



E-ISSN: 2320-7078

P-ISSN: 2349-6800

JEZS 2017; 5(6): 1748-1754

© 2017 JEZS

Received: 25-09-2017

Accepted: 26-10-2017

**Syed Shanaz**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**TAS Ganai**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Sheikh Firdous Ahmad**

Division of Animal Genetics, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, Uttar Pradesh, India

**Feroz Din Sheikh**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Saba B**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Aadil Ayaz**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Tavsief Sheikh**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Mir Shabir**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Ruksana Shah**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Ishraq Hussain**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Zaffar Iqbal**

Division of Animal Genetics and Breeding, F.V.Sc. &amp; A.H. SKUAST, Kashmir, India

**Correspondence****Sheikh Firdous Ahmad**

Division of Animal Genetics, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, Uttar Pradesh, India

## Understanding fibre related genes and their association with fibre quality attributes in small ruminants – A review

**Syed Shanaz, TAS Ganai, Sheikh Firdous Ahmad, Feroz Din Sheikh, Saba B, Aadil Ayaz, Tavsief Sheikh, Mir Shabir, Ruksana Shah, Ishraq Hussain and Zaffar Iqbal**

### Abstract

Sheep and goat are two species of small ruminants that produce different kinds of fibres that differ in their characteristics mainly on the breed-wise basis. On one hand, Pashmina breeds produce the fine type of fibre while breeds of South India produce fibre that is not much fine. Cashmere and Mohair are important fine fibres having immense demand in international markets. Understanding the pathways for genesis, development and differentiation of fibres have the potential to help us in manipulating the breeding plans for efficient fibre production from these sheep breeds. Keratin forms an important part of the wool fibre and determines the most part of its structure and physical characteristics. Different studies have aimed at elucidating the polymorphism and association thereby with different fibre characteristics. Two multi-gene families have been reported for Keratin, the type I (acidic) and type II (basic) families. Application of results from these studies is surely going to help reap rich benefits if applied meticulously into the existing breeding plans for these species. A standard set of abbreviated coding pattern has been proposed recently regarding the nomenclature of different KAP genes and proteins.

**Keywords:** Association, cashmere, KAP, Keratin

### 1. Introduction

Human societies have benefited immensely ever since the domestication of farm animal species. Animal rearing has improved the livelihood, thus it still remains highly relevant in present times, where everything is seen through an economic prism. On one hand, large animals are mainly reared for milk production, the small ruminants, mainly sheep and goat, have significance in their own ways. One of the main outputs is the production of the fibre of different types. A number of attempts have been made to understand the genetics and phenotypic parameters of wool and fibre growth in various species.

Wool fibres are of different kinds, produced from small animals, mainly sheep, goat, rabbit and a few other species. Even different breeds, within a single species, produce different kinds of fibres. These fibres differ significantly in terms of structural, mechanical and other characteristics. Of these fibres, Cashmere and Mohair are highly relished and are being used for various purposes all over the world. Due to less productivity per animal and ever-increasing demand, this forms a hot-cake in the small animal genetic studies. Different interrelated genes and pathways are thought to be responsible for different fibre characteristics like fibre yield, fineness, fibre diameter, staple length, fibre weight and colour and others. However, other parameters like tensile strength, moulting, spatial and temporal expression are some other factors important for our understanding and for any manipulations targeted for rich future reaps.

#### 1.1 Pashmina fibre

Pashmina is a fine, undercoat of the Cashmere goat (*Capra hircus*), which serves as a layer of insulation during the cold winter months. During the spring, the Cashmere moults spontaneously and is harvested by the farmer by combing of animals while it is entangled with primary fibres. *Pashmina*, produced in India, especially in the Jammu and Kashmir State, is known for its quality all over the world. The fineness of fibres varies from 11.30  $\mu$ <sup>[1]</sup> to 13.51  $\mu$ <sup>[2]</sup>. Similarly, fibre length also shows considerable variation and has been reported to

be 4.0 to 6.20 cm<sup>[1]</sup>, 4.95-5 cm<sup>[3]</sup>, 5.80 cm<sup>[4]</sup>, 4.86 cm<sup>[5]</sup>. However, the Cashmere fibres are rather weak and about 10% below the strength of the finest wool and about 40% weaker than fine Mohair<sup>[6]</sup>.

*Pashmina* fibres are non-medullated and lack crimps. On an equal weight basis, *Pashmina* possesses three times more insulating capacity as that of wool<sup>[6]</sup>. The common natural colours of *Pashmina* are grey, brown, black and white. The Cashmere traits of industrial importance are the fibre diameter, fibre length, and fibre yield, fibre weight and colour. Among all shades, white fetches the highest price because of its rarity. There is sparse information on the genes involved in *Pashmina* fibre production and quality. For analyzing the genetic association of particular gene polymorphism with production traits, studies which focus on associations between genetic variation within candidate genes and phenotypes are required. Hence, searching for the effects of candidate gene polymorphisms on Cashmere production traits is important to develop markers for selection and /or alleles of interest influencing *Pashmina* fibre for goat industry. Some quality attributes and related genes found to be associated with Cashmere traits shall be reviewed below.

