Chapter 3
Genetic Control/Involvement in Hair Fiber Traits

Abstract The focus in this chapter is on hair form or fiber diameter and curvature and on hair color or pigmentation. These important hair characteristics are controlled by single nucleotide polymorphisms which are single nucleotide changes in genes. The three primary hair forms today (African, Asian and Caucasian) and their hair pigmentations arose from genetic mutations that are consistent with geographic migrations of Asians and Caucasians. Therefore, these hair forms and pigmentations are probably remnants of prior adaptations to temperature, sun exposure and other environmental influences. Other hair traits related to genetics including different alopecia and several genetically involved hair abnormalities are described along with a brief summary of current directions in forensic science which has expanded into DNA analysis and is moving into the analysis of SNPs.

3.1 Introduction

Traits or characteristics of human hair fibers under genetic control include different hair forms or shapes such as curvature, ellipticity and coarseness, hair colors or pigmentation, and types of baldness, and hair diseases including certain genetically related hair abnormalities. In addition, Heywood et al. [1] suggested evidence for genetic involvement in hair quality. These areas are the subject of the following sections of this chapter. However, the focus of this chapter is on hair form and hair color or pigmentation with regard to single nucleotide polymorphisms (SNPs) which are single nucleotide changes in a gene. Several genetically involved hair abnormalities are also included in this chapter as well as a brief summary of the current direction in forensic science which over the last two decades has expanded dramatically into DNA analysis and is currently moving into the analysis of SNPs. Chapter 2, in the section entitled *Major Protein Fractions of Hair and Gene Expression*, contains a summary of the chromosomes and genes for the important Intermediate Filament proteins (keratin proteins) and KAP (keratin associated proteins) proteins of human hair.

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The term race applies to sub-populations or groups of people similar in several biological characteristics. In the past, races developed and persisted because travel over large distances was limited, thus, similar peoples interacted and procreated. The geographic or racial differences that are found today in hair and skin type are most likely remnants of prior adaptations to temperature, sun exposure and other environmental influences.

The words ethnic and ethnicity have been misused in the cosmetic industry. Ethnicity relates more to similarities in or shared social customs. Race relates more to similarities in physical characteristics. In the following pages I refer to geo-racial or geo-ethnic groups linking geographic origin to race or ethnicity. I will try to refrain from using the phrase ethnic hair, but I will sometimes inadvertently use the term geo-ethnic group. The cosmetic industry frequently refers to these three primary geo-racial hair types: African type hair originates primarily from south, west, or central Africa and the donors with a few exceptions tend to have heavily pigmented skin. Asian type hair originates from mid-eastern and south East Asia and the donors tend to have light to medium skin pigmentation. Caucasian hair originates from northern Europe or North Africa and the donors tend to have lightly pigmented skin, but some may have heavily pigmented skin. So, the influence of geography is recognized and persists in this important classification because the names of two of these three groups still retain their geographic origin.

These geo-racial groups will be referred to frequently in the sections involving hair fiber shape focusing on fiber diameter, ellipticity and hair fiber curvature in Chap. 9. Fiber curvature and cross-sectional shape as well as pigmentation variations of human scalp hair are largely controlled genetically. These fiber shape characteristics control much of the cosmetic and physical behavior of human hair. Therefore, geo-racial information on hair characteristics can and has been useful to the cosmetic scientist, although a century from now it will likely be less useful than the hair characteristics themselves.

Other classifications such as by curvature type will ultimately become more important to cosmetic science than the three geo-racial groups because curvature is so important to all cosmetic hair assembly properties as discussed in Chap. 10. Consider the fact that the cosmetic behavior of scalp hair of a Caucasian of Curly type IV hair by the Segmentation Tree Analysis Method (STAM) [2] (see the section entitled, *Measuring Hair Fiber Curvature* in Chap. 9) has more in common with Curl types IV of the African and Asian groups than with a curl Type I or II of their own geo-racial group. The commonality is in the way their hair behaves with regard to the more important cosmetic hair assembly properties described later in Chap. 10.

During the latter days of this century and the next, populations of Curl types III, IV and V will likely increase and Curl types I and VIII will decrease. So, in the future we must learn to type hair even better by its physical characteristics and become more quantitative with regard to its relationships to its important cosmetic hair assembly properties. Table 3.1 summarizes the general qualitative characteristics of the scalp hair of the three major geo-racial groups.

Table 3.1 Hair fiber characteristics by geo-racial group

Fiber characteristics [3, 4]				
Geo-race	Coarseness	Curvature	Cross-Sectional Shapte	Color
Caucasian	Fine	Straight to curly	Nearly round to slightly oval	Blond to dark brown
African	Coarse	Wavy to wooly	Slightly oval to elliptical	Brown-black to black
Asian	Coarse	Straight to wavy	Nearly round to slightly oval	Dark brown to brown-black

See Fig. 9.18

3.2 The Genetics of Hair Form: Hair Diameter and Curvature

3.2.1 Evolution to Hairless Bodies, Dark Skin and Highly Coiled Scalp Hair

The current ice age began about 2.6 million years ago producing a large scale climate change across the earth. Along with colder temperatures was a decline in rainfall. The densely wooded areas that our early ancestors occupied became tropical or sub-tropical grasslands with scattered trees and drought-resistant undergrowth. Consequently, the fruits, tubers and seeds and fresh water that these vegetarian hominids thrived on became scarce.

So, these vegetarians had to change their lifestyle, relocate and mutate to survive. They became hunters and fishermen traveling longer distances in search of food and water [5]. The elevated activity required for hunting and traveling for food and water increased the risk of overheating. So, this hominid adapted by losing its chimpanzee-like body fur. It developed many more sweat glands that were more efficient (for cooling) over most of its body compared with its chimpanzee-like ancestors. Montagna [6] explained that the sweat glands of fur bearing chimpanzees and gorillas do not respond to heat stimulation as in humans. Equally important, our ancestors' hairless skin became highly pigmented to protect against over-exposure from the sun in the tropics. They developed hair on the head that was highly coiled with a longer life cycle and therefore of greater length than the head fur of their predecessors.

Rogers et al. [7] concluded from studies of the human MC1R gene, involved in skin and hair pigmentation, that primitive humans lost most of their body hair by before 1.2 million years ago. Rogers et al. concluded that loss of fur had to occur before dark skin pigmentation because the specific variant of the MC1R gene that is always in dark skinned Africans originated about 1.2 million years ago.

Jablonski and Chaplin [8, 9] explained that skin color tends to correlate with latitude or the region of the earth that determines the intensity of UV radiation. These two scientists explained this effect by the fact that dark skin protects against the breakdown of folate which is essential for fertility and fetal development. Dark skin also protects against other but lesser effects with regard to reproductive success

such as protection of sweat glands, from UV damage [8], and protection against skin cancers. Jablonski and Chaplin explained further that humans in different geographical regions have evolved to be dark enough to protect folate, in the blood stream, from decomposition by UV-A radiation yet light enough to allow sufficient UV in the skin to catalyze the production of vitamin D, an essential vitamin for maternal and fetal bones. Furthermore, skin color through tanning is highly adaptive and can change at a faster rate than hair form or hair color.

3.2.2 Helpful Websites for SNP Nomenclature and Its Relationship to Hair Form and Pigments

Single nucleotide polymorphisms (SNP's) are mutations or changes that occur in a gene at a specific location. The nomenclature for SNP's in the scientific literature is variable and complex. Therefore, I recommend the following website as helpful for reading different papers dealing with SNPs because of the many different ways that gene mutations are described: www.hgvs.org/mutnomen/recs.html.

For example, sometimes a coding for the DNA sequence is used which is usually but not always described with a "c." beginning, for example (c.76 A > T) means that nucleotide 76 which was Adenine has been replaced by Thymine. Sometimes the coding is for the corresponding RNA sequence change which would be (r.76 a > u) which means that at nucleotide 76 Adenine has been replaced by Uracil. However, more frequently the coding for the protein sequence change will be designated. In that case, the coding would be (p.Lys76Asn) or p.K76N or K76N or 76N which means that at position 76 the amino acid Lysine has been replaced by Asparagine.

Another helpful website is: www.ncbi.nlm.nih.gov/sites/entrez?db=snp.

Much information can be obtained from this website including information for the DNA change, the RNA change and the protein change and much more from the rs number.

