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<thead>
<tr>
<th><strong>Allele</strong></th>
<th>chi</th>
</tr>
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<tbody>
<tr>
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</tr>
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</tr>
<tr>
<td><strong>Base Change (assembly)</strong></td>
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<tr>
<td><strong>Gene</strong></td>
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<tr>
<td><strong>Gene Name</strong></td>
<td>tyrosinase-related protein 1</td>
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<tr>
<td><strong>Synonym(s)</strong></td>
<td>Tyrp. isa, Oca3, TRP1, TRP-1</td>
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**Science Writers**: Anne Murray  
**Authors**: Adam Dismang, Tiana Purrington  
**Illustrators**: Peter Jurek  
**Last Updated**: 04/23/2019 7:45 PM by Diantha La Vine  
**Record Created**: 05/01/2013 8:28 AM by Adam Dismang  
**Record Posted**: 10/28/2013
Phenotypic Description

The *chi* mutation was induced by ENU mutagenesis on the C57BL/6J (black) background and was discovered in G3 animals. The mutant mice exhibit a brown coat color and black eyes (**Figure 1**).
Nature of Mutation

Whole exome HiSeq sequencing of the G1 grandsire identified 63 mutations. Among these, only one affected a gene with known effects on pigmentation, *Tyrp1*. The mutation in *Tyrp1* was presumed to be causative because the *chi* hypopigmentation phenotype mimics other known alleles of *Tyrp1* (see MGI for a list of *Tyrp1* alleles). The *Tyrp1* mutation was identified as an A to G transition at base pair 80840778 (v38) on chromosome 4 in the GenBank genomic region NC_000070 encoding *Tyrp1*. The mutation corresponds to residue 1159 in the mRNA sequence (NM_031202.2) in exon 4 of 8 total exons.

![Mutation diagram](image)

The mutated nucleotide is indicated in red. The mutation results in a conversion of tyrosine (Y) to cysteine (C) at residue 296 of the tyrosinase-related protein 1 (Tyrp1).

Protein Prediction

[Flash Content]

*Figure 2. Domain structure of tyrosinase-related protein 1 (Tyrp1).* The *chi* mutation results in a substitution of tyrosine (Y) to a cysteine (C) at residue 296. SP, signal peptide; EGF-like, epidermal growth factor-like domain; TM, transmembrane; CT, cytoplasmic tail. Glycosylation and copper binding sites are indicated in light pink and purple, respectively. The EGF-like/Cysteine-rich domain (EGF-like) is labeled. A central cysteine-rich (Cys-rich) region is between the copper binding regions (CuA and CuB; the exact amino acid residues that comprise the Cys-rich region are not documented). The CuA, Cys-rich, and CuB regions comprise the catalytic domain of Tyrp1. Image is interactive, click on the image to view an incidental mutation found in *Tyrp1* (R0011: *Tyrp1*).
The tyrosinase-related protein (TRP) family consists of Typr1 (Trp1, gp75), tyrosinase (Tyr; see the records for ghost, pale rider, and siamese), and Typr2 [alternatively, DOPAchrome tautomerase (DCT)]. Typr1 shares ~40-52% amino acid sequence homology with Tyr [reviewed in (1;2)]. The TRP proteins share homologous domains including two copper binding regions, an EGF-like/cysteine (Cys)-rich domain, a central cysteine-rich region, a transmembrane domain, a signal sequence and six putative glycosylation sites [Figure 2; (3-7); reviewed in (1;2;8;9)]:

- The N-terminal 24 amino acid signal peptide of Typr1 is essential for the correct processing of Typr1 [reviewed in (1)].

- The two copper-binding regions (CuA and CuB) are highly conserved among the three TRP family members (7). Each domain contains three histidine residues that are required for copper binding [(7); reviewed in (1)]. Studies have shown that, in Tyr, copper binding is essential for catalytic activity (10), however, the extent of copper binding to Typr1 is minimal (7).

