International Journal of Agriculture and Biosciences 2025 14(6): 1240-1245.
https://doi.org/10.47278/journal.ijab/2025.096
This is an open-access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
RESEARCH ARTICLE
eISSN: 2306-3599; pISSN: 2305-6622

Level of TRY Gene Expression in Morphs Albino in Ball Python (*Python regius*)

Ratchanok Kumsiri [1], Thanet Sophonnithiprasert [2] and Panan Kanchanaphum [2,*]

[1]Rangsit University, Faculty of Science, Pathobiology Unit, Pathumthani, Thailand
[2]Rangsit University, Faculty of Science, Biochemistry Unit, Pathumthani, Thailand
*Corresponding author: panan.k@rsu.ac.th

ABSTRACT

Ball pythons or *Python regius* are well-known exotic pets, because of their gorgeous colors and patterns, particularly the albino morphs. There are different types of albino ball pythons, including the Candy and Candino variants, which differ in color intensity. In the Candino morph, the yellow color compared with the standard albino morph becomes a dark yellow, and the white stripe turns purple. In contrast, the Candy variants show a gold color that is more intense than both the standard albino and Candino morphs. The variation of the tyrosinase gene (TRY gene) expression is the major cause of the difference in coloration of the albino morph. This study is the first to report the expression levels of the TRY gene in these two albino morphs, Candy and Candino. The results indicate that the TRY gene expression in both variants is significantly lower than in wild-type ball pythons. Specifically, expression is reduced by a factor of 7.88 for the Candy variety and by 36.93 for the Candino variety. This means that the TRY gene expression in Candy is 4.69 times higher than in Candino. These results suggest that the TRY genes in both Candy and Candino morphs are still active and capable of expression.

Keywords: Ball python, *Python regius*, Tyrosinase, Level of expression

Article History
Article # 25-117
Received: 12-Mar-25
Revised: 17-Jun-25
Accepted: 01-Jul-25
Online First: 06-Jul-25

INTRODUCTION

One of the famous exotic pets is the ball python (*Python regius*) because of their beautiful colors and patterns, as well as the wide variety of these traits. The different color and pattern variations are referred to as "morphs." The morph albino is one of the most favored morphs, which features reduced melanin in its skin. The skin color of albino ball pythons is white and yellow, unlike the black and brown found in their wild-type ball python. There are several genes involved in melanin synthesis in ball pythons, such as the tyrosinase gene (TYR gene), as noted in studies by Oetting et al. (1998), Miura et al. (2018), Brown et al. (2022), Kokiattrakool et al. (2024) and Garcia-Elfring et al. (2025). Another important gene is oculocutaneous albinism type 2 or OCA2, which encodes a chloride channel necessary for maintaining the pH of melanosomes. Several transporter proteins, such as the solute carrier (SLC) group of membrane transport proteins, are believed to be involved in the biosynthesis of melanin in ball python, including SLC7A11, SLC23A5, and SLC45A2 (Ginger et al., 2008; Vitavska & Wieczorek, 2013; Nicholas et al., 2014; Lavoro et al., 2023; García-Elfring et al., 2025). However, the most significant gene regulating melanin synthesis is the TYR gene. The albinism in ball python is the recessive homozygote of the mutant TYR gene (Kokiattrakool et al., 2024).

Brown AR and his colleagues (Brown et al., 2022) hypothesized that the primary reason for albinism in ball pythons is the inactivity of the TYR gene, also known as the tyrosinase gene, which encodes the enzyme responsible for catalyzing the most crucial step in melanin biosynthesis. The researchers identified three haplotypes of the TYR gene in albino pythons, each carrying a different loss-of-function variant. The first variant is a missense mutation in the third coding region of TYR, resulting in an exchange from aspartic acid to glycine (D394G) (Brown et al., 2022). The second variant is also a missense mutation in the same area, resulting in a proline-to-leucine exchange (P384L). This particular mutation is similar to a variant (P384A) associated with oculocutaneous albinism in humans (Simeonov et al., 2013). The last variant