The important thing to remember in all of this discussion is that we are looking for changes in specific genes at specific locations that create changes in the proteins that are derived from these genes. Further, these proteins play a significant role in accelerating or retarding enzymatic or non-enzymatic reactions such as pH control, or the transport of key ingredients involved in the biosynthetic scheme for the formation of hair pigments, hair form or any other trait. In the case of hair pigments, oftentimes the number and size of the melanosomes will be determined and these will ultimately become hair pigment granules.

To date, more than 100 SNP's in 24 genes have been shown to be involved in hair, skin or eye color of humans and many more in mice. Now this is just hair color. Hair and skin color are closely related in a number of ways, however, there are differences too. For example, both hair and skin pigments are formed in melanocytes in structures called melanosomes. Hair and skin pigments both involve

many of the same genes. Schwan-Jonczyk [10] has shown that melanin granules in hair from people of African descent are larger than those from East Asians which are larger than those from light haired blonde or red haired Europeans. In skin, melanin is produced in melanocytes similar to those in hair. The melanocytes in African skin appear similar to those in Europeans but they are much more reactive and the melanin granules that are formed are larger and more numerous in Africans [11] analogous to those in hair.

Among the several associations between hair color and skin color are the following: Red heads are almost always fair skinned. However, the reverse is not generally true; very light hair people normally have very light skin, however the reverse is not generally true; and dark skin people normally have dark hair, however the reverse is not commonly true.

One of the most important differences between hair and skin pigmentation has been pointed out by Slominski and Tobin [12]. For example, Slominski and Tobin [12] described that melanogenesis in hair coordinates with the hair cycle and is affected strongly by age which ultimately involves the graying of hair. On the other hand, skin melanogenesis is continuous not cyclic and is not as strongly affected by age. In hair follicles, melanogenic activity is directly related to the anagen stage of the hair cycle [12]. In the telogen follicle, melanocytes are mitotically quiescent. The complex and large number of biological controls of melanogenesis are summarized in this paper by Slominski and Tobin [12]. These same scientists suggested that a small number of melanocytes in a single anagen cycle produce enough melanin pigments for a hair shaft of one or more meter or longer. Furthermore, single scalp hair follicles continue to produce hair pigments for about 7–15 cycles before the onset of graying. Graying is due to a reduction of the activity of melanocytes in the hair bulb. See this paper by Slominski and Tobin [12] for additional details on the mechanism of melanogenic activity and graying.

3.2.3 Evolution of Coiled Scalp Hair to Straighter Hair Forms

The hair of the people indigenous to Africa today is highly coiled to kinky and highly elliptical. This hair type was developed several hundred thousand years before these hominids migrated out of Africa. This highly coiled hair continued to be the dominant hair form up to the early migrations out of Africa about 50,000 years ago [13, 14]. A primary reason for highly coiled and longer hair on the scalp in hot tropical high ultraviolet (UV) Africa was to provide a protective insulating layer to the head to help prevent overheating of the brain [8]. Thermal protection of the head was important because prior to these migrations, the brain size of this hominid increased by a factor of more than two. Furthermore, the head (in addition to the shoulders) is the most directly exposed part of the body to thermal and UV radiation for a bipedal upright animal and thermal protection of the brain is much more important than for the shoulders.

Highly coiled hair was preferred over straight hair in the tropics because coiled hair allows more rapid loss of water from the scalp than straight hair. This effect is because straight hair fibers mat together with water which inhibits evaporation, and thus inhibits cooling. Highly coiled and longer hair also provides a more effective thermal insulating layer to the ever increasing brain size. This hominid continued to develop in its behavior, but changed little in skin and hair development for the next few hundred thousand years.

Straight, thicker more round hair evolved in the Far East but wavy to straight, less elliptical hair evolved in Europe (less elliptical than African hair). We will speculate on the advantages of straighter hair in cold climates as possible reasons for its evolution; however it is possible that straight hair was linked to another property like teeth or sweat glands or skin pigmentation and straighter hair just went along for the ride in a process called phenotypic hitchhiking [15].

One possible advantage of straight to wavy hair in cold climates is that straight hair grows longer in length than highly coiled African hair primarily because of the fragility of the latter type of hair. Straight hair hangs down over the neck and the sides of the head and ears to cover those body parts more effectively. Therefore, longer straight hair that grows fast provides better thermal protection to the neck and the ears than highly coiled hair. Insulation of the neck (analogous to a scarf) facilitates thermal regulation of the upper spinal cord, while the ears are one of the most vulnerable parts of the body to frostbite. Tobin and Paus [16] described the following advantage to long straight hair and attributed this rationale to Hardy. The early migrations of our species to the Far East and Europe occurred along the seacoast, more so to the Far East. Therefore, these migrants survived on a diet high in seafood which contains toxic metals which bind to melanins in hair. Therefore toxic heavy metals can be detoxified quickly by selectively binding to melanin in hair which could provide a selective advantage for longer rapidly growing, melanin rich, and straight scalp hair as in Far Easterners.

Highly coiled hair is also more effective in scattering radiation and minimizing its contact with the skin an advantage only in the tropics. Iyengar [17] proposed and showed that hair fibers to some extent can function as fiber optic strands transmitting light to the melanocytes. Furthermore, coiling in optical strands interferes with light transmission. But, whether or not straight hair fibers can function sufficiently to transmit a meaningful amount of UV to the skin to facilitate vitamin D production in clothed humans in northern latitudes remains to be seen. There is no agreement today of whether hair form has occurred by natural selection or if it is coupled to another trait controlled by selection. But, its geographic specificity does lead one to believe that natural selection was somehow involved.

3.2.4 The Genes and SNPs Involved in Hair Form

The people of Japan, China and Amerindians have been shown to have a mutation involving a simple substitution in the EDAR gene (sometimes referred to as

1540T/C or 1540C or 370A) which has been associated with hair thickness of East Asian and Amerindian populations [15, 18, 19]. In addition, Fujimoto et al. [20] determined that the FGFR2 gene is also associated with hair thickness in East Asian populations. Equally important, Mou et al. [18] demonstrated that elevation of EDAR activity via this EDAR mutation in transgenic mice decreases the number of kinks in the hair fibers as well as increasing fiber diameter. Therefore this variant gene is involved in producing straighter-more coarse hair in East Asian populations.

This EDAR gene substitution does not occur in Africans and it is at very low frequency in most of the people of Central/South Asia, Europe and the Middle East as shown by Bryk et al. [15] and Fujimoto et al. [19]. As of this writing, I have not been able to identify whether or not this substitution occurs to a significant degree in the people of India. However, I suspect it only occurs in a small percentage via the Tibetan-Burma population in the north-eastern part of India. This conclusion is based on the fact that the curvature of the main population of India tends to be more Caucasian-like than East Asian and hair diameter studies on small numbers of people from India suggests that Asiatic Indians do not have hair as coarse as East Asians.

The straight hair of Europeans and East Asians appears to have occurred independently, analogous to the independent evolution of light skin in Europeans and East Asians after these two groups of humans separated in their respective migrations. Migrations to Europe are believed to have occurred about 40,000 years ago, a few thousand years after migrations to the Far East. As indicated, the thick-straight hair of East Asians is linked to the Asian specific allele variants of the EDAR and FGFR2 genes [19, 20]. These gene variants are either not in or at very low frequencies in the hair of Europeans [15]. However, Medland et al. [21] demonstrated an association of the trichohyalin gene with straight hair in Europeans. Furthermore, these trichohyalin gene variants are highest in frequency in Northern Europeans and are specific to populations of Europe and western-central Asia. Medland et al. suggested that in this regard, these trichohyalin gene variants "parallel the distribution of the straight-hair EDAR variant in Asian populations".

The geographic specificity of the EDAR gene for hair form in combination with the trichohyalin gene variants in Europe and the Middle East support the East Asian and West Eurasian Sweeps hypothesis suggested by Coop et al. [22]. The EDAR gene is at high frequencies in Chinese, Koreans, and Japanese and Amerindian populations consistent with the geographic migrations of these populations and contributed to the hair form of the hair type we call Asian. In addition, the trichohyalin variants in Europeans and Middle Easterners are consistent with the migrations of these populations as suggested by Coop et al. and contributed to the hair form of the hair type that we call Caucasian. Also see the next section in this Chapter entitled, *Hair Pigmentation and Genetics*.