- Seventeen cysteine residues present in Typr1 are clustered into two Cys-rich regions. The N-terminal Cys-rich region is also an EGF-like domain; the central Cys-rich region is within the catalytic domain between the two-copper-binding regions. The EGF-like/Cys-rich domain is proposed to play a role in protein-protein interactions [(11); reviewed in (1;9)]. Typr and Typr1 form heterodimers, possibly through the EGF-like motif (4;12-14). Typr, Typr1, and Typr2 form a multi-enzyme complex within the ER and Golgi as well as in the early and late melanosomes (4;13;15-17). PKC-mediated phosphorylation of Typr may promote complex formation between Typr1 and Typr (17). Both Typr1 and Typr2 help to stabilize Typr within the complex (4;12;14). Consistent with this, the brown mutation of Typr1, C86Y located in the N-terminal EGF-like domain, leads to decreased stability of Typr in melanocytes (4;18;19), thereby affecting Typr activity. Studies have reported that Typr1 can either increase (4;14;20) or decrease (16) Typr activity. Kobayashi et al. found that in mouse melanocytes, Typr1 expression increased Typr stability and melanogenesis (i.e., melanin synthesis) (4). However, Orlow et al. determined that dissociation of the Typr1-Typr complex resulted in an increase in Typr activity, suggesting that Typr1 inhibits Typr activity (16). Wu et al. propose that the changes in Typr1-Typr association observed by Orlow et al. could be due to the use of a detergent treatment when assaying for Typr activity (17).

- Disulfide bonds (and other non-covalent interactions sensitive to thermal denaturation) stabilize Typr1 [(11); reviewed in (1)]. Although the cysteine residues that participate in disulfide bonds are unknown, proper disulfide bond pattern and protein conformation are essential for Typr1 trafficking from the ER (11). Treatment of Typr1-expressing mouse B16 melanoma cells with dithiothreitol (DTT) resulted in prolonged interaction of Typr1 with ER chaperones (e.g., calnexin and BiP) and subsequent targeting of Typr1 for degradation (11).

- The transmembrane domain of Typr1 (amino acids 479-501) functions in proper trafficking to the melanosome and incorporation into the melanosome-limiting membrane (12;21).
Typr1 has six potential N-linked glycosylation sites (i.e., Asn-X-Ser/Thr; X is any amino acid) at the luminal domain: Asn96, 104, 181, 304, 350, and 385 (22). However, Xu et al. determined that, in mouse, there are only five residues that are N-glycosylated: Asn96, 181, 304, 350, and 385; Asn104 is not glycosylated (22). N-linked glycosylation at Asn181, 304, and 385 influences intracellular transport of Typr1, while N-glycosylation at Asn350 influences the stability of Typr1 in the endocytic pathway (22). Inhibition of the early steps of N-glycosylation by N-butlydeoxyxojirimicin (NB-DNJ; inhibitor of -glucosidase I) resulted in only a slight reduction of Typr1 DOPA oxidase activity, while the same treatment caused Tyr to be synthesized as an inactive form [(5); for more information about Typr1 and DOPA oxidase activity see “Background”, below]. Furthermore, changes in Typr1 glycan processing did not result in changes to Typr1 conformation near the active site (5).

The C-terminal 36 amino acids (amino acids 501-537), along with the transmembrane domain, are required for intracellular retention and sorting of Typr1 (21). Deletion of 27-33 of the amino acids of the cytoplasmic tail resulted in targeting of Typr1 to the cell surface instead of to the endosome/lysosome (23). In fibroblast transfectants, residues 511-517 (NQPLLTD) were necessary for sorting Typr1 in the endocytic pathway (21). The QPLLTD sequence containing the “di-leucine motif” is conserved among melanosomal membrane proteins (21). The C-terminal tail of Typr1 interacts with GIPC/SEMCAP-1, a PDZ domain-containing protein, within and near the Golgi (24). The interaction of Typr1 with GIPC is proposed to function during intracellular sorting and targeting of Typr1 to the melanosome (24).

Studies have determined that mature Typr1 can exist both as an intracellular form (75-80 kDa) and a secreted form (78-88 kDa) [(25); reviewed in (1; 8)]. Intracellular Typr1 has the N-terminal signal peptide, a long N-terminal luminal domain with the N-linked glycosylation sites, a transmembrane region, and the C-terminal domain (25). In contrast, soluble Typr1 lacks the transmembrane domain, the C-terminal tail, and a small region in the luminal domain (25).

The chi mutation resides within the catalytic domain of Typr1, a domain that contains the copper-binding motifs and one of the EGF-like domains. A mutation within the catalytic domain could alter the association of Typr1 to Tyr and/or the DHICA oxidase function of Typr1.