Cite this Article as: Kumsiri R, Sophonnithiprasert T and Kanchanaphum P, 2025. Level of TRY gene expression in morphs albino in ball python (*Python regius*). International Journal of Agriculture and Biosciences 14(6): 1240-1245. https://doi.org/10.47278/journal.ijab/2025.096

A Publication of Unique Scientific Publishers

does not contain any coding or splicing site alterations (Brown et al., 2022). Based on Brown et al.'s (2022) hypothesis regarding the variant that lacks coding or splicing sites. Recently, Kokiattrakool et al. (2024) succeeded in using the PCR primers designed to target the splicing regions of the TYR gene to distinguish between the wild type and heterozygous albino phenotypes in ball pythons. Kumsiri et al. (2025) used PCR and qPCR to discriminate between the wild type and heterozygous piebald phenotypes in ball python.

Additionally, various mutations in the TYR gene have been linked with milder phenotypes. For instance, the phenotype of Himalayan llamas is linked to different mutations that cause temperature-regulated activity of the TYR gene, resulting in cooler areas of the body being pigmented white, while warmer parts remain unpigmented (Anello et al., 2019). Similar examples can be seen in rabbits (Aigner et al., 2000), cats (Lyons et al., 2005) and mice (Kwon et al.,1989; Kulathunga et al., 2021).

In ball pythons, there are many types of albinos, such as albino, Candino or Toffino, Candy or toffee, as shown in Fig. 1.

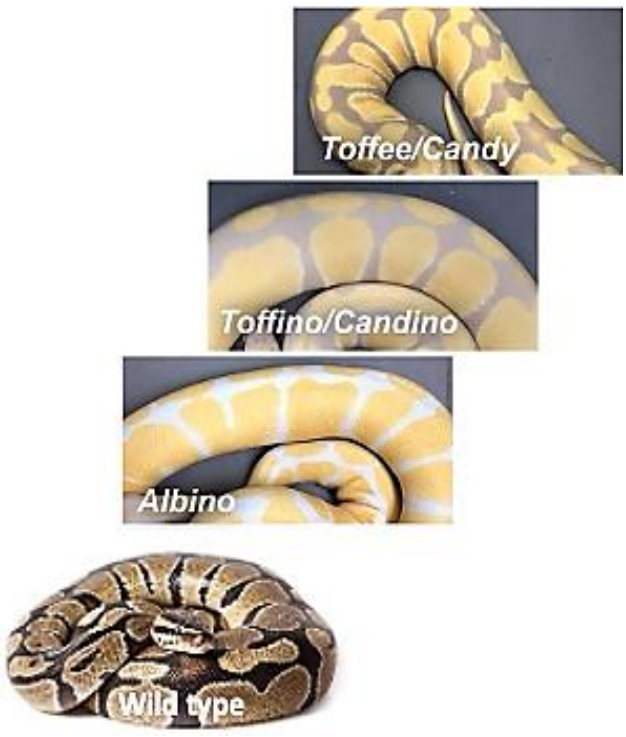

Fig. 1: The variant types of morph albino in ball pythons.

The type of albinos is divided depending on the intensity of the color. In Fig. 1, the morph Candino, the yellow color (in morph albino) changes to a dark yellow. Additionally, the white stripe in albino becomes purple in Candino. In Candy variants, the yellow (in morph albino) turns into a gold color, which is more intense than in both albino and Candino. The stripe color in Candy is a light brown. The variation of the color in morph albino is based on the amount of melanin in the skin. So, this study focuses on the level of tyrosinase gene expression in the albino variant.

MATERIALS & METHODS

Sampling and RNA Extraction

Ethical Approval

Before starting the experiment, the Ethics Review Board for Animal Research at Rangsit University approved this study (RSU-AEC 001-2022).