Another useful study involving hair form was conducted by Eriksson et al. [23] where 10,000 European subjects were surveyed with a questionnaire for 22

common traits including hair curl, hair color and red hair (red to not red on a scale of 4). Hair curl was evaluated with 6° of curl based on a verbal description with accompanying photographs. After the questionnaire saliva samples were taken from each subject and tested for 580,000 SNP's. These data were then tested for associations. This study revealed four genes with significant association with hair curl in Northern Europeans. Among these four genes was the rs17646946 SNP near the Trichohyalin gene (TCHH), the minor allele being associated with straighter hair and first implicated with hair curl in Europeans by Medland et al. [21]. The rs7349332 SNP near WNT10A, the minor allele (T) was associated with slightly curlier hair and rs1556547 near OFCC1 was also associated with straight hair.

Shimomura et al. [24] also suggested with some evidence that the IRS specific epithial keratin genes KRT71-74 may be involved in the determination of hair texture, particularly with regard to coiled hair of different mammalian populations.

3.3 Hair Pigmentation and Genetics

We know that highly pigmented hair is both geographically/racially related (geo-racially) suggesting genetic involvement. For example those of African and Asian origin tend to have larger amounts of eumelanin in their hair while those of Caucasian extraction especially originating from Northern Europe tend to have less pigment such as eumelanin and more pheomelanin. Schwan-Jonczyk [10] suggested that melanin granules are ovoid or spherical and that the size and density of the granules are smaller and lower in Caucasians; that is the total melanin content and type of melanin [eumelanin (brown-black) versus pheomelanin (yellow-red)]. She concluded that Black African hair contains large agglomerated eumelanin granules about 0.8 μm along their major axis, while Japanese hair has smaller melanin granules about 0.5 μm and blonde European hair contains even smaller primarily pheomelanin granules about 0.3 μm. These observations on melanin size and race are consistent with those by Swift [25] for African versus Caucasian hair. Thus, the intensity or depth of color is related to both the size of the melanin granules and the total melanin content (the melanin granule density) while the proportion of eumelanin to pheomelanin is believed to be involved in determining the shade of hair color.

Melanins are synthesized in melanocytes (melanin producing cells) from the amino acid tyrosine and pheomelanin from tyrosine and cysteine and packaged into melanosomes in the melanocytes. The melanin containing melanosomes ultimately become melanin granules after being transferred into keratinocytes, cells that form the shaft of hair fibers. A more complete discussion of the biosynthesis and proposed structures for hair melanins is covered in Chap. 5.

3.3.1 Melanin Granules of Different Hair Types

From cross-sections of African hair versus dark-brown Caucasian hair the melanin granule density clearly appears higher in African hair. Two papers on melanin granule size and density in human hair, both Japanese papers by Kita et al. [26, 27], indicated a higher melanin density in the outer cortex versus the inner cortex. This melanin distribution effect is also typical of Caucasian and African hair. These scientists found no difference in melanin granule size and density in infant hair versus 20–30 year olds, but significant differences at age 60–70 wherein the minor axis of the melanin granules was smaller than for the other age groups. The density (number per square cm) of the melanin granules was lower at the advanced age [26, 27].

There is a wider range of natural pigment shades for Caucasian hair than for any other geo-racial group. We know that several genes are involved in the production of hair pigments. Furthermore, many of these genes function differently in different populations. But, the primary mechanisms of these genes are to control the size, aggregation state and the ratio of eumelanin to pheomelanin in the melanosomes which ultimately become the pigment granules of hair fibers.

3.3.2 The More Important SNPs and Genes for Hair Pigments

In 2010 Valenzuela and Brilliant [28] described 75 SNP's in 24 genes that have been associated with human or animal pigmentation for hair, skin and or eye color. These scientists analyzed these 75 SNP's by ANOVA and concluded that 31 were from 13 genes associated with either total melanin content or the ratio of eumelanin to pheomelanin in human hair fibers [28]. Multiple regression modeling by Valenzuela and Brilliant considering SLC24A5, SLC45A2 and HERC2 for total scalp hair melanin accounted for 76.3% of the variance. Modeling for the ratio of eumelanin to pheomelanin considering SLC24A5, SLC45A2 and MC1R accounted for 43.2% of the variance. So, these four genes (SLC24A5, SLC45A2, HERC2 and MC1R) are clearly among the more important genes to hair coloring, see Tables 3.2 and 3.3. However, since three of these genes, SLC24A5, SLC45A2 and MC1R explain less than half of the variance for the ratio of eumelanin to pheomelanin (the shade or color factor) and the fact that other genes are likely linked to the action of these genes highlights the fact that genes, in addition to these four, are obviously important to hair color.

Table 3.2 summarizes data from a few of the more important genes that have been implicated in pigmentation of human hair. At least three of these genes are believed to be involved in membrane transport. SLC45A2 produces the membrane-associated transporter protein (MATP) which has been suggested by Yuasa et al. [38] to be involved in the transport of melanosomal proteins to the melanosomes. The SLC24A5 gene (NCKX5) which stands for $Na^+/Ca^{++}/K^+$ exchanger 5 has been

Table 3.2 Some important genes/SNP's involved in hair color for major geo-ethnic groups

		Frequencies for populations of these groups (%)		
Gene	SNP/allele variant	East Asians	Africans	Caucasians
SLC45A2	rs16891982 (374L)	98.9 [29, 30]	98.9 [29]	1.7 [29]
	rs16891982 (374F)	1.1 [29, 30]	1.1 [29]	98.3 [29]
SLC24A5	rs1426654A = Thr^{111}	1.9 [29]; 36₮ [31]	4 [31]	97.8 [30]; 100₮ [31]
	rs1426654G = Ala^{111}	93–100 [32]	93–100 [32]	0₮ [31]
OCA2/HERC2	rs12913832C = i86			74 [33]
	rs12913832T			26€ [33]
P gene	rs1800414 (H615R)	44 J [34]; 54 J [35]	100 [34]	100 [34]
		54 C [35]		
ASIP	rs6058017G (g.8818G)	28 [36]	80 [36]; 60 [29]	12 [36]; 24 [29]
	rs6058017A		39.6 [29]	75.8 [29]
MC1R	rs885479 (R163Q)	75.5 [37]	0 [37]	4.6ʃ 1.6%€ [37]
	rs1805007 (R151C)		0 [37]	5.8 [37]

ʃ Northern Europeans, € Southern Europeans, ₮ Italians, *J* Japanese, *C* Chinese

suggested by Lamason et al. [32] to regulate the Ca^{++} concentration in the melanosomes. In addition, the P protein which is encoded by the OCA2 locus is another multi-transmembrane protein involved in the formation of melanin. Its function is unknown at this time, however, it has been suggested by Chen et al. [39] to involve the transport of tyrosinase (the enzyme involved in the formation of melanin pigments from tyrosine). Variants of the MC1R and to some extent the ASIP genes have been shown to be involved in determining the ratio of eumelanin to pheomelanin in the melanosomes.

Earlier in this chapter in the section on hair form entitled, *Evolution of Scalp Hair to Coiled and Straight Hair Forms*, the concept by Coop et al. [22] of East Asian and West Eurasian Sweeps was presented. This concept links genetics to geographic migrations out of Africa. The first migration was to the Far East (China, Korea, Japan and Mongolia) then to the Americas (Amerindians). The second migration was through the Middle East and then westward to Europe forming the Caucasian group. The p.A111T (THR^{111}) variant of the SLC24A5 gene for light skin and hair is at a high frequency in Europeans (Caucasians) and at low frequencies in East Asians and Africans [22, 31] supporting the East Asian Sweep, see Table 3.2. While the R163Q variant of the MC1R gene for dark hair is at a high frequency in East Asians and Amerindians and at low frequencies in Europeans and Africans supporting the West Eurasian Sweep [22, 37], see Table 3.2.