TGF-1 inhibits the activity of Typr1

Transforming growth factor (TGF)-1 is a multifunctional cytokine that regulates several processes, including proliferation, differentiation, adhesion, and migration, in many cell types [reviewed in (26; 27)]. TGF-1 negatively regulates the activities of both Typr1 and Tyr in mouse melanoma cells by reducing their abundance; Typr2 activity is not changed (28). Martinez-Esparza et al. propose that the TGF-1-mediated changes to the Typr1 protein level are due to post-translational events (28). Other factors that regulate the expression of Typr1 are described in "Expression /Localization", below.
Expression/Localization

Tyrp1 is localized in melanosomes of the skin, hair follicle, inner ear, choroid, iris, and ciliary body as well as in the retinal pigment epithelium (RPE) [reviewed in (29)]. For more information on the localization of Tyrp1, please see “Transport of Tyrp1 in the melanosome” in the Background section, below.

The first exon of Tyrp1 is noncoding and, along with the first intron, is required for efficient gene expression, but not for pigment cell specificity [(30); reviewed in (1;29)]. The TRP proteins can be regulated by several stimuli including vitamins, interleukins (31), prostaglandins (32), sex steroids (33), interferons (34), ultraviolet light (35), and melanocyte stimulating hormone (36).

The TRP proteins all contain an M-box motif (AGTCATGTGCT) upstream of the TATA box (between positions -44 and -34) in their respective promoters that can bind to microphthalmia transcription factor (MITF), a basic helix-loop-helix transcription factor [(37-41); reviewed in (8;9;29)]. Binding of MITF to the Tyrp1 promoter increased Tyrp1 promoter activity (37). cAMP (cyclic AMP) facilitates the upregulation of MITF and the subsequent association of MITF with Tyrp1 (37). cAMP-elevating agents stimulated the transcriptional activity of the Tyrp1 promoter, subsequently leading to an increase in Tyrp1 mRNA; the protein levels were also increased (37). Bertolotto et al. determined that the cAMP-elevating agents stimulated the transcription of Tyrp1 via the cAMP-dependent protein kinase (PKA) pathway (37).

T-box factor Tbx2 by binds to two elements, MSEu and MSEi, to negatively regulate Tyrp1 expression (42;43). The MSE elements are comprised of a six nucleotide sequence, GTGTGA. Pax3, a member of the paired box (PAX) family of transcription factors, also binds the Tyrp1 promoter at the MSE elements, subsequently upregulating Tyrp1 activity in melanocytes (40).

Promoter analysis determined that Tyrp1 expression is regulated by different factors in melanocytes of the skin, hair follicle, inner ear, choroid, iris, and ciliary body versus the RPE (41). For example, the homeobox factor, Otx2, controls RPE-specific expression of Tyrp1 (44). Murisier et al. identified a highly conserved region at -15 kb that acts as a melanocyte-specific enhancer of Tyrp1 expression; the transcription factor Sox10 binds and transactivates this enhancer (41).
Background