The shed skins of the ball python samples were kindly provided by commercial breeders in Thailand, specifically Reptile Collector by docjavet and Morph Hunter. All samples were kept at -20°C to prevent any insect larvae from infesting the sheds. The total set of animals included seven wild types, seven albinos, seven candinos, and seven candies. We cut a size of 1.5 cm x 1.5 cm piece from each shed sample, which was then submerged in a lysis buffer (1M Tris-HCl, pH 7.5, and 10% SDS) and crushed using a stirring rod. The resulting solution was then used for RNA extraction. The RNA extraction was performed using GENEzol™ Reagent (Geneaid, New Taipei City, Taiwan). After mixing the solution with GENEzol™ Reagent, chloroform was added, and the mixture was vigorously shaken. The solution was then centrifuged at 10,000g for 10min. The upper phase was transferred to a new tube, and isopropanol was added in an equal volume to that of the upper phase. This mixture was centrifuged again at 10,000g for 10min, after which the supernatant was removed. The RNA pellet was washed with cold 70% ethanol and centrifuged at 10,000g for 3min. After allowing the pellet to air dry, 25µL of DEPC water was added and the solution was stored at -80°C until further use.

cDNA Synthesis

After extraction, the RNA was measured for concentration using the Nanodrop (Thermo Scientific, Massachusetts, USA). The RevertAid First Strand cDNA Synthesis Kit (Thermo Scientific, Massachusetts, USA) was used for first-strand cDNA synthesis. The oligo dT primer from the kit and 2•g of each RNA sample were employed to synthesize the first strand of cDNA. After that 1xTaq DNA polymerase, a buffer and a mixture of deoxynucleotide triphosphates (dATP, dTTP, dCTP, and dGTP) were added to synthesize the second strand of cDNA. The resulting cDNA was then stored at -20°C until further use.

qPCR Reaction and Gene Expression Analysis

The primers of the PCR reaction in this study were based on the work of Kokiattrakool et al. (2024), which is shown in Table 1. To increase the specificity of the qPCR reaction, Luna Universal qPCR Master Mix (New England BioLabs, Massachusetts, USA) was applied. The qPCR amplification reaction mixture included Luna Universal qPCR Master Mix and 0.8µM of the forward primer (TYR-F), reverse primer (TYR-R), and cDNA extract as a template, in a final volume of 10µL. The PCR amplification conditions consist of an initial denaturation at 95°C for 3min, followed by 35 cycles of denaturation at 90°C for 30s, annealing at 55°C for 30s, and extension at 72°C for 30s. The expression levels of the TYR gene were analyzed in the cDNA of wild-type, albino, Candino, and Candy samples. The

Glyceraldehyde-3-phosphate dehydrogenase gene (GAPDH) served as the reference gene. Each sample was tested in triplicate during the qPCR reaction.

Table 1: The sequence of PCR primers in this study

Primer name	Sequence 5'-3'
TYR-F	TGG TAG CTT CTG GCC TCT CT
TYR-R	GAG TGT GCA GAA TCA CCC CA

RESULTS

qPCR Reaction and Gene Expression Analysis

PCR products of the housekeeping gene GAPDH and the TRY gene were observed in every sample. The melting curves were analyzed to confirm a single PCR product. NTC controls showed no PCR product. The results presented in Table 2 indicate that the expression of the TRY gene in Candy was consistently lower than that in the wild-type. Specifically, the average expression level of the TRY gene in Candy was found to be 7.88 times lower than that in the wild-type.

Table 2: The comparison of TRY gene expression between wild-type and Candy

	Candy 1	Candy2	Candy3	Candy 4	Candy 5	Candy 6	Candy 7
Repeat 1	3.71	3.09	5.46	5.31	2.38	6.45	12.13
Repeat 2	9.51	11.88	15.45	2.43	15.14	9.25	15.35
Repeat 3	3.61	2.97	17.15	2.77	10.41	8.75	2.23
Average	5.61	5.98	12.69	3.50	9.31	8.15	9.90

Similarly, Table 3 showed that the expression of the TRY gene in Candino was also lower than in the wild-type. In this case, the average expression level of the TRY gene in Candino was 36.93 times lower than that of the wild-type.