### 1.2 Fibre Structure

The undercoat *Pashmina* fibres microscopically consist of the epidermis and the cortical layer and are free of any medullation. The epidermis scales are more distinct in *Pashmina* fibre than in Mohair, but less than wool. In the very fine *Pashmina* fibres, one or two scales encircle the entire fibre shaft. The scale margins are relatively far apart, averaging 6 to 7 per 100 microns, and have smooth edges. Scales with crenate edges are very rarely found.

The cortical layer of the white and light coloured fibre shows distinct longitudinal striations which are covered up by the colour pigment in the dark fibres. The distribution of pigment is generally uniform in the light coloured Chinese and Mongolian fibres, whereas in many of the dark brown and black Iranian fibres asymmetrical distribution of the pigment is common, indicating the presence of the two distinct portions, the ortho-cortex and the meso-cortex<sup>[6]</sup>.

## 2. Understanding the genetics underlying the fibre related characteristics in animals

### 2.1 Keratin Genes

Keratin forms a major part of fibre and hair structures in mammals giving them intense strength. Keratin and keratin associated genes are responsible for various aspects of skin and fibre development in mammals. Different proteins and underlying proteins have been studied for the developmental pathways and characteristics of wool and hair in animals and humans. The Keratins proteins are divided into two groups- the keratin intermediate filament (KIF) proteins and the keratin-associated proteins (KAPs). The keratin and Keratin-associated proteins are among few of the largest multigenic families in mammalian genomes. These, in turn, encode a heterogeneous group of proteins that make up about 90% of the Cashmere fibre i.e. Keratin associated proteins<sup>7</sup>. Furthermore, the individual KAP genes are small in size less than 1 kb and consist of a single exon, most of the times. It is apparent with our current understanding of wool fibre structure that in vertebrate epidermal cells, regardless of their keratinization status, the intermediate filaments of their cytoskeletal base is composed of Keratin proteins. The hair keratins represent 2 major multigene families i.e., type I (acidic) and type II (basic). They copolymerize to form the 8-

10 nm intermediate filaments (KIF) of trichocytes that are eventually differentially expressed throughout the hair/fibre development<sup>[8]</sup>.

### 2.2 Keratin associated proteins (KAPs)

Keratin-associated proteins are reported to be coded by a large multiple-gene families. This seems to be the most probable reason for the immense variation in their content and structure. However, the keratin content, being coded by only multiple gene families is found to vary within a narrow range in the fibre of animals. The KAP genes are small, between 0.6 and 1.5 kb in size and are intron-less<sup>[9]</sup>. The KAPs have been divided into three major groups on the basis of their amino acid components:

- i. The high sulphur group (16-30 mol % cysteine) that are encoded by the KAP1.n, KAP2.n and KAP3.n multi-gene families<sup>[10, 11]</sup>. These proteins are 11-26 kDa and contain up to 30 % cysteine<sup>[12]</sup>.
- ii. The ultra-high sulphur group protein (>30 mol % cysteine) and are encoded by the KAP4.n and KAP5.n multi-gene families<sup>[10, 11]</sup>.
- iii. The high glycine-tyrosine group proteins are encoded by the KAP6.n, KAP7.n and KAP8.n multi-gene families<sup>[9, 11]</sup>. These are 6-9 kDa and contain up to 15 and 30 moles % of these amino acids, respectively<sup>[12]</sup>. These kinds of proteins are reported to vary significantly at individual and species levels. The ranges of 1% to 12% were reported for sheep wool; while it was around 18% in mouse hair and above 30% in echidna quills<sup>[13]</sup>.

### 2.3 Keratin intermediate filaments (KIFs)

In Mammalian epidermal cells, Keratin proteins were reported to be in the range of 50-67 kDa and they represent a category of intermediate filaments of 8-10 nm in diameter<sup>[14]</sup>. KIF's are ideally low-sulphur proteins, classified into type I keratins (acidic) and type II (non-acidic) keratins<sup>[9]</sup>. Wool keratin IF type I genes were reported to be 4-5 kilobase long with six introns in its sequence, whereas the type II gene sequence covered 7-9 kilobase length with eight introns. The two KIF macromolecule families (polypeptide) were reported to be large in size and includes 10-20 proteins<sup>[15]</sup>. KIF type I genes have also been reported in inner root sheaths of the hair follicle in humans<sup>[16]</sup>. However, the expression levels in different species are bound to vary and this may follow trends at individual, population and other levels as well. Individual KIF type I and II keratin genes have been isolated from bovine<sup>[17]</sup>, mouse<sup>[18]</sup> and human<sup>[19, 20]</sup>.

## 3. Chromosomal Location of KAP and KIF genes

### 3.1 Humans:

Two genes encoding KIF Type I and K16 besides three genes encoding K14 were clustered in two distinct regions of chromosome 17<sup>[21]</sup>.