Figure 3. Biochemical pathway leading to the synthesis of eumelanin and pheomelanin. The TRP proteins are labeled in red. Tyrp1 primarily functions as a 5,6-dihydorxyindole 2-carboxylic acid (DHICA) oxidase.
Figure 4. Transport of Tyrp1 in the melanosome.
Premelanosomes arise from the late secretory or endosomal pathway. Stage 1 premelanosomes (depicted here as "Early endosome/Stage I" for simplicity) lacking pigment are thought to correspond to the coated endosome, an intermediate between early and late endosomes densely coated on one face with clathrin.
PMEL17, a structural component of the melanosome on which melanins are deposited (not depicted) accumulates in stage I and II; PMEL17 is masked by melanin in later stages. Melanin synthesis begins in Stage II premelanosomes that contain regular arrays of parallel fibers that give these organelles a striated appearance by electron microscopy. During Stage III, these fibers gradually darken and thicken (red arrows, inset) as eumelanin is deposited along them, such that by Stage IV no striations are visible and the melanosome is filled with melanin; this action has been illustrated in the inset. All cargoes required for melanin synthesis, processing, and transport (OCA2, SLC45A2, Rab32, Rab38, DCT (alternatively, Tyrp2), Tyr, and Tyrp1) derive from the Golgi and traverse vacuolar and/or tubular elements (not shown) of early endosomes en route to the stage III melanosome. Adaptor protein-3 and -1 as well as biogenesis of lysosome-related organelle complex-1 (BLOC-1) and BLOC-2 regulate the intracellular trafficking of Tyrp1. SLC45A2 and OCA2 function in the trafficking of Tyrp1 and DCT to melanosomes. OCA2 maintains the proper pH in the melanosomes and transports glutathione, a protein necessary for Tyr and Tyrp1 trafficking to melanosomes. Black arrows represent transport of vesicles; red arrows represent protein-mediated regulation at a specific transport step as indicated in the key. Tyrp1 expression is regulated by the microphthalmia transcription factor (MITF). See the text and Table 1 for more details about the proteins shown in this image. The image is interactive, click to reveal mutations in several of the proteins.
Several mouse models with mutations in components of the pigment-producing pathway are shown below; the mutation name (black) and mutated gene (red) are indicated. The melanosome pathway has been adapted from several sources including: Raposo, G. and Marks, M.S. (2007), Nat. Rev. Mol. Cell Biol., 8:786 and Lakkaraju, A. et al. (2009), J. Cell Biol., 187:161.
The production of melanin in the skin, hair follicle, inner ear, choroid, iris, ciliary body, and RPE results in pigmentation [reviewed in (29)]. Tyr, Tyrp1, and Tyrp2 are Cu\(^{++}/\)Zn\(^{++}\) metalloenzymes that function in melanogenesis leading to the formation of two types of pigments, eumelanins (brown or black) and pheomelans (yellow or red) [Figure 3; reviewed in (4; 8; 13; 45)]. The pigments are synthesized in melanosomes, which arise from the endosomal or secretory pathway and progress through four stages of maturation (I-IV), as defined by their electron microscopic appearance (46). Melanin synthesis begins with the chemical conversion of tyrosine to dopaquinone, a reaction catalyzed by Tyr. Both eumelanin and pheomelanin derive from dopaquinone, thus Tyr determines the rate and total amount of melanin production. Pheomelanin production proceeds spontaneously following dopaquinone production, while eumelanin production further requires Tyrp1 and Tyrp2 [reviewed in (46; 47)]. Tyrp2 catalyzes the non-decarboxylative rearrangement of L-dopachrome to 5,6-dihydroxyindole-2-carboxylic acid (DHICA); the function of Tyrp1 is described below (48). For more information about melanogenesis, please see the record for ghost.

Several enzymatic activities have been attributed to murine Tyrp1: tyrosine hydroxylase and DOPA oxidase activities (49-51), DOPAchrome tautomerase function (along with Tyrp2) (52), DHICA oxidase activity (53; 54), and catalase activity (hydrogen-peroxide:hydrogen-peroxide oxidoreduction) (55). The primary function attributed to Tyrp1 is that of a DHICA oxidase (53; 54), catalyzing the oxidation of DHICA to indole-5,6-quinone-2-carboxylic acid, a product eventually converted to eumelanin (54). The role of TYRP1 in human melanocytes, in contrast, is currently unclear (17). For example, Boissy et al. found that human TYRP1 did not have DHICA oxidase activity (56). In addition, Zhao et al. determined that human TYRP1 did not exhibit DOPA oxidase activity; TYRP1 exhibited tyrosine hydrolase activity in this study (51).

**Transport of Tyrp1 in the melanosome**

Tyrp1 is synthesized in the ER, transported to the Golgi where it undergoes post-translational processing, then from the trans-Golgi network (TGN) to an endosomal compartment [Figure 4; (57-60)]. Early endosomes are requisite intermediates in the trafficking of Tyrp1 from the Golgi to the late stage melanosomes (61). Within the endosomal intermediate, Tyrp1 is sorted away from both late endocytic and pre-melanosomal cargoes (61). Tyrp1 associates with several proteins that are essential for proper trafficking of Tyrp1 to melanosomes including Rab7, Rab38, Rab32, ESCRT-I, Varp (VPS9-ankyrin-repeat protein), syntaxin-3, PI3-kinase, BLOC (biogenesis of lysosome-related organelles complex)-1, BLOC-2, and AP-1 [Table 1; (58; 59; 62-65)]. Whereas the dileucine motif of tyrosinase interacts with the adaptor complex AP-3 (see the record for bullet gray), studies have shown that AP-3 does not interact with Tyrp1 (66-68). In AP-3 deficient melanocytes, tyrosinase is mislocalized, but Tyrp1 is properly targeted (66; 67).