Table 3: The comparison of TRY gene expression between wild-type and Candido

	Candino 1	Candino 2	Candino 3	Candino 4	Candino 5	Candino 6	Candino 7
Repeat 1	16.91	14.32	30.91	13.18	47.18	23.1	21.11
Repeat 2	29.86	31.78	35.27	47.18	47.5	18	36.25
Repeat 3	94.35	78.79	30.48	31.56	32.45	23.43	72
Average	47.04	41.63	32.22	30.64	42.38	21.51	43.12

Fig. 2 showed that the decrease in TRY gene expression in Candino was greater than the decrease in TRY gene expression in Candy. These results indicated that the TRY gene expression in Candy is higher than in Candino.

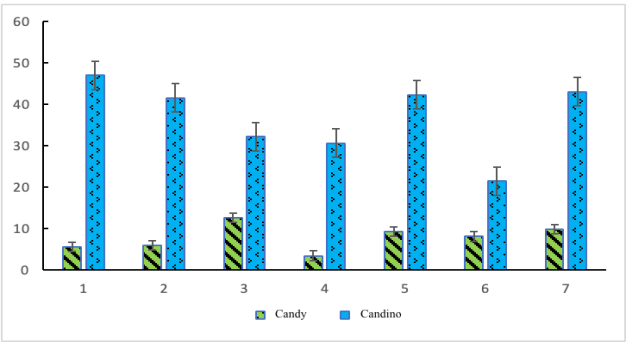

Fig. 2: The comparison of the decline of TRY gene expression between Candy and Candino. The numbers 1-7 are each ball python morph Candy and Candino.

DISCUSSION

Brown AR and his colleagues (Brown et al., 2022) hypothesized that the primary cause of albinism in ball pythons is the absence of function of the TYR gene, also known as the tyrosinase gene. This gene encodes the enzyme tyrosinase, which catalyzes the main reaction of melanin biosynthesis. Tyrosinase is the copper-containing enzyme that regulates the first two steps in the melanin biosynthesis pathway, changing tyrosine into L-dihydroxyphenylalanine (DOPA) and subsequently transforming DOPA into DOPA quinone, a precursor of melanin (Cieslak et al., 2011). The TYR gene is commonly referred to as the albino locus since mutations in this gene lead to albinism in several species. In addition, some mutations of the TYR gene have been associated with milder phenotypes. For instance, the Himalayan phenotype in mice is linked to different mutations that alter the temperature-regulated activity of the TYR gene, resulting in pigmentation in the cooler parts of the body while the warmer areas remain white (Anello et al., 2019). An additional case is the chinchilla allele in mice, which translates a tyrosinase enzyme with only one-third to one-half the activity of the normal enzyme. This reduced activity is due to a point mutation in the TYR gene. As a result, chinchilla mice typically display a grayish color (Lamoreux et al., 2001). This example is relevant to our study. Another point mutation in the TYR gene majorly causes the platinum phenotype in mice, resulting in nearly complete loss of pigmentation (Orlow et al., 1993). Two near-white TYR alleles have been identified in mice, known as Dhoosara and Chandana, both of which are characterized by significantly low pigment synthesis in the body and eyes (Challa et al., 2016).

Pös et al. (2021) described copy number variants (CNVs) as tools for molecular diagnosis of various diseases and in non-invasive prenatal care, but their full potential is still emerging. López et al. (2015) discuss the relationship between copy number variation and the TRY gene in humans. Copy number variation is a molecular phenomenon in which sequences of the genome are repeated, with the number of repetitions varying among individuals of the same species (Lauer and Gresham 2019).

The biological effects of CNV can vary significantly, ranging from having no impact on common physiological traits (Zhang et al., 2009) to causing morphological variations (Wright et al., 2009; Henkel et al., 2019; Wang et al., 2023). In ball pythons, the coloration of the Candy and Candino morphs is darker than that of the standard albino, as shown in Fig. 1. This effect depends on the level of TRY gene expression. However, there is currently no evidence to show that the variation in TRY gene expression among ball pythons is due to copy number variation (CNV).

Another interesting evidence for the diversity of color in animals is the melanocortin 1 receptor or MC1R locus, which is located on chromosome 2 (EquCab3.0 chr3:36,979,313-36,980,266). This locus plays an important role in determining the production of eumelanin and pheomelanin, which are responsible for black and red pigments, respectively. These pigments contribute to the

formation of black, bay, or chestnut base colors in horses (Hammons et al., 2021).

