and has the accession number KP682502

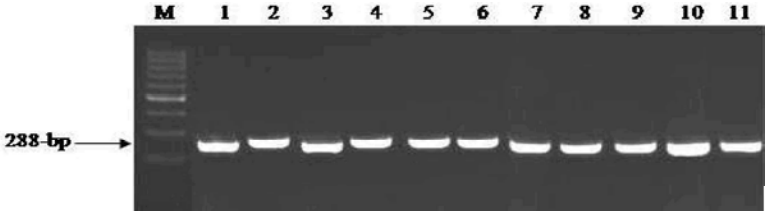

Fig. 1: Agarose gel stained with ethidium bromide showing the PCR product of *FGF-5* gene
M: 100-bp ladder. Lanes 1-11: 288-bp PCR product of *FGF-5* gene.

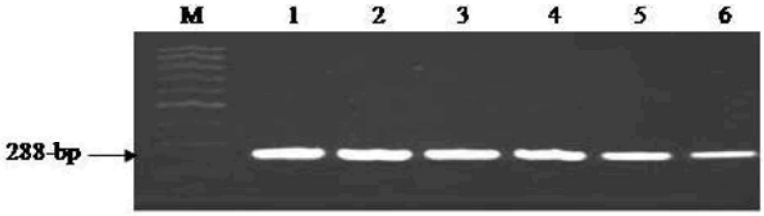

Fig. 2: Elecrophoretic pattern of *FGF-5* PCR product after digestion with *Taq*I endonuclease
M: 100-bp ladder. Lanes 1-6: TT homozygous genotype with intact fragments at 288-bp.

CCTATGCCTCAGCAATACATAGAACTGAGAGAACAGGGCGGGAGTGGTATGTGGCC
TTGAACAAACGAGGGAAAGCAAAGCGAGGCTGCAGCCCACGGGTCAAACCTCAGC
ACGTCTCTACCCATTTTCTACCAAGATTCAAGCAGTCGGAGCAGCCAGAACTTTCCT
TTACTGTTACTGTTCCTGAAAAGAAAAAGCCGCCCAACCCTATCAAGCCAAAGGTTC
CCCTTTCTGCACCTCGGAGAAGTCCCAACACAGTGAAATACAGACTCAAGTTTCGCT
TTGGAT

Fig. 3: The nucleotide sequence of *FGF-5* allele T in rabbits reared in Egypt

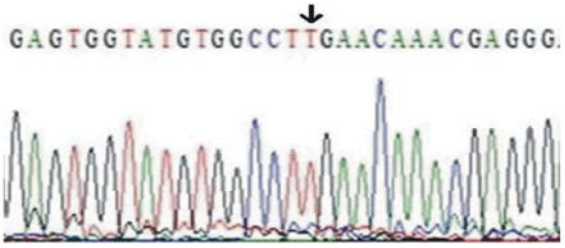

Fig. 4: The fixed nucleotide T at position 58 in the amplified fragments

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A:     1 CCTATGCCTCAGCAATACATAGAACTGAGAGAACAGGGCGGGAGTGGTATGTGGCCTTGA 60
B:     1 CCTATGCCTCAGCAATACATAGAACTGAGAGAACAGGGCGGGAGTGGTATGTGGCCTTGA 60
C:     1 CCTATGCCTCAGCAATACATAGAACTGAGAGAACAGGGCGGGAGTGGTATGTGGCCTTGA 60
D:     1 CCTATGCCTCAGCAATACATAGAACTGAGAGAACAGGGCGGGAGTGGTATGTGGCCTTGA 60
         ************************************************************

A:    61 ACAAACGAGGGAAAGCAAAGCGAGGCTGCAGCCCACGGGTCAAACCTCAGCACGTCTCTA 120
B:    61 ACAAACGAGGGAAAGCAAAGCGAGGCTGCAGCCCACGGGTCAAACCTCAGCACGTCTCTA 120
C:    61 ACAAACGAGGGAAAGCAAAGCGAGGCTGCAGCCCACGGGTCAAACCTCAGCACGTCTCTA 120
D:    61 ACAAACGAGGGAAAGCAAAGCGAGGCTGCAGCCCACGGGTCAAACCTCAGCACGTCTCTA 120
         ************************************************************

A:   121 CCCATTTTCTACCAAGATTCAAGCAGTCGGAGCAGCCAGAACTTTCCTTTACTGTTACTG 180
B:   121 CCCATTTTCTACCAAGATTCAAGCAGTCGGAGCAGCCAGAACTTTCCTTTACTGTTACTG 180
C:   121 CCCATTTTCTACCAAGATTCAAGCAGTCGGAGCAGCCAGAACTTTCCTTTACTGTTACTG 180
D:   121 CCCATTTTCTACCAAGATTCAAGCAGTCGGAGCAGCCAGAACTTTCCTTTACTGTTACTG 180
         ************************************************************