<table>
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<th>Tyrp1-associated function</th>
<th>References</th>
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<table>
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<tr>
<th>Protein</th>
<th>Function Description</th>
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<td>Transporter protein (see the record for <em>cardigan</em>)</td>
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<td>Rab7</td>
<td>Mannose-6-phosphate receptor</td>
<td>58; 59; 69</td>
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<td>Rab38 &amp; Rab32</td>
<td>GTPases (see the record for <em>fenrir</em> for information about Rab38)</td>
<td>63; 70</td>
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<tr>
<td>Phosphatidylinositolide (PI) 3-kinase</td>
<td>Various functions, including regulation of protein trafficking</td>
<td>57; 71</td>
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<tr>
<td>ESCRT-I</td>
<td>Component of the endosomal sorting complex machinery</td>
<td>61</td>
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<td>Mutagenetix Phenotypic Mutation 'chi'</td>
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<td>--------------------------------------</td>
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<td><strong>Varp</strong></td>
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<td>Rab32/38 binding protein and guanine nucleotide exchange factor for Rab21. Varp interacts with the vesicle SNARE VAMP7.</td>
<td>Facilitates, along with Rab32/38, trafficking of Tyrp1 (e.g., transport from an endoplasmic reticulum [ER] to the Golgi, transport from endosomes or the trans-Golgi network, tethering, docking, and/or fusion of Tyrp1-containing vesicles to melanosomes)</td>
<td>(63; 64)</td>
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<td><strong>Syntaxin-3</strong></td>
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<td>Target (t)-SNARE in intracellular vesicle trafficking</td>
<td>Trafficking to peripheral melanosomes. Syntaxin-3 and SNAP23 on melanosomes interact with VAMP7 on Tyrp1-containing vesicles to regulate Tyrp1 trafficking.</td>
<td>(62)</td>
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<td><strong>BLOC-1</strong></td>
<td></td>
<td></td>
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<tr>
<td>Protein complex that regulates intracellular trafficking (see the records for <em>salt and pepper</em> and <em>minnie</em> for information about members of the BLOC-1 complex)</td>
<td>Promotes the transit of Tyrp1 from endosomes to melanosomes. Lack of a subunit of BLOC-1 resulted in mislocalization of Tyrp1 to early endosomes and at the cell surface.</td>
<td>(65; 72)</td>
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**BLOC-2**

Protein complex that regulates intracellular trafficking (see the record for *pam gray*, *toffee*, and *stamper-coat* for information about the members of the BLOC-2 complex) Promotes the transit of Tyrp1 from endosomes to melanosomes. Tyrp1 expression is reduced in BLOC-2-deficient melanocytes. *(65; 72; 73)*

**AP-1**

Clathrin adaptor complex that sorts proteins in the TGN (see the record for *bullet gray* for information about AP-3) Tyrp1 sorting *(66; 74; 75)*

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**TYRP1** mutations cause hypopigmentation

Mutations in *TYRP1* are linked to oculocuaneous albinism type III [OCA3; OMIM: #203290; *(76; 77)*] and variations in skin/hair/eye pigmentation linked to 9p23 in Melanesians [OMIM: #612271; *(78)*]. Individuals with OCA3 have reduced pigment of the skin, hair, and eyes *(76)*. Melanocytes isolated from a patient with OCA3 did not express TYRP1, subsequently resulting in reduced melanin production; TYR transcription and translation were normal *(76)*. Tyrp1 mutations have also been linked to pigmentation changes in domestic cats *(79; 80)*, dogs *(81; 82)*, cattle *(83)*, horses *(84)*, and mice (see “Putative Mechanism”, below).

**Additional functions of Tyrp1**

In addition to its role in melanogenesis, Tyrp1 also promotes melanocyte viability/survival *(15; 85-87)*, protects melanocytes against oxidative stress *(88)*, and is a melanocyte differentiation marker *(8; 89)*.
Tyrp1 functions to protect melanocytes from the cytotoxicity of melanin intermediates produced by Tyr; Tyrp1 does not protect against Tyr-mediated cell death in nonmelanocytic cells (15; 90). Through the formation of the Tyr-Tyrp1-Tyrp2 complex in melanocytes, the leakage of toxic melanin intermediates is decreased [see “Protein Prediction”, above, for information about the Tyr-Tyrp1-Tyrp2 complex] (12; 14; 16). Luo et al. propose that Tyrp1 participates in scavenging cytotoxic melanin intermediates via an interaction with Lamp1 (87).