One more interesting example of the color diversity mechanism is presented by Liu et al. (2025). The multi-omics analyses indicated the crucial roles of pathways involved in antioxidant and lipid metabolism. Specifically, tyrosine metabolism, melanogenesis, fatty acid metabolism, fatty acid elongation, and the biosynthesis of unsaturated fatty acids were identified as key factors influencing the variation in levels of skin color among the leopard coral grouper (*Plectropomus leopardus*).

Our results indicated that the expression of the TRY gene in Candy and Candino varieties is significantly lower compared to the wild type, specifically 7.88 times and 36.93 times lower, respectively. Additionally, the TRY gene expression in Candy is 4.69 times higher than that in Candino. Our findings suggest that there are some TRY genes still active and capable of expression. The aligns with the study by Anello et al. (2019), who compared the expression levels of the TRY gene across three groups of llama: non-diluted llamas, diluted llamas, and llamas with a white phenotype. The results indicated that the expression of the TRY gene in the white phenotype llamas was absolutely lower than that in the non-diluted group.

Another interesting albino phenotype, characterized by a critical loss of melanin, is accompanied by two other albino phenotypes that also exhibit reduced melanin in the skin and eyes: lavender and ultramel. The lavender phenotype shows with the lavender-colored patches on the skin instead of the usual brown or black. The researchers (Gardner et al., 1992) have indicated that this lavender phenotype results from a loss of function in the OCA2 gene. When the OCA2 protein disappears or loses function, the enzymes responsible for melanin synthesis become less active, resulting in only small amounts of melanin synthesis (Puri et al., 2000; Ni-Komatsu and Orlow 2006). The ultramel phenotype is characterized by tan or light brown skin patches, contrasting with the darker shades of brown or black commonly observed. This phenotype results from the functionlessness of five genes, including TYR1, TYR2, SLC7A11, SLC24A5 and SLC45A2 (Puri et al., 2000). The TYR1 and TYR2 genes translate enzymes crucial for melanin biosynthesis (Lai et al., 2018). SLC7A11 translates a transporter that imports cystine into the cell (Sato et al., 1999), while SLC24A5 translates a K+-dependent Na+-Ca2+ exchanger (Nicholas et al., 2014; Apar et al., 2024). The SLC45A2 gene translates a putative sugar transporter (Chintala et al., 2005). The absence of proteins translated by these genes decreases melanin production through mechanisms that may involve defects in the regulation of melanosome pH (Nicholas et al., 2014; Bin et al., 2015; Wu et al., 2023).

Additionally, there are several white morphs of ball pythons, such as the Blue Eye Leucistic (BEL), Ivory, and Superfire, as illustrated in Fig. 3. While these morphs are not albino, their mostly skin appears white due to the absence of pigment. However, the interesting issue is that the parents of BEL, Ivory, and Super Fire have distinct colors and patterns, as shown in Fig. 4.

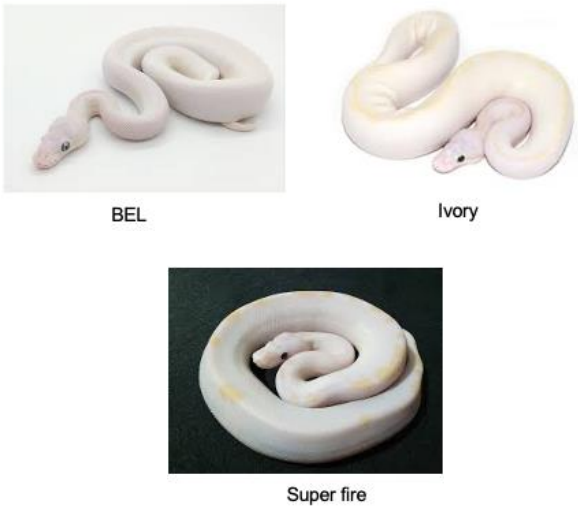

Fig. 3: The white morph: Blue Eye Leucistic (BEL), Ivory, and Super fire.