### 3.2 Sheep

Sheep type I and type II genes are at 11q 25-q29 and 3q l4-q 22<sup>22</sup> with the type I gene about 4-5 kb in length and containing 6 introns and the Type II gene about 7-9 kb in length and containing 8 introns<sup>[10]</sup>. The KIF type II, KRT2.10 and KRT2.13 are located on chromosome 3<sup>[11]</sup>. The high glycine/tyrosine KAPs (KAP 6.1, 7, 8) are located on chromosome 1, the high-sulphur group KAP1.1, 1.2, 1.3 and 3.2 are located on chromosome 11 and the ultra-high sulphur group KAP5.1 is located on chromosome 21<sup>[11]</sup>. Three B2 high-sulphur keratin genes (new name KAP1.n family)

KAP1.1 (B2A), KAP1.3 (B2C) and KAP1.4 (B2D) were cloned in Charon 4A breed of sheep. The results from this study reported that the B2A and B2D genes were closely linked in the genome, only 1.9kb apart and are transcribed in the same direction [23].

### 3.3 Nomenclature of KAP genes

Previous studies have reported *KAPs* in their studies using the abbreviations *KAP1.n* through *KAP23.n* for these members known at that time with n referring to a number identifying individual members, also subdivided into 23 distinct families [24], more than 100 *KAP* genes have been isolated from human and other mammalian species. Genetic markers for the keratin and keratin-associated protein genes have been associated with variation in fibre diameter and staple strength [11]. Due to this, variation in the sequences also needs to be incorporated into the standard nomenclature of Keratin and keratin associated genes. A standard nomenclature was advocated as using the abbreviation of model sp-KAPm-nL\*x for *KAP* proteins and sp-*KRTAPm-n(p/L)\*x* for *KAP* genes [25]. In this system “sp” refers to the species-specific unique letter-based code as described by the protein knowledge-based UniProt. The gene or protein family is identified by the letter “m: whereas “n” is a constituent member of that family. A pseudogene in the family is identified as “p” and alphabet “L” refers to a naive gene/protein that is yet to be assigned any place in any family. The alphabet “x” signifies a genetic variant or allele.

### 4. Approaches to studying KAP genes

For any attempt for an efficient understanding of fibre based traits at the molecular level, different genetic parameters are needed to be studied. Several of these aspects are still naive and not yet studied properly. Studying various genetic aspects of Keratin and Keratin Associated proteins (*KAPs*) in host species formed the basic step. This approach surely has helped in our approach, moving ahead in understanding regarding *KAPs*. Studying the polymorphism and underlying association (if any) of Keratin, *KAP* and *KIF* genes has helped in the development of strong molecular markers for selection and other procedures.

Candidate gene approach is the major technique to study the effects of *KAP* genes on fibre related genes. *KAP6*, *KAP7* and *KAP8* genes were studied as candidate genes in Chinese sheep breeds and realized the potential of SNP based variations to be effectively associated with fibre related traits<sup>26</sup>. These can thus be used as candidate genes for wool quality based genetic studies. The polymorphisms of *KAP13.1* gene were investigated and corresponding associations with cashmere production traits (diameter, cashmere yield, down Cashmere thickness) were reported [27].

Another approach of identifying the underlying genes responsible for fibre related traits is the transcriptome analysis. Based on the relative and differential expression based studies, the underlying genes can be identified. In this way, the genes responsible for hair and fibre traits along with unique expression patterns can be elucidated. The keratin-associated genes were studied via transcriptome approach and concluded that hair growth is associated with upregulation and downregulation of these genes [28]. Similarly, a related study on transcriptome analysis was done, studying the seasonal patterns of the eruption of Keratin based functions in *Leptobranchium boringii* [29]. These approaches along with the supplementation of other techniques have helped in better understanding the genetics of wool and fibre growth and other

related traits in animal species. One more advanced approach that needs to be taped is the relative spatial and temporal based studies on various keratin and *KAP* genes in sheep and goat species. *HGT-1* and *HGT-2* were reported to be unique in Glycine/tyrosine-rich *KAP* genes and they were probably involved in spatial and temporal regulation of fibre development along with other characteristics [30].

A still highly advanced approach is that of transgenesis into smaller but evolutionarily related species. At many instances, the gene segments found to be associated with fibre characteristics can be introduced in other species like mice or in other species and the expression patterns can be studied in depth. In this regard, a study was conducted on a few aspects of keratin genes by using transgenic model, though the study was aimed at differentiating skin development based on keratin genes [31]. They studied differential expression patterns of Keratin 16 in Progenitor Basal Cells and its role in skin maturation. Similarly, tissue and differentiation-specific patterns of keratin 14 were reported [32]. In fibre associated traits, the role of *FST* (Follistatin) gene was studied [33, 34]. However, disrupting the normal functioning of fibre associated genes (Keratin or Follistatin) need to be studied extensively before applying any major biotechnological intervention into them.