A:   181 TTCCTGAAAAGAAAAAGCCGCCCAACCCTATCAAGCCAAAGGTTCCCCTTTCTGCACCTC 240
B:   181 TTCCTGAAAAGAAAAAGCCGCCCAACCCTATCAAGCCAAAGGTTCCCCTTTCTGCACCTC 240
C:   181 TTCCTGAAAAGAAAAAGCCGCCCAACCCTATCAAGCCAAAGGTTCCCCTTTCTGCACCTC 240
D:   181 TTCCTGAAAAGAAAAAGCCGCCCAACCCTATCAAGCCAAAGGTTCCCCTTTCTGCACCTC 240
         ************************************************************

A:   241 GGAGAAGTCCCAACACAGTGAAATACAGACTCAAGTTTCGCTTTGGAT 288
B:   241 GGAGAAGTCCCAACACAGTGAAATACAGACTCAAGTTTCGCTTTGGAT 288
C:   241 GGAGAAGTCCCAACACAGTGAAATACAGACTCAAGTTTCGCTTTGGAT 288
D:   241 GGAGAAGTCCCAACACAGTGAAATACAGACTCAAGTTTCGCTTTGGAT 288
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Fig. 5: The nucleotide sequences and alignment between four rabbit animals with different body weights. A (2.445 kg), B (2.080 kg), C (1.37 kg) and D (1.290 kg)

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Query  27   GAGAGAACAGGGCGGGAGTGGTATGTGGCCTTGAACAAACGAGGGAAAGCAAAGCGAGGC  86
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1    GAGAGAACAGGGCGGGAGTGGTATGTGGCCTTGAACAAACGAGGGAAAGCAAAGCGAGGC  60

Query  87   TGCAGCCCACGGGTCAAACCTCAGCACGTCTCTACCCATTTTCTACCAAGATTCAAGCAG  146
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  61   TGCAGCCCACGGGTCAAACCTCAGCACGTCTCTACCCATTTTCTACCAAGATTCAAGCAG  120

Query  147  TCGGAGCAGCCAGAACTTTCCTTTACTGTTACTGTTCCTGAAAAGAAAAAGCCGCCCAAC  206
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  121  TCGGAGCAGCCAGAACTTTCCTTTACTGTTACTGTTCCTGAAAAGAAAAAGCCGCCCAAC  180

Query  207  CCTATCAAGCCAAAGGTTCCCCTTTCTGCACCTCGGAGAAGTCCCAACACAGTGAAATA  265
            |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  181  CCTATCAAGCCAAAGGTTCCCCTTTCTGCACCTCGGAGAAGTCCCAACACAGTGAAATA  239
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Fig. 6: The alignment between our sequence and the published sequence

This result showed that all tested animal with different body weights possess the same genotype TT. In going for searching about the association between body weight and single nucleotide polymorphism in *FGF-5* gene, we chose 4 animals; two of them with the highest (2.445 and 2.080 kg) and the other two with the lowest (1.370 kg and 1.290 kg) body weights at age week 12 for sequencing analysis. The sequences of *FGF-5* exon 3 for these four animals were aligned using ClustalW2. The result declared that all four sequences possess 100% identity between them without any SNP (Fig. 5). Our sequence of *FGF-5* exon 3 was aligned with the published sequence of this gene (Accession No.: AY230009.1). The results showed 100% identity between these two sequences in shared fragments with 239-bp (Fig. 6).

The fibroblast growth factor 5 gene (*FGF-5*) is a member of the FGF gene family and represents a candidate gene for hair length because of its role in the regulation of the hair follicle growth cycle [6]. *FGF-5* was originally identified as a human oncogene [19], belonging to a family of 23 related *FGF* genes [20,21]. Fibroblast growth factor-5 is known to be expressed in the embryo [22-24]. The analysis of defects at this locus in angora animals of different species should thus be of help in elucidating the role of fibroblast growth factor 5 in embryonic development. Angora recessive mutations that cause the production of abnormally long hair have been detected in several species, including mice, rabbits, goats, dogs and cats [11]. So, most studies which were carried out on *FGF-5* polymorphism were focused on its association with hair length in different animals.

Kehler *et al*. [25] determined the genetic regulation of hair length in the domestic cat using a whole-genome scan in a multigenerational pedigree in which the long-haired phenotype was segregating. The markers that demonstrated the greatest linkage to the long-haired trait flanked an estimated 10-Mb region on cat chromosome B1 containing *FGF-5* gene, a candidate gene implicated in regulating hair follicle growth cycle in other species. Sequence analyses revealed 4 separate mutations predicted to disrupt the biological activity of the *FGF-5* protein. Association analyses of genotyped breed and non-breed cats were consistent with mutations in the *FGF-5* gene causing the long-haired phenotype in an autosomal recessive manner.