Loss of TYRP1 expression in cutaneous neoplastic melanocytes is linked to the appearance of transformed melanocytes in the underlying dermis (39; 91). TYRP1 mRNA and protein expression are reduced in several melanoma cell lines and specimens due to decreased expression of MITF (39; 91-93). In TYRP1-melanoma cells, binding of MITF to the TYRP1 M box is inhibited due to activation of factors that interfere with binding (39). Gene profiling in skin and lymph nodes (i.e., the most frequent sites of melanoma metastases) revealed an inverse correlation between the level of TYRP1 expression and patient survival (94).

**Putative Mechanism**

To-date 58 mouse Tyrp1 mutant alleles have been documented (MGI). Homozygous Tyrp1 mutants [e.g., brown, MGI:1855960; cordovan, MGI: 1855961; light, MGI:1855962; white-based brown, MGI: 1855963] exhibit a brown coat color on a non-agouti background [reviewed in (29)]. The brown mutation (Cys86Tyr) is within the EGF-like/Cys-rich domain and results in a mutant protein that is mislocalized and does not get delivered to melanosomes (95; 96). Kobayashi et al. propose that the mutant protein is unable to associate with Tyr, subsequently leading to decreased stabilization of Tyr and degradation of Tyr (4; 13). Melanosomes from brown homozygotes are round, particulate, and disorganized compared to the lamellar and regular structures observed in normal animals (4). The light mutation (Arg38Cys) results in premature death of follicular melanocytes due to pigment production-induced cytotoxicity (90). The light mouse has lightly (or non)pigmented hair at the tip; pigmentation is absent at the base of the hair. This phenotype persists for each hair cycle, but the light base progresses with age; older mice can have almost completely pale gray fur (90). Tyrp1 mRNA expression is normal in this model. Similar to the light mouse, the white-based brown mouse exhibits absence (or reduction) in pigment at the base of the hair (90; 97). The white-based brown mutation is an insertion of DNA or a chromosomal translocation at the 3' end of the first intron of Tyrp1; Tyrp1 transcripts are not produced (97). The white-based brown mutation leads to premature melanocyte death, similar to the light mutant. The chi mutation also results in hypopigmentation. It is unknown whether the chi mutation results in the death of follicular melanocytes. Tyrp1 expression and Tyrp1 localization have not been examined.

**Genotyping**

Chi genotyping is performed by amplifying the region containing the mutation using PCR, followed by sequencing of the amplified region to detect the single nucleotide transition.

**PCR Primers**

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Chi(F): 5’- ACACACTCACTGACTCCTTAGCAGG -3’
Chi(R): 5’- GGTGCTTAACGTGCAACTGCATTG -3’

**Sequencing Primer**

Chi_seq(F): 5’- TCACTGACTCCTTAGCAGGTAGAG -3’

**PCR program**

1) 94°C  2:00
2) 94°C  0:30
3) 55°C  0:30
4) 72°C  1:00
5) repeat steps (2-4) 40X
6) 72°C  10:00
7) 4°C

The following sequence of 456 nucleotides (from Genbank genomic region NC_000070 for linear DNA sequence of *Tyrp1*) is amplified:

```
1  acacactcac_tgactcctta_gcagg_tagag  agctaagga aaaggacacc agggctaagc
61 aagccagagg acaagatgtt agcagaagca gagaccacta atggatcttc atgatctagg
121 agatgctgca ggagccttct ttctcccttc cttactggaa ttttgcaact gggaaaaacg
181 tctgcgatgt ctgcactgat gacttgatgg gatccagaag caacttcgat tctactctta
241 taagccccaa ctcttgttct tctcaatgga gagtggtctg tgaatccttg gaagagt cga
301 ataccctggg aacacttttgt aacagtaaga cccaaatgac agctactatt cacaatttt
361 tatttctata atgactgtgt tgctgcttga gagtggcttg tgaatctttg gaagagt a cg
421 tcttcagaga atcaatcag atgctcctta aqcacc
```
Primer binding sites are underlined and the sequencing primer is highlighted; the mutated nucleotide is shown in red text.

References


97. Javerzat, S., and Jackson, I. J. (1998) White-Based Brown (Tyrp1B-w) is a Dominant Mutation Causing Reduced Hair Pigmentation Owing to a Chromosomal Inversion. *Mamm Genome.* 9, 469-471.