## 5. Polymorphism of Keratin and Keratin associated genes/proteins and association-based studies

### 5.1 Studies on Variants of KAP genes

A study reported *KAP8.1* gene to be strongly associated with three cashmere fibre traits including cashmere weight, cashmere length and hair length [13]. Another study aimed another variant i.e., *KAP1.4* gene and reported that the length of this gene was shorter in Sheep than Goat [35]. This sequence was found to be 30 kb in sheep (i.e. 10 amino acids shorter in protein notation) when compared to Goat. This difference was attributed to deletion of this segment from the Ovine genome during species divergence in evolutionary timescale. Similarly, the polymorphism of *KAP1.1*, *KAP1.3* and *K33* (*KAP1.2*) genes was reported to be polymorphic in Merino sheep [36].

### 5.2 Species-wise allelic variations of KAP and KIF genes

#### 5.2.1 Sheep

From sheep genomic library of the high-sulphur keratin genes *KAP 1.n* family (previously called B2 high-sulphur genes), four genes *KAP 1.1* (B2A), *KAP 1.2* (B2B), *KAP 1.3* (B2C) and *KAP 1.4* (B2D) were isolated [23]. All allelic variations were confirmed by DNA sequencing. Three alleles at *KAP1.1* locus, five alleles at *KAP1.2* locus and nine alleles at the *KAP1.3* locus were reported [36]. Two alleles at *KIF* type I have been reported in Indian sheep breeds [37], whereas nine alleles at *KAP1.4* were reported [38].

#### 5.2.2 Goat

Information on these genes in the goat genome is sparse. Three alleles at *KAP8.2* gene locus have been reported in Chinese Inner Mongolian Cashmere goats [39]. Three alleles at *KIF* type I have been reported in Xinjiang goat breeds [40]. In general, very scanty information is available on these genes and their allelic variants in sheep and information are even scantier in goats. This may be attributed to limited inventory of these animals maintained under specific climatic conditions only, along with the prevailing harsh climatic conditions and other factors like relative inaccessible nature of breeding tracts.

## 6. Polymorphism and association of KAP and KIF genes with Cashmere Traits

Genetic variation, a raw material for the animal breeders, is used to mold our domestic animal species to satisfy the needs of society. The genetic variations both between and within the breeds are described as the diversity within a species. The generation of information for estimation of genetic distance, variation in gene products from enzymes, blood group systems and leukocyte antigens has now been almost entirely superseded by polymorphisms at the molecular level. A recent trend is to use molecular techniques for characterization which detect the genetic variation at DNA level. DNA polymorphisms may be detected through a variety of ways, mostly based on restriction fragment length polymorphisms (RFLPs), randomly amplified polymorphic DNAs (RAPD) and a variable number of tandem repeats (VNTRs) in the form of minisatellites and microsatellites. Very recently, microsatellites and SNP-based studies have received significant attention in polymorphism and association-based studies. Their emergence may, in turn, be attributed to many specialities in their use as markers of choice. All these markers have been used for studies related to fibre characteristics.

Various characteristics define the properties of fibres and thereby their significance. The most important ones include the yield, fineness, mean fibre diameter, mean fibre length, guard hair percentage. Studies on their association and the incorporation thereby into the breeding policies and decisions may help realize the best potential of these breeds producing various kinds of fibres.

A study utilized candidate genes approach for identifying the alleles affecting the wool fibre quality and quantity in a Medium Peppin Merino sheep flock at two KAP loci (KAP6 and KAP8) [41]. The results of analysis between polymorphism of these two loci and production traits gave significant evidence of association with fibre diameter. The polymorphism and association of five KAP genes (KAP6.1, KAP8.1, KAP8.2, KRTAP9-2 and KAP16.4 [KAP16.4-1 and KAP16.4-2]) in Chinese Merino (Xinjiang type) sheep [42]. Based on their study, they strongly recommended SNP variations as potential markers for wool characters. Similarly, the polymorphism of KAP 8.2 nucleotide sequence was studied in Mongolian Cashmere goats to work out any associations between ascertained genotypes and fibre traits [39]. The fibre traits investigated were Cashmere fibre diameter, fibre weight, Cashmere fibre length and guard hair length. They reported significant ( $p < 0.01$ ) association between the genotypes present and fibre traits including Cashmere fibre diameter, Cashmere weight and hair length. Cashmere length was the sole fibre characteristic that did not show any association with the ascertained genotypes. The genotype AA (0.73) was found to be predominant in Inner Mongolian Cashmere goats and therefore the animals with this genotype had the thinnest Cashmere fibre diameter compared to different genotypes. These results urged that polymorphisms in KAP 8.2 cistron could also be a possible marker for Cashmere fibre diameter in Cashmere goats. The polymorphism of KIF Type I gene was studied with the aim to associate the observed polymorphism with Cashmere traits in 253 animals of three Xinjiang goat breeds using PCR-RFLP [40]. Two of the alleles have an impact on Cashmere traits (fineness, thickness, and yield and body weight). This study provided ample evidence of an association between different allelic variations and fibre diameters.