Han et al. [40], in 2008, conducted a genome-wide study among more than 10,000 European males and females. This study revealed 38 SNPs associated with hair color. The involved gene variants were located on six different chromosomes and involved eight different genes. Therefore, as Sturm [29] suggested, earlier anticipation that human pigmentation is dominated by a few TYR gene mutations that could control the formation of melanins has been shown to be a gross

Table 3.3 Genotype and hair color associations for variants in Southern Europeans [33]

Hair color by the percentage of the subjects of that color								
Gene/SNP	AA change	Genotype	N (%)	Red	Lt blonde	Lt brown	Dk brown	Black
SLC45A2/								
rs16891982	F374F	F/F	184 (81.4)	12	14.2	14.8	48.6	10.4
	F373F/F374L	F/L	40 (17.7)	5.1	7.7	7.7	56.4	23.1
	F374L	L/L	2 (0.9)	50	0	0	50	0
rs26722	E272E	E/E	211 (93.3)	10.5	12.9	14.3	51.4	10.9
	E272E/E272K	E/K	14 (6.2)	15.4	15.4	0	30.7	38.5
	E272K	E/K	1 (0.4)	100	0	0	0	0
SLC24A5/								
rs1426654	T111T	T/T	244 (99.1)	11.3	13.1	13.5	49.6	12.6
	T111T/T111A	T/A	2 (0.9)	0	0	0	100	0
	T111A	T/T	0 (0)	–	–	–	–	–
OCA2-HERC2/								
rs12913832		[a]C/C	57 (25.3)	8.8	28.1	17.5	40.4	5.3
		[a]C/T	108 (48)	11.2	11.2	15.9	51.4	10.3
		[a]T/T	60 (26.7)	13.6	1.7	5.1	55.9	23.7
MC1R/								
Homozygous wild type₸		+/+₸	86 (38.1)	0	10.5	20.9	47.7	20.9
Heterozygous wild type		€r/+	69 (30.5)	0	14.5	10.1	63.8	11.6
		€r/r	12 (5.3)	0	0	8.3	83.3	8.3
		¥R/+	26 (11.5)	20.8	16.7	16.7	41.7	4.2
		¥R/r	13 (5.8)	38.5	38.5	0	23.1	0
		¥R/R	20 (8.8)	75	5	0	20	0

[a]Nucleotide changes not amino acid changes

₸Wild type is + and is also referred to as consensus or the most common genotype; €r is V60L, V92M and R163Q; ¥R is R142H, R151C, I155T, R160W and D294H

oversimplification. Table 3.3 has been modified from a similar but larger table tabulating effects on skin and eye pigmentation as well as hair pigmentation by Cook et al. [33].

Another interesting study was conducted by Eriksson et al. [23] where 10,000 Northern European subjects were surveyed with a questionnaire for 22 common traits including hair color (blonde to black on a 7 point scale) and red hair (red to not red on a scale of 4 choices ("before I went gray, if I am gray now")). The hair color results revealed that rs12913832 of the OCA2/HERC2 region explains 12.2% of the variance for hair color in Northern Europeans, rs16891982 of SLC45A2 explains 2.7% of the variance and several SPN's of MC1R and two of ASIP are involved in red versus non-red hair color, results consistent with other studies.

Masui et al. [34] concluded that the MC1R gene and the P gene can serve as indicators of the origin of individuals in some populations. These scientists started with 18 SNP's, 11 from the MC1R gene and 7 from the P gene and narrowed down to 4 SNP's, the R163Q SNP from MC1R (rs885479) the IVS5+1001, IVS13+113 and H615R (rs1800414) from the P gene. Masui et al. combined the P gene SNP's versus the R163Q (rs885479) into a factor called CG which showed clear distinction between Asian populations (Japan, China, Korea and Mongolia combined) versus European or African populations. Interestingly, there appears to be a small distinction between Japanese versus the Chinese, Korean and Mongolian populations combined also.

Of the several genes involved in human hair, skin and eye color, the MC1R gene has shown the largest number of mutations and has been studied most thoroughly. In 2008, Savage et al. [37] published a paper describing allele frequency data on 55 SNP's of the MC1R gene from seven geographic populations of 2,306 persons. Savage et al. found a frequency of 75.5% for the R163Q protein (c.488 G > A allele variant; rs57758262) among 343 Asians including 282 Japanese and 50 Chinese with frequencies less than 5% for any other group for this same protein-allele. The next MC1R allele with a high frequency was for the T314T protein produced by the c.942 A > G allele; a dark hair allele with a frequency of 44.4% for the African population of 117 subjects 13.3% for the Asian group, 13.2% for the Asiatic Indians and 18.75% for the Papua New Guinea population [37].

A variety of different hair colors can be produced by different genotypes of the MC1R alleles. Among the MC1R alleles of Table 3.3, the homogeneous wild type (the consensus or most common) produces the highest percentage of black hair. Of the MC1R variants, the r variants do not produce red hair, but only dark brown to blonde hair. The heterozygous wild type with r and the homogeneous r/r genotypes produce from 75% to 92% dark brown to black hair. On the other hand, the R variants produce increasing percentages of red hair from 21% to 75% of the subjects with the highest percentage for the R/R homozygous subjects.

Lu et al. [41] showed that the MC1R gene can function to produce lighter shades of pigment via agouti-signaling involving another gene variant that produces a protein that antagonizes or inhibits the α-melanocyte stimulating hormone (α-MSH). Valverde et al. [42] in 1995 concluded that mutations of the MC1R gene are involved in red hair formation in humans and the mechanism involves increasing the ratio of pheomelanin to eumelanin in the melanosomes. This type of genetic variation is highest among Europeans with red hair and fair skin [43]. Branicki et al. [43] determined that at least 5 MC1R variants are involved in red hair production: C451T (rs1805007) providing an amino acid change of p.R151C, C478T (rs1805008) providing an amino acid change of R160W, C252A, (rs1805006) providing an amino acid change of D84E, G425A providing an amino acid change of R142H and G880C providing an amino acid change of D294H (rs1805009).

The major role was played by the first two of these gene variants for people of Polish descent and has been show by Savage et al. [37] to be at higher frequencies among European and US populations. The C451T variant has been shown by Savage et al. to occur at 5.6% in Northern Europeans, at 3.16% in Southern

Europeans and at 6.42% in the United States while the C478T variant at 8.3% in Northern Europe, at 1.9% in Southern Europe and at 7.2% in the United States. Box et al. [44] showed that the G178T variant (rs1805005) that provides an amino acid change of p.V60L is associated with fair or blond and light brown hair. This variant has been shown by Savage et al. [37] to occur at a frequency of 10.7% in Northern Europeans, at 15.75% in Southern Europeans and at 13.21% in the United States.

Savage et al. [37] and others described that in most regions of the genome there is greater genetic variation in African populations than most other populations. But the MC1R gene is an exception to this rule of thumb. This exception occurs because of the greater variation in hair pigments and skin pigments of people of European descent versus those of African descent.

Kanetsky et al. [45] provided evidence that the ASIP gene is also involved in the production of dark hair and brown eyes in European Americans. Bonilla et al. [46] suggested that the specific SNP of the ASIP gene described as g.8818A>G (SNP# rs6058017) is believed to function by producing a protein that binds to MC1R and promotes formation of eumelanin and darker skin color in African Americans. Zeigler-Johnson et al. [36] demonstrated that the allele of ASIP g.8818 G is involved in this type of agouti-signaling to promote eumelanin production and occurs at a high frequency (0.80) in West Africans, at 0.62 in African Americans, 0.28 in East Asians and at a frequency of 0.12 in European Americans. Harding et al. [47] concluded that the MC1R gene is "under strong functional constraint in Africa" and any change would be harmful from an evolutionary perspective.

Branicki et al. [48] demonstrated that the SLC45A2 gene also called MATP for membrane associated transporter protein is involved in hair color and in particular the L374 allele significantly increases the likelihood of black hair color in Europeans. The L374F (rs16891982, c.1122C > G) polymorphism of SLC45A2 has been suggested by Yuasa et al. [38] as a possible important factor in hypo-pigmentation in Caucasian populations. This SNP occurs at a high frequency in German, French and Italian populations and is virtually absent in African and East Asian populations [38]. It also occurs at low frequencies in Indians from New Delhi (14.7%) and Bangladeshi (5.9%) important populations of India.

The SLC24A5 gene has been found to affect pigmentation in zebrafish and humans and has been implicated in hair color by Lamason et al. [32] and confirmed by Valenzuela and Brilliant et al. [28]. The frequency for the p.A111T (rs63750629, c.331G > A) has been shown to be high in European populations (0.975) and low in Chinese (0.019) by Soejima and Koda [30].