Comparative cDNA and genomic DNA sequencing of long- and short-haired cats revealed four non-synonymous polymorphisms in the *FGF-5* coding sequence [14]. A missense mutation (194C>A) was found in the homozygous state in 25 long-haired cats and 55 short-haired cats had zero or one copy of this allele. A second *FGF-5* exon 1 missense mutation (182T>A) was found exclusively in long-haired Norwegian Forest cats and it is considered a second *FGF-5* mutation responsible for long hair in cats. A frame-shift mutation (474delT) was found with a high frequency in the long-haired Maine Coon breed. A missense mutation (475A>C) was also associated with the long-haired phenotype in some breeds.

The cloning, sequencing and characterization of the full-length *FGF-5* cDNA of Chinese Merino sheep were carried out by Zhang *et al.* [6]. They found that the *FGF-5* gene spanned 21,743 bp of genomic DNA and consisted of 3 exons and 2 introns, both of which differed from those of a previously annotated *FGF-5* genomic sequence from sheep. Also, this result declared that the expression of the *FGF-5* mRNA was restricted to the brain, spleen and skin tissue. The single-nucleotide polymorphism analysis of the genomic sequence revealed 72 genetic variants of the *FGF-5* gene in Chinese Merino sheep.

Mulsant *et al.* [11] used two pairs of primers which were chosen in the human *FGF-5* coding sequence in order to amplify two fragments of the rabbit gene from exons 1 and 3. Polymorphism of the two fragments was analyzed on a random sample of unrelated angora and wild-type control animals using PCR-RFLP. The polymorphism in the putative exon 1 corresponded to the insertion at position 217 in the slow allele of three nucleotides, creating a supplementary in phase TCT (serine) codon in a serine stretch. The mutation of the slow allele creates an additional *Ear*I site. A single variation was also observed in the 288 bp putative exon 3 fragment, with a T (slow allele) or C (fast allele) at position 58. This transition replaces the leucine present in the slow allele by a serine in the fast allele. It corresponds to a *Taq*I polymorphism, with 0 or 1 digestion site in the slow or fast allele, respectively.

Single nucleotide polymorphism in exon 1 and 3 of *FGF-5* gene was studied by DNA sequencing in Yingjing angora rabbit, Tianfu black rabbit and California rabbit [16]. A frame-shift mutation (TCT insert) at base position 217 (site A) of exon 1 and a missense mutation (T/C) base position 59 (site B) of exon 3 were found in Yingjing angora rabbit with a high frequency. A same-sense mutation T/C at base position 3 (site C) of exon 3 was found with similar frequency in three rabbit breeds. Least square analysis showed that different genotypes had no significant association with wool yield in site A and had high significant association with wool yield in site B ($P<0.01$) and significant association with wool yield in site C ($P<0.05$).

In conclusion, due to the negative association between *FGF-5* exon 3 with body weight in rabbits reported in this study, we need further studies to find another molecular marker associated with body weight in rabbits for using it in marker assisted selection program (MAS) as a step toward the production improvement of this animal in Egypt.

REFERENCES

1. Powers, C.J., S.W. McLeskey and A. Wellstein, 2000. Fibroblast growth factors, their receptors and signaling. Endocrine-Related Cancer, 7: 165-197.
2. Hébert, J.M., T. Rosenquist, J. Gotz and G.R. Martin, 1994. FGF5 as a regulator of the hair growth cycle: evidence from targeted and spontaneous mutations. Cell, 78: 1017-1025.
3. Vatner, S.F., 2005. FGF induces hypertrophy and angiogenesis in hibernating myocardium. Circ. Res., 96: 705-707.
4. Chantry-Darmon, C., C. Urien, H. Rochambeau, D. Allain, B. Pena, H. Hayes, C. Grohs, E.P. Cribiu, S. Deretz-Picoulet, C. Larzul, J.C. Save, A. Neau, P. Chardon and C. Rogel-Gaillard, 2006. A first-generation microsatellite-based integrated genetic and cytogenetic map for the European rabbit (Oryctola guscuniculus) and localization of Angora and albino. Anim. Genet., 37: 335-341.