The polymorphism of KRTAP 1-4 (B2D), a gene encoding a

member of KAP1-n family was studied in ovine species using PCR-SSCP [38]. A total of 14 SNPs were identified as clustered in two regions from this study. Of the 13 SNPs found in the coding region, nine were non-synonymous SNPs and would result in amino acid changes. The variations detected may have an impact on the structure of KAP1.4 and hence affecting the wool traits. The polymorphism in KAP 13.1 gene was reported and association studies were carried out with Cashmere traits in three Local Goat Breeds (Nanjing, Xinjiang, Bogeda) of China [27]. In another similar study, characterization and expression analysis of KAP 7.1 and KAP 8.2 genes were carried out in Liaoning new-breeding Cashmere goat [43]. qRT-PCR results showed that the expression of KAP7.1 and KAP8.2 genes within the secondary hair follicles was considerably higher than that of primary follicles. Furthermore, semi-quantitative RT-PCR results revealed that KAP 7.1 and KAP 8.2 template RNA were not present in other tissues including heart, liver, spleen, respiratory system and urinary system, demonstrating that KAP7.1 and KAP8.2 were exclusively expressed in hair follicles. Moreover, the results indicated that during the formation of Cashmere and wool fibres, the differential expression of above two genes within primary and secondary hair follicles could possibly have a crucial role in the regulation of fibre diameter. A missense mutation of KAP16.6 sequence was detected in three goat breeds in China and studied the polymorphism and its associations with Cashmere fibre traits [40]. In Xinjiang goat population, the statistical evaluation revealed significant differences ( $p < 0.05$ ) between the fibre diameter and Cashmere yield trait of GG genotype. In Nanjiang Cashmere goat population, no significant differences ( $p > 0.05$ ) between Cashmere production traits were observed.

The polymorphic analysis of KAP 8.1 gene was carried out in two breeds of Chinese Cashmere goats [44]. The polymorphism was detected by PCR-SSCP and results showed that there were two mutations 63T > G and 66C > G in KAP 8.1 gene. The study also indicated that the polymorphism might be relevant to fibre diameter. According to one other study, three alleles were present in the KAP8.2 sequence of Chinese Inner Mongolian Cashmere goats [39]. They studied polymorphism of KAP 8.2 gene to determine associations between discovered genotypes and fibre traits in 542 animals of Chinese Inner Mongolian Cashmere goats using polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP) techniques. There was significant ( $p < 0.01$ ) association between the different genotypes with Cashmere fibre diameter, Cashmere weight and guard hair length. Cashmere length was the only trait that was not associated with the observed genotypes. The genotype AA (0.73) was found to be predominant in Inner Mongolian Cashmere goats and the animals with this genotype had the thinnest Cashmere fibre diameter compared with other genotypes. These results suggested that polymorphisms in KAP 8.2 gene may be a potential marker for Cashmere fibre diameter in Cashmere goats.

The polymorphisms in the keratin-associated protein 1.1 (KAP1.1) gene was explored by PCR-SSCP and DNA sequencing methods in Liaoning Cashmere goat and Inner Mongolia white Cashmere goat [45]. One SNP was detected at the KAP1.1 gene and resulted in three different genotypes. A novel SNP (g.688T>C) was found in the sequence of TT genotype and caused synonymous mutation for the amino acid sequence. Statistical analysis demonstrated for Cashmere yield, body weight and Cashmere fineness of Liaoning

Cashmere and Inner Mongolia White Cashmere goat, TT genotype was significantly higher than CC and CT genotype for Cashmere yield and body weight). However, there was no difference between three genotypes for Cashmere fineness, these results showed that TT genotype could be a favourable marker for early breeding selection of the Liaoning and Inner Mongolia White Cashmere goat.

An association study was carried out between the polymorphism of KAP 9.2 gene and Cashmere traits, together with the variation and expression of KAP9.2 gene affecting Cashmere trait in goats [46]. DNA sequencing revealed a novel C/T polymorphism of KAP9.2 gene from a genomic DNA pool. Quantitative real-time PCR analysis revealed that the expression level of KAP9.2 was reduced in the individuals bearing genotype CC compared with TT individuals, suggesting that C was the nucleotide causing decreased expression of KAP9.2 or was in linkage disequilibrium with the causative SNP. They proposed that the 586C/T SNP found in this study might control translation or stability of KAP9.2 mRNA, which would be beneficial for marker-assisted selection in Cashmere goat breeding.

Another study investigated the genetic basis underlying the development of Cashmere fibres by sequencing the transcriptomes of primary and secondary hair follicles [47]. Based on an annotated set of goat genes, they generated and compared transcriptomic data from secondary hair follicles (which produce the Cashmere fibre) with data from primary hair follicles of the Inner Mongolia Cashmere goat, shedding light on the genetic basis of the formation of Cashmere fibres. Notably, two out of the 29 keratin genes and ten out of the thirty KAP genes were differentially expressed on a consistent basis between primary and secondary hair follicles in all 3 sample sets. Furthermore, each of above genes was expressed in higher proportions in secondary than in primary follicles. They concluded that the KAP genes may additionally be vital in deciding the physical and mechanical structures of Cashmere fibres. On the similar lines, the differential gene expression patterns were reported in primary and secondary hair follicles of Inner Mongolian Merino sheep [48].