The HERC2 gene sometimes called OCA2/HERC2 (Table 3.2) has been suggested by Sulem et al. [49] to be involved in expression of the OCA2 gene that reduces pigmentation in the hair of Europeans. The rs12913832 allele of the HERC2 gene has been shown by Valenzuela and Brilliant [28] to be involved in hair pigmentation and by Eiberg et al. [50] to be involved in brown eye color by inhibiting OCA2 expression. The OCA2 gene is involved in the most common form of albinism. Rebbeck et al. [51] determined that mutations of the P gene are also involved in eye color by association of these mutations with the OCA2 gene.

3.4 Some Other Hair Traits Related to Genetics

Shimomura and Christiano [52] reviewed genetically involved hair diseases in a comprehensive review entitled, *Biology and Genetics of Hair*. I refer the interested reader to this review for a description of several more hair diseases with genetic involvement than are described in this chapter. The most interesting to this author are the possible connections to the development of "normal" non-diseased hair such as those involved in pigmentation (in the previous section) and hair form. One example is the paper by Shimomura et al. [24] suggesting the possible involvement of IRS specific epithial keratin genes KRT71-74 in the determination of hair texture, particularly with regard to coiled hair of different mammalian populations.

With respect to androgenetic alopecia, the most common form of hair loss, several genes have been implicated. Hillmer et al. [53] demonstrated that the androgen receptor gene (AR) on the X chromosome is the primary requirement for early-onset androgenetic alopecia. The fact that location of this important gene is on the X-chromosome signifies the significance of the maternal line to androgenetic alopecia. A genome wide linkage study by Hillmer et al. [54] of 95 families of German descent provided evidence for linkage to chromosome 3q26. The susceptibility to male pattern baldness has also been shown to relate to five SNPs on chromosome 20pll by Brent Richards et al. [55] and Hillmer et al. [56]. This study by Hillmer et al. [56] suggested no interaction with the androgen receptor on the X-chromosome suggesting an androgen independent role from the product of these genes. Chromosomes 5 and 2 which harbor genes encoding the two 5α-reduction isoenzymes were found by Ellis et al. [57] to not be associated with male pattern baldness, therefore, the authors suggested that a "polygenic etiology should be considered" for the role of 5α-reductase in male pattern baldness.

Ahmed and Christiano et al. [58] identified a hairless gene (hr) on chromosome 8p12 that is associated with alopecia universalis in humans and Nothen et al. [59] have mapped the locus on chromosome 8p21-22. Martinez-Mir and Christiano et al. [60] have conducted a genome wide scan for linkage to alopecia areata implicating at least four susceptible loci on chromosomes 6, 10, 16 and 18 using more than one statistical approach.

Heywood et al. [1] working with hair from 292 female Caucasians characterized the hair of these subjects by amino acid analysis, dry tensile elastic modulus, two-dimensional electrophoresis of hair protein extracts and the perception of hair quality by the panelists themselves. The results from protein analysis provided a string of 66 kDa proteins that correlated with higher perceived hair quality. These scientists also noted a decrease in the low molecular weight (14–29 kDa) proteins with the use of hair coloring products.

Amino acid analysis revealed that the perception of hair quality was associated with higher levels of the amino acids serine and threonine. Higher elastic modulus was significantly higher in hair of higher perceived quality. Serine is an amino acid that occurs at very high levels in the ultra high sulfur proteins of hair. There are also threonine rich keratin associated proteins [61]. Therefore, higher concentrations of

these amino acids may suggest higher concentrations of the ultra high sulfur proteins or related keratin associated proteins which are likely under genetic control. From these results, these scientists hypothesized that hair quality is likely to be genetically determined.

3.5 Hair Abnormalities

Abnormalities in this section are classified as diseases involving growths on the hair and diseases of genetic origin that affect the structure of the hair fiber. Lice and Piedra are discussed in the last part of this section because they produce nodules on the hair shaft as well as affect the scalp in contrast to dandruff, a disease primarily of the scalp discussed in Chap. 6.

The sections in Chap. 1 entitled *Intermediate Filaments* and in Chap. 2 entitled *Type I and Type II Keratin Proteins (IF Proteins) of Human Hair* discusses only the Type I acidic keratins and the Type II neutral-basic keratins that are essential structures of the human hair fiber. Langbein and Schweitzer [62] described that IF proteins of human hair are involved in a few diseases such as monilethrix and certain hair follicle derived tumors. Six different types of IF proteins are described in the review paper on intermediate filaments and disease authored by Eriksson et al. [63]. Type III IF proteins include vimentin and desmin, Type IV IF proteins include nestin, synemin and the neurofilament triplet proteins, Type V IF proteins are the nuclear lamins and Type VI IF proteins of the eye lens cell are not considered in the discussion in this current Chapter. Nevertheless IF family members all share a central helical coiled-coil rod with variable Nitrogen and Carbon terminal groups that provides huge structural diversity. The IFs of human hair fiber are structural proteins while the other IF types are located in epithelia, muscle, neuron and eye lens cells. To date, the IF proteins of human hair fiber involve a few defective keratins in hair fibers and a few hair follicle derived tumors [63]. Numerous diseases of other tissues involve these other Types of IF proteins and include neurodegenerative diseases such as Lou Gehrig's disease, and Parkinson's disease, muscular dystrophy, liver disease and cataracts [63] all connected in some way to Intermediate Filaments.

Monilethrix, pili torti, pili annulati, trichorrhexis nodosa, Menke's disease and trichothiodystrophy are somewhat rare structural anomalies in human hair under genetic influence. The structural changes occurring in these anomalies are so large that they may be observed microscopically.

Monilethrix is a congenital, hereditary disease resulting in abnormal human scalp hair. Monilethrix is also called moniliform hair or beaded hair, and it produces hair fibers with the appearance of a twisted ribbon, as illustrated by the light micrograph of Fig. 3.1. However, in spite of its casual appearance detailed examination shows that monilethrix does not exhibit severe twists and it is thus distinguishable from pili torti. This disease is also characterized by dry, fragile hair fibers. Therefore, in monilethrix, hair length generally does not exceed a few centimeters,

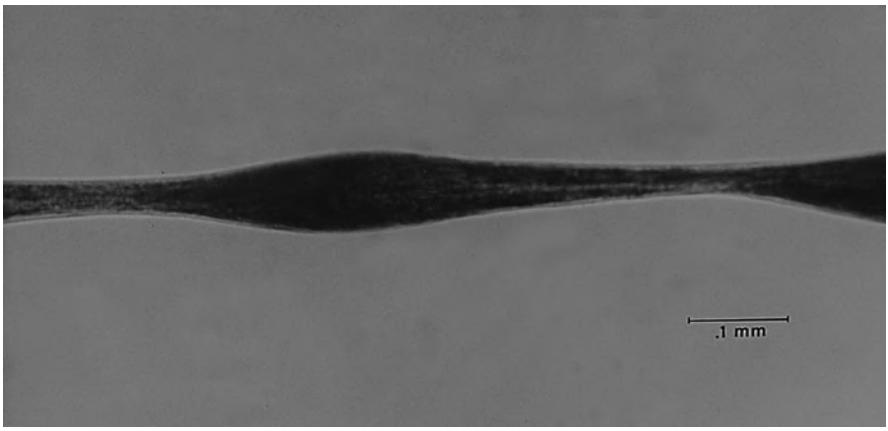

Fig. 3.1 Monilethrix, a congenital and hereditary structural anomaly of human scalp hair (Kindly provided by John T. Wilson)

particularly hair with narrow internodes. Healy et al. [64] studied two families with autosomal dominant monilethrix and excluded linkage to the type I keratin gene cluster on 17q, but provided evidence that this disorder is linked to the type II keratin cluster on 12q. Genes for basic trichocyte keratins are found on this latter gene. Congenital monilethrix produces defects in keratin intermediate filaments (hHb6 and hHb1) [62], the filamentous proteins in the cortex, see this paper by Langbein and Schweitzer [62] and the references therein. The most frequent mutations for monilethrix are E413K, E402K and E413D for hHb6 and E402K for hHb1 although other less frequent mutations have been described [62]. These mutations interfere with assembly or adhesion of the coiled coil dimers in the intermediate filaments resulting in very brittle, dry hair. Langbein and Schweitzer [62] concluded further that in addition to monilethrix those potential hair disorder candidates for the inability of mutated keratin proteins to form stable IF structures include pili annulati, wooly hair, numerous hypotrichoses and nail diseases.