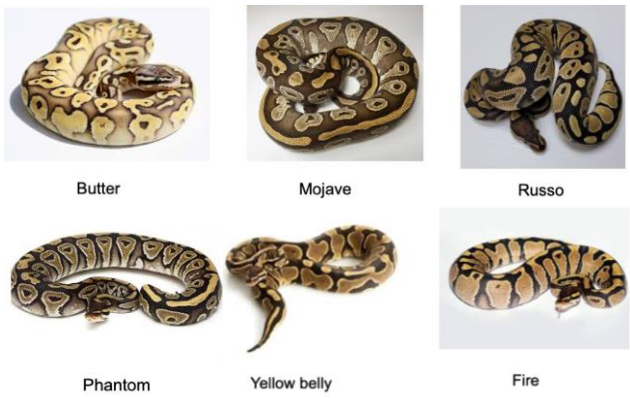

Fig. 4: These morphs of ball pythons are capable of breeding BEL, Ivory, and Super Fire.

The offspring of the Butter, Mojave, Russo, and Phantom morphs, which have yellow, brown, and black colors with distinct patterns, are called BELs. BELs have completely white skin and no patterns. The parents of the Ivory morph, which is mostly white with a yellow line on its back, are Yellow Belly, known for their color and pattern. Similarly, the parents of the Super Fire morph, which is predominantly white with some yellow dots on its skin, are Fire morphs, which have a brown and yellow coloration with patterns. This phenomenon is very interesting. Future work will involve studying the expression of the TRY gene in BEL, Ivory, and Super Fire morphs to gain a better understanding of the mechanisms behind this phenomenon.

Conclusion

The study is the first report on the ball python indicating that the TRY gene is expressed in both Candy and Candino. However, the level of TRY gene expression is higher in Candy compared to Candino. This difference in expression corresponds to the phenotypic characteristics of the ball pythons, as Candy exhibits a darker coloration than Candino.

DECLARATIONS

Funding: This work was supported by the Fundamental Fund (Grant no.4770963/2568), Thailand Science Research and Innovation (TSRI).

Acknowledgement: We would like to sincerely thank Mr. Stewart Miller for critically correcting our English grammar.

Conflict of Interest: All authors declare that they have no conflicts of interest.

Data Availability: The entire data set that supports the results of this study was published in the article itself.

Ethics Statement: This study was approved by the Ethics Review Board for Animal Research at Rangsit University (RSU-AEC 001-2022).

Author's Contribution: R.K. contributed to sample collection, conducted laboratory experiments, performed data analysis, and wrote the initial draft of the manuscript. T.S. participated in the laboratory experiments and data analysis. P.K. supervised the project, secured funding, conducted laboratory experiments, performed data analysis and interpretation, and critically revised the manuscript for intellectual content. All authors have reviewed and approved the final version of the manuscript for submission.

Generative AI Statement: The authors declare that no Gen AI/DeepSeek was used in the writing/creation of this manuscript.

Publisher's Note: All claims stated in this article are exclusively those of the authors and do not necessarily represent those of their affiliated organizations or those of the publisher, the editors, and the reviewers. Any product that may be evaluated/assessed in this article or claimed by its manufacturer is not guaranteed or endorsed by the publisher/editors.

REFERENCES

Aigner, B., Besenfelder, U., Müller, M., & Brem, G. (2000). Tyrosinase gene variants in different rabbit strains. *Mammalian Genome,* 11(8), 700-702. https://doi.org/10.1007/s003350010120

Anello, M., Fernández, E., Daverio, M.S., Vidal-Rioja, L., & Di Rocco, F. (2019). *TYR* Gene in Llamas: Polymorphisms and expression study in different color phenotypes. *Frontiers in Genetics,* 10, 568. https://doi.org/10.3389/fgene.2019.00568

Apar, R., Ye, X., & Lv, X. (2024). Transcriptome-based screening and validation of key genes for wool color in cashmere goats. *Genes & Genomics*, 46(10), 1239-1252. http://doi.org/10.1007/s13258-024-01562-2