KAP 1.4 cistron was explored for its characterization in Changthangi (pashmina producing), Bakerwal and native Kargil (non-pashmina) goats [35]. In comparison to published sequences of sheep, goat sequences explored were differing at positions 174, 462 and 568 & at these positions. G, T & T, present in sheep were replaced by A, C & C, respectively. They reported the effects of the genotypes on pashmina and guard fibre diameter and length in these goats to be non-significant ( $P > 0.05$ ). The non-significance association reported herein could have been due to small sample size.

## 7. Recommendations

Based on the available literature and the research experience of the authors, it may be advocated that different Keratin and Keratin associated genes have a definite impact (positive or negative) on fibre characteristics including fibre fineness, length, yield and others, but ample scope remains to tap so the real production potential at the molecular levels. Aggressive research approach needs to be taken up at the earliest on various aspects of these gene families (i.e., KAP's and KIF's genes). Only some of the KAP's viz. KAP 1.1, 1.3, 1.4, KAP 2, KAP 4, KAP 6, KAP 7.1, KAP 8, KAP 8.1 and KAP 8.2 has been molecularly characterized and their polymorphism associated with fibre attributes in sheep. Only four KAP's 7.1, 8.1, 8.2 and 13.1 had been explored in goats

and polymorphisms of these genes have been associated with fibre diameter, combed fibre weight, fibre length and guard hair length traits. KIF Type I gene has been molecularly characterized and their polymorphism stands associated with fibre traits both in sheep and goats. However, from KIF Type I group of genes, only KIF 2.10 and K33 have been studied only in sheep. In short, sparse research has been carried out in goats with regard to KAP and KIF families of genes and their polymorphism. Keeping in view the importance of KIF and KAP families of genes in controlling the variability existing between different animals with regard to various fibre traits, characterization of these genes in goats in general and Pashmina goats in particular and exploration of polymorphism in these genes, if any is warranted. The association of the polymorphism, if present, with quality traits, is essentially required to develop any molecular marker for fibre traits.

The structural characterization of extra genes and also the assessment of their levels of polymorphism in numerous goat populations are going to be necessary to elucidate the genetic factors fully that modulate the fibre production. This may, in addition, facilitate unveil the intricate network of interactions that are established by these genes for their expression. By careful selection experiments, there is scope for increasing the frequencies of the desired allele in relevant livestock populations.

In Pashmina goats of Ladakh, selection by conventional technique has improved the traits of interest to some extent. However, due to limitations posed by harsh climatic conditions and difficulty in accurate data recording, the improvement has been static for few decades. The Polymorphic marker-based selection also known as Marker Assisted Selection (MAS) offers an excellent opportunity as it not only reduces the time interval to obtain maximum genetic gain but also increases the accuracy of selection. Further, selection based on markers can play important role in genetic improvements of animals before expressing the actual target traits, sometimes before birth or at the time of birth. Ultimately MAS increases the genetic gain if it is coupled with the conventional breeding programme. Certain polymorphisms have been identified in goats by various workers and some are under study to see their influence in the production status.

Since the production performance of Cashmere goats remains confined mainly to the cold regions of the world, whether Ladakh (J&K), Tibet or Mongolia, the field of epigenetics, nutrigenomics and nutrigenetics hold a great promise. To this date, no major research of such kind is reported, however, it seems to possess the potential to greatly enhance our understanding of production aspects of these fibres.

## 8. Conclusion

Fibre coat and characteristics of animals are very important for normal physiology and sometimes survival of animals. Fibre traits play an important role in the welfare of human beings and their protection during adverse climatic conditions. These traits assume peculiarity with immense demand in national and international markets for fine fibres like Cashmere and Merino and our understanding is important regarding the selection and breeding of animals for these traits. Studying and understanding various aspects of fibre growth and development will help in the efficient manipulation of these pathways for proper realization and better utilization of production potentials of these animals.

## 9. Acknowledgement

This study was supported by the FVSc & AH, SKUAST-K, and we thank them for providing the necessary funding and support. The authors would also wish to acknowledge the help and support rendered by Dean, FVSc & AH; Head, Division of Animal Genetics and Breeding, FVSc & AH, SKUAST-K, Kashmir for providing access to necessary facilities to carry out this work.