Pili torti is a rare congenital deformity of the hair characterized by flattened fibers with multiple extensive twists. In some cases, the hair grows to a normal length, although frequently this deformity produces short, twisted, broken hairs presenting the appearance of stubble. Pili torti provides a high frequency of rotation (usually about 180°) and can resemble mildly affected monilethrix hair shafts (see Fig. 3.2) but its distinguishable by the severe twists of pili torti which show up better in SEM than in light microscopy see Fig. 3.3. Figure 3.3 shows three different pili torti hairs compared with one monilethrix hair. The extremely twisted hair on the left has been called corkscrew hair by Whiting et al. [65]. Price [66] identified two human DXL genes in the TDO locus (DLX3 and DLX7) and identified mutations in DLX3 in tricho-dento-osseous (TDO) syndrome patients. These genes are located on chromosome 17q21. TDO syndrome exhibits kinky curly hair, thin-pitted enamel, taurodontism and thickening of cortical bone.

Figure 3.4 illustrates Pili annulati, sometimes called ringed hair. Ringed hair is a rare hereditary condition characterized by alternating light and dark bands along the hair fiber axis described in the previous section entitled, *Medull*a. Giehl et al. [67] studied three families with 40 subjects affected by pili annulati to narrow the locus which was mapped to chromosome 12q24.34-24.33. These scientists "reduced the critical interval of pili annulati to 2.9 Mb". They also used sequence analysis to exclude mutations in the coding region of 36 potential candidate genes.

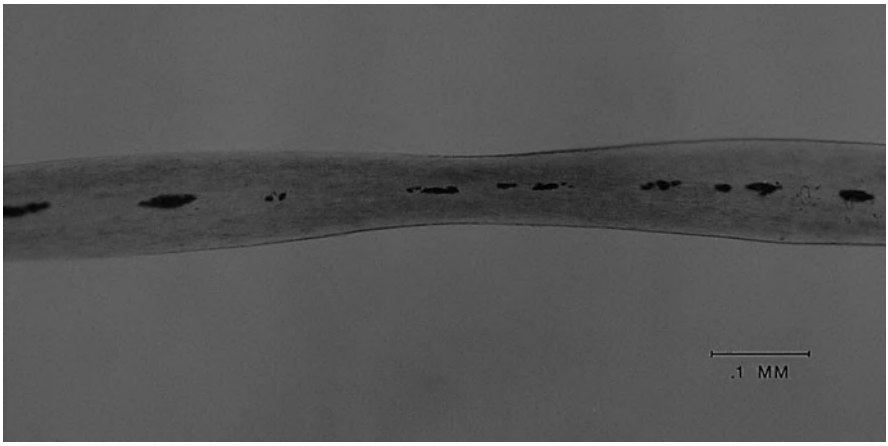

Fig. 3.2 Pili torti, an uncommon hair shaft anomaly, see also Fig. 9.12 (Kindly provided by John T. Wilson)

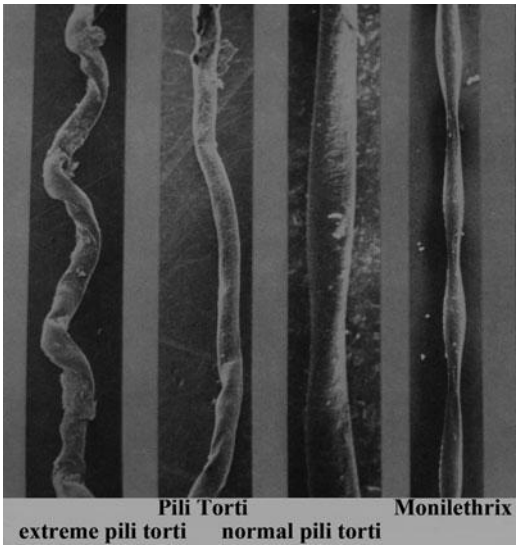

Fig. 3.3 Three different pili torti hairs and one monilethrix hair [58] (Reprinted with permission of Praeger Publishers, New York, NY)

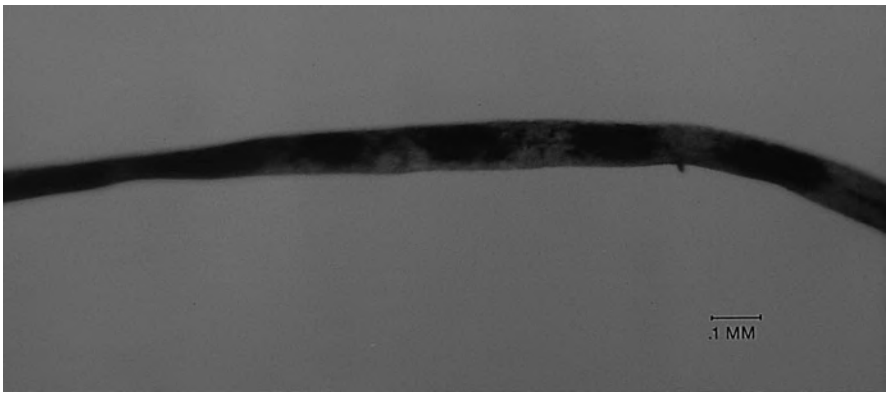

Fig. 3.4 Pili annulati (ringed hair). An uncommon inherited hair shaft anomaly (Kindly provided by John T. Wilson)

Netherton's syndrome is a skin disorder characterized by several hair shaft abnormalities two of which provide the appearance of nodes on the hair. Trichorrhexis invaginata involves the invagination of a short portion of the root of the hair into a short part of the tip of the hair providing the appearance of a node. Trichorrhexis nodosa forms the appearance of nodes on the hair provided by expansion of the cortical cell/cell membrane complex regions. These nodes are usually, but not always, fragile regions along the hair shaft. Dermatologists often refer to fragile hair as "Acquired trichorrhexis nodosa" and separate it into two disorders. Hairs with Proximal trichorrhexis nodosa break near the scalp. This condition is more common in African hair. Proximal trichorrhexis nodosa is exacerbated by hair straightening and braiding.

Distal trichorrhexis nodosa is more common in European or Asian hair with breaks occurring closer to the tips. This disease is exacerbated by chemical treatments, prolonged sun exposure and mechanical stress. It is often corrected over time and can be helped by the use of conditioners and care. Congenital trichorrhexis nodosa is a genetic disease involving a disorder of the urea cycle producing multiple nodes along the hair shaft, see Fig. 3.5. This genetic disorder occurs more often in facial hair than scalp hair, and produces bulbous type nodes appearing as irregular thickenings along the hair shaft. These nodes are actually partial fractures, which under stress crack more completely forming broom-like breaks illustrated by Fig. 3.6. Netherton's disease or syndrome has been shown by Bitoun et al. [68] to involve mutations of SPINK5 as the defective gene on chromosome 5q32 encoding the serine protease inhibitor Kazal-type 5 protein (LEKTI).