5. Hattori, Y., M. Yamasaki and N. Itoh, 1996. The rat FGF-5 mRNA variant generated by alternative splicing encodes a novel truncated form of FGF-5. Biochim. Biophys. Acta, 1306(1): 31-33.
6. Zhang, L., S. He, M. Liu, G. Liu, Z. Yuan, Z. Liu, X. Zhang, N. Zhang and W. Li, 2015. Molecular cloning, characterization and expression of sheep FGF5 gene. Gene, 555(2): 95-100.
7. Colin, M. and F. Lebas, 1996. Rabbit meat production in the world. A proposal for every country. In Proc.: 6th World Rabbit Congress, Toulouse, France, pp: 323-330.
8. Rangoju, P.K., S. Kumar, A.P. Kolte, R. Gulyani and V.K. Singh, 2007. Assessment of genetic variability among rabbit breeds by random amplified polymorphic DNA (RAPD)-PCR. World Rabbit Sci., 15: 3-8.
9. Amie Marini, A.B., K. Aslinda, R. Mohd Hifzan, A.B. Muhd. Faisal and K. Musaddin, 2012. HaeIII-RFLP Polymorphism of growth hormone gene in Savanna and Kalahari goats. Mal. J. Anim. Sci., 15: 13-19.
10. Miller, S.M., D.D. Dykes and H.F. Polesky, 1988. A simple salting out procedure for extracting DNA from human nucleated cells. Nucleic Acids Res., 16(3): 1215.
11. Mulsant, P., H. Rochambeau and R.G., 2004. A note on linkage between the angora and FGF5 genes in rabbits. World Rabbit Sci., 12: 1-6.
12. Zhang, L., S. Kharbanda, J. Hanfelt and F.G. Kern, 1998. Both autocrine and paracrine effects of transfected acidic fibroblast growth factor are involved in the estrogen-independent and antiestrogen-resistant growth of MCF-7 breast cancer cells. Cancer Res., 58: 352-361.
13. Nguyen, C., D. Roux, M.G. Mattei, O. de Lapeyriere, M. Goldfarb, D. Birnbaum and B.R. Jordan, 1994. The FGF-related oncogenes hst and int.2 and the bcl.1 locus are contained within one megabase in band q13 of chromosome 11, while the fgf.5 oncogene maps to 4q21. Oncogene, 3(6): 703-708.
14. Drögemüller, C., S. Rüfenacht, B. Wichert and T. Leeb, 2007. Mutations within the FGF5 gene are associated with hair length in cats. Anim. Genet., 38(3): 218-221.
15. Cadieu, E., M.W. Neff, P. Quignon, K. Walsh, K. Chase, H.G. Parker, B.M. Vonholdt, A. Rhue, A. Boyko, A. Byers, A. Wong, D.S. Mosher, A.G. Elkahloun, T.C. Spady, C. André, K.G. Lark, M. Cargill, C.D. Bustamante, R.K. Wayne and E.A. Ostrander, 2009. Coat variation in the domestic dog is governed by variants in three genes. Science, 326(5949): 150-153.
16. Li, C.X., M.S. Jiang, S.Y. Chen and S.J. Lai, 2008. Correlation analysis between single nucleotide polymorphism of FGF5 gene and wool yield in rabbits. Yi. Chuan., 30(7): 893-899.
17. Allain, D. and C. Renieri, 2010. Genetics of fibre production and fleece characteristics in small ruminants, Angora rabbit and South American camelids. Animal, 4(9): 1472-1481.
18. Roca, A.L., Y. Ishida, N. Nikolaidis, S.O. Kolokotronis, S. Fratpietro, K. Stewardson, S. Hensley, M. Tisdale, G. Boeskorov and A.D. Greenwood, 2009. Genetic variation at hair length candidate genes in elephants and the extinct woolly mammoth. BMC Evol. Biol., 9: 232-242.
19. Zhan, X., B. Bates, X.G. Hu and M. Goldfarb, 1989. The human FGF-5 oncogene encodes a novel protein related to fibroblast growth factors. Mol. Cell Biol., 8(8): 3487-3495.
20. Katoh, M., 2002. WNT and FGF gene clusters. Int. J. Oncol., 21: 1269-1273.
21. Katoh, Y. and M. Katoh, 2005. Comparative genomics on FGF16 orthologs. Int. J. Mol. Med., 16: 959-963.
22. Haub, O. and M. Goldfarb, 1991. Expression of the fibroblast growth factor-5 gene in the mouse embryo. Development, 112: 397-406.
23. Hébert, J.M., C. Basilico, M. Goldfarb, O. Haub and G. Martin, 1990. Isolation of cDNAs encoding four mouse FGF family members and characterisation of their expression patterns during embryogenesis. Devl. Biol., 138: 454-463.
24. Hébert, J.M., M. Boyle and G.R. Martin, 1991. mRNA localisation studies suggest that murine FGF-5 plays a role in gastrulation. Development, 112: 407-415.
25. Kehler, J.S., V.A. David, A.A. Schaffer, K. Bajema, E. Eizirik, D.K. Ryugo, S.S. Hannah, S.J. O'brien and M. Menootti-Raymond, 2007. Four independent mutations in the feline fibroblast growth factor 5 gene determine the long-haired phenotype in domestic cats. J. Hered., 98(6): 555-566.