## 10. References

- Sahni KL. Project coordinators report of 1980. Central Institute of Research on goat Makhdoom. 1981, 17.
- Wani SA, Ishrat Y, Salahuddin M, Malik AH. Processing and Product development from cashmere fibre. In National seminar on Angora rabbit wool and cashmere production and utilization. 2004, 25-26.
- Darokhan MD, Tomar NS. Studies on pashmina yield of Changthang goats [India]. Indian Veterinary Journal. 1983.
- Deb SM. Performance of pashmina (cashmere) goats on Kumaon Himalayas. Indian journal of animal sciences. 1998; 68(9):954-6.
- Ganai TA, Kirmani MA, Ganai NA, Tundup T. Pashmina goat in Changthangi goats beyond period of the longest and shortest day. In Proceedings of the conference of Indian Society of Animal Genetics and Breeding and Nutritional Symposium on conservation of livestock and Poultry. 2004.
- Von-Bergen W. Wool Hand Book. (In 3rd Edn). Inter Science Publisher, London. John Wiley and Sons. 1963, 343.
- Rogers MA, Langbein L, Winter H, Ehmann C, Praetzel S, Schweizer J. Characterization of a first domain of human high glycine-tyrosine and high sulfur keratin-associated protein (KAP) genes on chromosome 21q22. 1. Journal of Biological Chemistry. 2002; 277(50):48993-49002.
- Langbein L, Rogers MA, Winter H, Praetzel S, Schweizer J. The catalog of human hair keratins II. Expression of the six type II members in the hair follicle and the combined catalog of human type I and II keratins. Journal of Biological Chemistry. 2001; 276(37):35123-32.
- Powell BC. Differentiation in hard keratin tissues: hair and related structures. Keratinocyte Handbook. 1994, 401-36.
- Powell BC, Rogers GE. The role of keratin proteins and their genes in the growth, structure and properties of hair. Exs. 1997; 78:59-148.
- McLaren RJ, Rogers GR, Davies KP, Maddox JF, Montgomery GW. Linkage mapping of wool keratin and keratin-associated protein genes in sheep. Mammalian genome. 1997; 8(12):938-40.
- Crewther WG. Primary structure and chemical properties of wool. Proceedings of the Fifth International Wool and Textile Research Conference, Aachen, 1976; 1(1):101.
- Liu H, Yue CW, Zhang W, Zhu X, Yang G, Jia Z. Association of the KAP 8.1 gene polymorphisms with fibre traits in inner mongolian cashmere goats. Asian-Australasian Journal of Animal Sciences. 2011; 24(10):1341-7.
- Yoon KH, Yoon M, Moir RD, Khuon S, Flitney FW, Goldman RD. Insights into the dynamic properties of keratin intermediate filaments in living epithelial cells. The Journal of cell biology. 2001; 153(3):503-16.
- Lazarides E. Intermediate filaments: A chemically heterogeneous, developmentally regulated class of proteins. Annual review of biochemistry. 1982; 51(1):219-50.
- Bawden CS, McLaughlan C, Rogers G, Nesci A. A unique type I keratin intermediate filament gene family is abundantly expressed in the inner root sheaths of sheep and human hair follicles. Journal of investigative dermatology. 2001; 116(1):157-66.
- Lehnert ME, Jorcano JL, Zentgraf H, Blessing M, Franz JK, Franke WW. Characterization of bovine keratin genes: similarities of exon patterns in genes coding for different keratins. The EMBO journal. 1984; 3(13):3279.
- Krieg TM, Schafer MP, Cheng CK, Filpula D, Flaherty P, Steinert PM *et al.* Organization of a type I keratin gene. Evidence for evolution of intermediate filaments from a common ancestral gene. Journal of Biological Chemistry. 1985; 260(10):5867-70.
- Johnson LD, Idler WW, Zhou XM, Roop DR, Steinert PM. Structure of a gene for the human epidermal 67-kDa keratin. Proceedings of the National Academy of Sciences. 1985; 82(7):1896-900.
- Tyner AL, Eichman MJ, Fuchs E. The sequence of a type II keratin gene expressed in human skin: conservation of structure among all intermediate filament genes. Proceedings of the National Academy of Sciences. 1985; 82(14):4683-7.
- Rosenberg MA, Ray Chaudhury AM, Shows TB, Le Beau MM, Fuchs E. A group of type I keratin genes on human chromosome 17: characterization and expression. Molecular and cellular biology. 1988; 8(2):722-36.
- Dolling CH, Brooker MG. A viable hypotrichosis in Poll Dorset sheep. Journal of Heredity. 1966; 57(3):87-90.
- Powell BC, Sleigh MJ, Ward KA, Rogers GE. Mammalian keratin gene families: organisation of genes coding for the B2 high-sulphur proteins of sheep wool. Nucleic acids research. 1983; 11(16):5327-46.
- Rogers GE, Powell BC. Organization and expression of hair follicle genes. Journal of investigative dermatology. 1993, 101.
- Gong H, Zhou H, McKenzie GW, Yu Z, Clerens S, Dyer JM *et al.* An updated nomenclature for keratin-associated proteins (KAPs). International journal of biological sciences. 2012; 8(2):258.
- Liu YX, Shi GQ, Wang HX, Wan PC, Tang H, Yang H *et al.* Polymorphisms of KAP6, KAP7 and KAP8 genes in four Chinese sheep breeds. Genet. Mol. Res. 2014; 13:3438-45.
- Fang Y, Liu WJ, Zhang FQ, Shao YG, Yu SG. The polymorphism of a novel mutation of KAP13. 1 gene and its associations with cashmere traits on Xinjiang local goat breed in China. Asian Journal of Animal and Veterinary Advances. 2010; 5(1):34-42.
- Wakame K, Komatsu KI, Nakata A, Sato K, Takaguri A, Masutomi H *et al.* Transcriptome Analysis of Skin from SMP30/GNL Knockout Mice Reveals the Effect of Ascorbic Acid Deficiency on Skin and Hair *in vivo*. 2017; 31(4):599-607.
- Zhang W, Guo Y, Li J, Huang L, Kazitsa EG, Wu H. Transcriptome analysis reveals the genetic basis underlying the seasonal development of keratinized nuptial spines in *Leptobranchium boringii*. BMC genomics. 2016; 17(1):978.
- Fratini A, Powell BC, Rogers GE. Sequence, expression, and evolutionary conservation of a gene encoding a