Menke's syndrome is a genetic disorder producing very kinky human hair in which the sulphydryl groups are only partly converted to disulfide bonds (about 50% oxidized) and is linked to a copper deficiency caused by a mutation in a protein involved in copper transport. Another symptom of Menke's syndrome is deterioration of the nervous system. Menke's syndrome is an X-linked recessive disorder involving a gene that encodes a copper-transporting ATPase located at Xq13 as

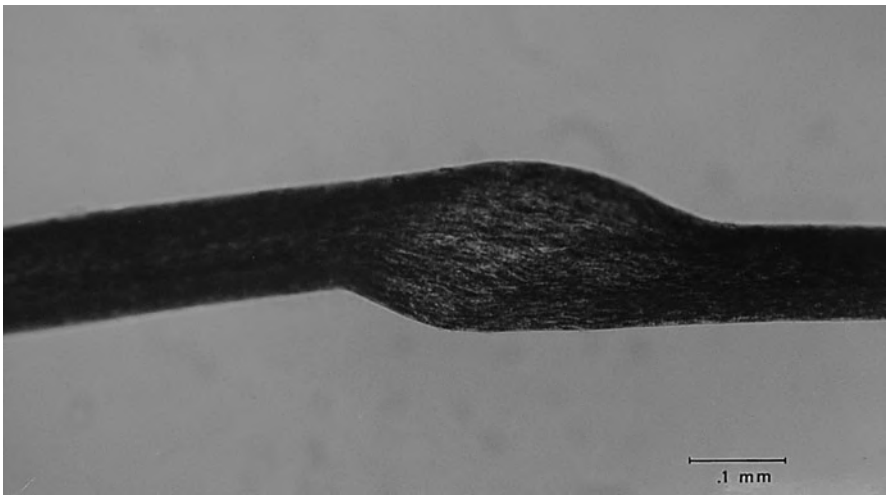

Fig. 3.5 An intact hair fiber illustrating the condition of trichorrhexis nodosa (Kindly provided by John T. Wilson)

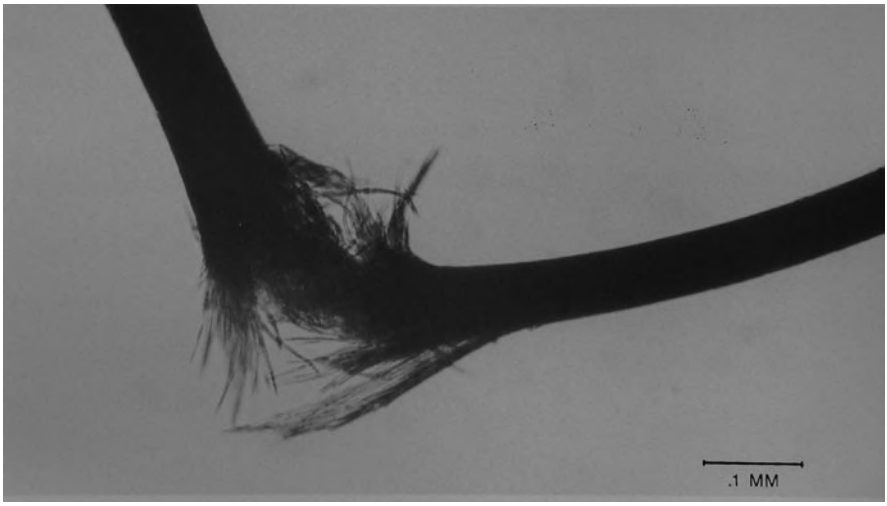

Fig. 3.6 Trichorrhexis nodosa. "Broomlike" fractures at the "nodes" are symptoms of this hair shaft anomaly (Kindly provided by John T. Wilson)

shown by Vulpe et al. [69]. Menke's kinky hair disorder occurs primarily on males because males have only one X chromosome and the probability for both X chromosomes of a female being affected is very low. Subcutaneous injections of copper if done early are sometimes helpful.

Trichothiodystrophy (TTD) is a number of syndromes affecting both the hair and the nails and other organs resulting from mutations producing sparse and brittle hair, nail dystrophy, mental and growth retardation, ichthyosis, decreased fertility and cutaneous photosensitivity. There are several forms of nonphotosensitive TTD and photosensitive TTD. Amish brittle-hair syndrome is characterized by short stature, mental retardation, hair with very low sulfur content and decreased male fertility. Other forms of nonphotosensitive TTD include Pollitt syndrome and Sabinas brittle-hair syndrome with similar clinical conditions. Nakabayashi et al. [70] determined one gene involved in nonphotosensitive TTD as C7orf11 which maps to chromosome 7p14 and is expressed in hair follicles. In TTD the hair contains only about one half the cystine content of normal hair. Such low cystine cross-link levels account for the brittleness of the hair in this disorder.

Jones and Rivett [71] described maple syrup urine disease or branched chain keto-aciduria (MSUD) as a rare genetic defect involving a lack of the enzyme that synthesizes 18-methyl eicosanoic acid from isoleucine. This enzyme is involved in a necessary biological process for eliminating excessive branched chain amino acids from the body. In MSUD, branched chain amino acids can build up to toxic levels. Some of the symptoms of MSUD are maple syrup odor in cerumen at 12–24 h after birth, elevated levels of branched chain amino acids by 12–24 h, ketonuria, irritability and poor feeding by 2–3 days and in some cases coma and respiratory failure by 7–10 days [72]. Strauss et al. [72] in their thorough review of MSUD describe three types of MSUD, the disease characteristics, diagnosis and testing and treatment as well as its genetic basis. MSUD Type I involves the chromosomal locus 19q13.1-q13.2 and the gene symbol BCKDHA and is found in certain Mennonite populations. MSUD Type II involves the chromosomal locus 6q14 and the gene symbol BCKDHB and has been found in the Ashkenazi Jewish population. MSUD Type III involves the chromosomal locus 1p31 and the gene symbol DBT.

MSUD patients lack 18-methyl eicosanoic acid in hair. In MSUD, this unique branched chain fatty acid is substituted by linear saturated fatty acids, mainly C16, C18 and C20. Smith and Swift [73] found that hair from persons with MSUD does not cleave cleanly at the Beta-Delta layers as with normal hair and therefore it provides more endocuticular failure. MSUD is described in more detail in Chapter 1 in the section entitled “The cuticle-cuticle CMC”.

Lice and Piedra are two diseases that occur primarily, but not exclusively among pre-pubertal children. Both of these diseases produce nodules on hair shafts that contain eggs for the former and spores for the latter.

Lice nodules may appear on hair on most areas of the body, such as the scalp, the eyebrows or even the pubic region (crabs). The human head louse, *Pediculus capitis*, is a very small wingless parasitic insect that survives on the blood of humans. The louse has a flattened body, about 3 mm long, with a claw on the end of each leg which it uses to cling to the hair of its host. Female lice lay whitish eggs called nits. The nits are bound to the hair of the host with an adhesive material. In most cases it is easier to find nits than adult lice because of the immobility of the former and the high mobility of the latter. Nits are generally laid close to the scalp. Since nits are “permanently” attached to the hair shaft, they can be found near the

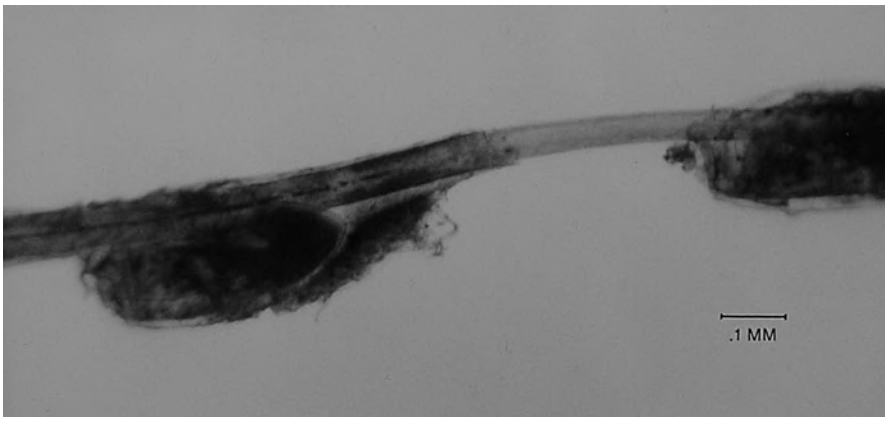

Fig. 3.7 Light micrograph illustrating empty nits of the head louse *Pediculus capitis* on a human scalp hair (Kindly provided by John T. Wilson)

tip ends of long hair from growth, after long attachment times. The eggs hatch in about a week after attachment. Three molts in only 2–3 weeks' produces a mature adult louse. Figure 3.7 is a light micrograph illustrating the empty nit sacs of the human head louse.

When the insect bites the host a small amount of a mild toxin is released. The bite usually leaves a tiny red spot that with scratching can cause larger sores. Louse infection occurs frequently and should be considered as a possible causative agent in cases of prolonged scalp itching. The resultant pruritus can lead to excoriation and secondary infection. After several bites the victims may become sensitized to the toxin. Lice are also capable of transmitting several diseases including typhus and relapsing fever.