- glycine/tyrosine-rich keratin-associated protein of hair. *Journal of Biological Chemistry*. 1993; 268(6):4511-8.
31. Paladini RD, Coulombe PA. Directed expression of keratin 16 to the progenitor basal cells of transgenic mouse skin delays skin maturation. *The Journal of cell biology*. 1998; 142(4):1035-51.
  32. Vassar R, Rosenberg M, Ross S, Tyner A, Fuchs E. Tissue-specific and differentiation-specific expression of a human K14 keratin gene in transgenic mice. *Proceedings of the National Academy of Sciences*. 1989; 86(5):1563-7.
  33. Guo Q, Kumar TR, Woodruff T, Hadsell LA, DeMayo FJ, Matzuk MM. Overexpression of mouse follistatin causes reproductive defects in transgenic mice. *Molecular Endocrinology*. 1998; 12(1):96-106.
  34. Wankell M, Munz B, Hübner G, Hans W, Wolf E, Goppelt A *et al*. Impaired wound healing in transgenic mice overexpressing the activin antagonist follistatin in the epidermis. *The EMBO journal*. 2001; 20(19):5361-72.
  35. Shah RM, Ganai TA, Sheikh FD, Shanaz S, Shabir M, Khan HM. Characterization and polymorphism of keratin associated protein 1.4 gene in goats. *Gene*. 2013; 518(2):431-42.
  36. Itenge-Mweza TO, Forrest RH, McKenzie GW, Hogan A, Abbott J, Amofo O *et al*. Polymorphism of the KAP1. 1, KAP1. 3 and K33 genes in Merino sheep. *Molecular and cellular probes*. 2007; 21(5):338-42.
  37. Arora R, Bhatia S, Sehrawat A, Pandey AK, Sharma R, Mishra BP *et al*. Genetic polymorphism of type 1 intermediate filament wool keratin gene in native Indian sheep breeds. *Biochemical genetics*. 2008; 46(9-10):549-56.
  38. Gong H, Zhou H, Hickford JG. Polymorphism of the ovine keratin-associated protein 1-4 gene (KRTAP1-4). *Molecular biology reports*. 2010; 37(7):3377-80.
  39. Liu H, Li N, Jia C, Zhu X, Jia Z. Effect of the polymorphisms of keratin associated protein 8.2 gene on fibre traits in Inner Mongolia cashmere goats. *Asian Australasian Journal of Animal Sciences*. 2007; 20(6):821.
  40. Liu WJ, Fang Y, Li LJ. Polymorphism of KIFI gene associated with cashmere traits in Xinjiang goat breeds. *Journal of Animal and Veterinary Advances*. 2009; 8(12):2730-4.
  41. Parsons YM, Cooper DW, Piper LR. Evidence of linkage between high-glycine-tyrosine keratin gene loci and wool fibre diameter in a Merino half-sib family. *Animal genetics*. 1994; 25(2):105-8.
  42. Sulayman A, Mamat A, Taurusun M, Huang XX, Tian K, Tian Y *et al*. Identification of Polymorphisms and Association of Five KAP Genes with Sheep Wool Traits. *Asian-Australasian journal of animal sciences*. 2017.
  43. Jin M, Wang L, Li S, Xing MX, Zhang X. Characterization and expression analysis of KAP7. 1, KAP8. 2 gene in Liaoning new-breeding Cashmere goat hair follicle. *Molecular biology reports*. 2011; 38(5):3023-8.
  44. Zhao M, Chen H, Wang X, Yu H, Wang M, Wang J *et al*. aPCR-SSCP and DNA sequencing detecting two silent SNPs at KAP8. 1 gene in the Cashmere goat. *Molecular biology reports*. 2009; 36(6):1387-91.
  45. Zhang Y, He Y, Xue P, Chen Y. Sequence variant in the KAP 1.1 gene associate with cashmere trait in two Cashmere goat breeds. *African Journal of Agricultural Research*. 2011; 6(12):2889-94.
  46. Wang X, Zhao ZD, Xu HR, Qu L, Zhao HB, Li T *et al*. Variation and expression of KAP9. 2 gene affecting cashmere trait in goats. *Molecular biology reports*. 2012; 39(12):10525-9.
  47. Dong Y, Xie M, Jiang Y, Xiao N, Du X, Zhang W *et al*. Sequencing and automated whole-genome optical mapping of the genome of a domestic goat (*Capra hircus*). *Nature biotechnology*. 2013; 31(2):135-41.
  48. Zhu B, Xu T, Yuan J, Guo X, Liu D. Transcriptome sequencing reveals differences between primary and secondary hair follicle-derived dermal papilla cells of the Cashmere goat (*Capra hircus*). *PloS one*. 2013; 8(9):e76282.