Lice infection is usually treated by shampooing and combing frequently with a fine tooth comb to remove the nit sacs. Re-treatment in 7–10 days is essential to remove or kill the lice that hatch from the nits. Rubbing a product containing an insecticide into the hair and the scalp is even more effective. It is usually recommended to apply the treatment at night and to shampoo in the morning and then to repeat treatment in 7–10 days. Products are shampoos, crème rinses and hair/scalp creams. Leave in products are more effective than shampoos. Crème rinses are claimed to help remove nit sacs because they facilitate the comb out.

Insecticides such as permethrin, benzyl benzoate, lindane and pyrethrin have been used to treat lice. Pyrethrins are insecticides initially derived from certain species of chrysanthemum flowers. Synthetic pyrethroid insecticide is more stable with a similar activity and low mammalian toxicity and is called permethrin. Lindane (1,2,3,4,5,6 hexachlorocyclohexane) and benzyl benzoate have also been used as Pediculocides. Lice infection is spread by direct contact or by wearing the clothing of an infected person. The control of secondary bacterial infection may require an antibiotic.

Black Piedra "black stone" is caused by *Piedraia hortai*, a fungus that can affect scalp hair, and sometimes beard mustache or even body hair. This fungus penetrates

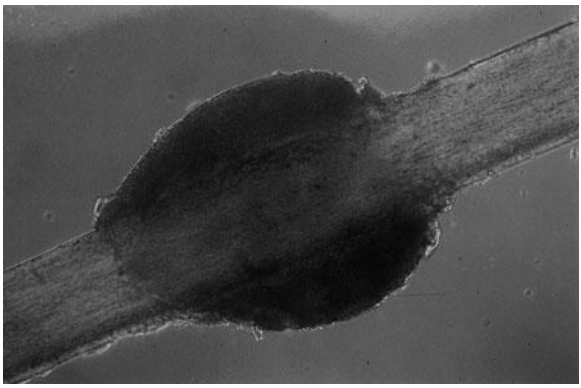

Fig. 3.8 Light micrograph of the spore sacs of the Black Piedra fungus on a human hair fiber

the cuticle resulting in adherent rough or granular black to brown nodules (see Fig. 3.8) that can be observed microscopically or even with the naked eye. These penetrating nodules can weaken the hair shaft and even lead to hair shaft fractures.

White Piedra is caused by *Trichosporin beigelii*, another fungus, and is found more often in pubic hair than in scalp hair. White Piedra can also weaken hair fibers and produce fractures. The whitish nodules from this fungus are easy to remove from the hair fiber, but are usually full of fungal spores. Black or white Piedra can be identified or diagnosed by microscopic examination or by cultures from infected hairs. Piedra usually occurs in tropical or humid climates such as tropical South America; however, white Piedra has also been identified in certain parts of Europe. Antidandruff products containing strong fungicides should be effective against Piedra. See the antidandruff section in Chap. 6 for a description of the most effective fungicides in hair products.

For additional details relevant to these hair shaft anomalies, see the review paper by Shimomura and Christiano [52] and the book edited by Brown and Crounse [74].

3.6 Hair Analysis for Drugs and Forensic Studies

Hair analysis for drugs of abuse has been described to detect cocaine [75–77], marijuana [75], nicotine [78], opiates [79] and amphetamines [78–81]. Originally drugs were extracted from the hair followed by gas chromatographic/mass spectrophotometric (GC/MS) analysis for the drug. More recently, the hair is dissolved and antibodies used in radioimmunoassay (RIA) act as specific agents for extraction/analysis [77, 82, 83]. The analysis is generally by GC/MS. Some distinct advantages exist in hair analysis over urinalysis, such as the detection of long term drug usage is more readily identified. However, drug usage over the most recent few days is not detectable by hair analysis. All analytical methods have limits. Although, hair analysis does appear to offer potential, however, the limits for hair analysis are still in the process of being defined [82].

A review of hair analysis for drugs of abuse is provided in the paper by Baumgartner [83] addressing some of these limits. Hair analysis for drugs of abuse such as ethyl alcohol, amphetamines, barbiturates, cocaine, ecstasy opiates, etc. can be determined [84]. If scalp hair is not available, hair from other areas of the body such as armpit, eyebrow, pubic or facial hair can be used; although differences in growth rates must be taken into consideration. Kelly et al. [85] examined hair analysis for three drugs, amphetamines, cocaine and cannabinoids and determined there is no bias introduced by hair color or racial effects for hair analysis of those drugs. One concern expressed in the literature for hair analysis deals with the potential for false positives created by contamination by passive environmental exposure, e.g. smoking of PCP or marijuana, etc. The review by Baumgartner speaks to this concern by pre-washing the hair to remove the passive contaminants and not the material deposited in the cortex through the bloodstream. For example, environmental contamination via passive smoke exposure should provide for only superficial sorption near the surface rather than deeply penetrated drugs taken internally.

3.6.1 Forensic Studies and DNA Analysis

Hair fibers are frequently found at crime scenes, and they are usually evaluated first for a large number of macroscopic and microscopic comparisons for identification as described by Gaudette [86, 87]. Characteristics such as color, pigment size, pigment distribution, pigment density, whether the fiber has been dyed, type of medulla, maximum and minimum diameter, type of cut at tip, length, scale count, and various cross-sectional characteristics are used in this evaluation. Such comparisons have been invaluable for either excluding or incriminating suspects in crimes. However, more recently, several newer techniques have been developed including blood group analysis [77], DNA analysis [88–95], and drug analysis (see the previous section), that together provide for even more conclusive evidence for either excluding or targeting a suspect.

For some DNA analysis, the specimen must be either plucked or shed, because it must contain root or root sheath material for DNA to be extracted for further workup and identification. ‘Extraction of DNA from the biological specimen has been described by Walsh et al. (of the Roche Molecular Systems, Emeryville, CA) [93]. After extraction, two methods are used for further analysis: restriction fragment length polymorphism (RFLP) [88] and the technique, polymerase chain reaction (PCR). The RFLP technique [88] was the first one developed and provided a very high discriminating power because it discriminates by size and the number of the fragment lengths of the DNA sample. However, it cannot be used with highly degraded DNA and requires much more DNA material than the PCR technique, generally more than is provided by a single hair fiber. So, primarily because of much higher sensitivity, the PCR method has replaced the RFLP method [96].

The PCR technique offers many advantages because it requires minimal amounts of DNA and even permits typing from degraded DNA. It can even be used on single hairs as shown by Higuchi et al. [90]. PCR analysis even permits DNA analysis over a large area of the hair shaft itself. For example, Heywood et al. [97] have shown that PCR amplification permits DNA to be found even in root end and tip ends of hair, although there are higher levels in the root end. These same scientists also found that hair treated with permanent hair colorants provide lower levels of DNA and surfactant washing also decreases DNA.

After extraction, the PCR technique is used to replicate specific sections of a strand of DNA to increase the amount of material for analysis. (For further information, see bulletins describing the Gene Amp Polymerase Chain reaction Technology and the AmpliType HLA DQα Forensic Typing Kit available from the Cetus Corporation, Emeryville, CA).

Budowle and van Daal [96] describe that the discrimination power of current PCR analysis has been increased by amplifying the typing of variable number of tandem repeat (VNTR) loci. The allele forms are then separated by electrophoresis and detected by silver staining [97]. Part of a subclass of the VNTR loci has replaced the earlier markers. These new markers or short tandem repeats (STRs) are now used worldwide [98–101]. Because the fragment length of the required DNA is much smaller than in the past (about less than 350 base pairs) some degraded samples are now capable of being typed. The analysis used today is sometimes called multiplex autosomal STR loci [101]. This procedure provides high sensitivity, specificity and the capability to analyze small and degraded samples in a semi-automated manner.

Even newer techniques are under development to permit quantitation and even faster and more convenient qualitative identification of DNA for forensic, archaeological, and clinical research [79, 80].

Another type of genetic marker that shows promise for typing degraded samples involves SNPs. SNPs are single nucleotide polymorphisms or a portion of DNA where one nucleotide base has been changed, inserted or deleted. It is not likely that SNPs will ever become the primary forensic markers but they show promise to provide useful forensic information especially on degraded samples. For additional information on SNPs in forensic research see the review paper by Budowle and van Daal [96] and the sections in this Chapter entitled *Evolution of Scalp Hair to Coiled and Straight Hair Forms* and *Hair Pigmentation and Genetics*.

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