Bin, B.H., Bhin, J., Yang, S.H., Shin, M., Nam, Y.J., Choi, D.H., Shin, D.W., Lee, A.Y., Hwang, D., Cho, E.G., & Lee, T.R. (2015). Membrane-Associated Transporter Protein (MATP) regulates melanosomal PH and influences tyrosinase activity. *PLoS One,* 6, e0129273. https://doi.org/10.1371/journal.pone.0129273

Brown, A.R., Comai, K., Mannino, D., McCullough, H., Donekal, Y., Meyers, H.C., Graves, C.W., & Seidel, H.S. (2022). BIO306W Consortium. A community-science approach identifies genetic variants associated with three color morphs in ball pythons (Python regius). *PLoS One,* 17(10), e0276376. https://doi.org.10.1371/journal.pone.0276376

Challa, A.K., Boitet, E.R., Turner, A.N., Johnson, L.W., Kennedy, D., Downs, E.R., Hymel, K.M., Gross, A.K., & Kesterson, R.A. (2016). Novel hypomorphic alleles of the mouse tyrosinase gene induced by CRISPR-Cas9 Nucleases cause non-albino pigmentation phenotypes. *PLoS One,* 11(5), e0155812. https://doi.org.10.1371/journal.pone.0155812

Chintala, S., Li, W., Lamoreux, M.L., & Wakamatsu, K. (2005). *Slc7a11* gene controls production of pheomelanin pigment and proliferation of cultured cells. *Proceedings of the National Academy of Sciences,* 102(31), 10964-10969. https://doi.org.10.1073/pnas.0502856102

Cieslak, M., Reissmann, M., Hofreiter, M., & Ludwig, A. (2011). Colours of domestication. *Biological Reviews of the Cambridge Philosophical Society,* 86(4), 885-99. https://doi.org.10.1111/j.1469-185X.2011.00177.x

García-Elfring, A., Roffey, H.L., Abergas, J.M., Hendry, A.P., & Barrett, R.D.H. (2025). GTP cyclohydrolase II (gch2) and axanthism in ball pythons: A new vertebrate model for pterin-based pigmentation. *Animal Genetics*, 56(2), e70011. https://doi.org.10.1111/age.70011

Garcia-Elfring, A., Roffey, H.L., Abergas, J.M., Wuyts, J., Hendry, A.P., Tzika, A.C., & Barrett, R.D.H. (2025). A Ball Python Colour Morph Implicates MC1R in Melanophore-Xanthophore Distribution and Pattern Formation. *Pigment Cell & Melanoma Research*, 38(1), e13215. https://doi.org.10.1111/pcmr.13215

Gardner, J.M., Nakatsu, Y., Gondo, Y., Lee, S., Lyon, M.F., King, R.A., & Brilliant, M.H. (1992). The mouse pink-eyed dilution gene: association with human Prader-Willi and Angelman syndromes. *Science,* 257(5073), 1121-1124. https://doi.org.10.1126/science.257.5073.1121

Ginger, R.S., Askew, S.E., Ogborn, R.M., & Wilson, S. (2008). SLC24A5 encodes a trans-golgi network protein with potassium-dependent sodium-calcium exchange activity that regulates human epidermal melanogenesis. *Journal of Biochemistry,* 283, 5486-5495. https://doi.org.10.1074/jbc.M707521200

Hammons, V., Ribeiro, L., Munyard, K., Sadeghi, R., Miller, D., Antczak, D., & Brooks, S.A. (2021). GWAS identifies a region containing the SALL1 gene in variation of pigmentation intensity within the chestnut coat color of horses. *Journal of Heredity,* 112(5), 443-446. https://doi.org.10.1093/jhered/esab037

Henkel, J., Saif, R., Jagannathan, V., Schmocker, C., Zeindler, F., Bangerter, E., Herren, U., Posantzis, D., Bulut, Z., Ammann, P., Drögemüller, C., Flury, C., & Leeb, T. (2019). Selection signatures in goats reveal copy number variants underlying breed-defining coat color phenotypes. *PLoS Genetics,* 15(12), e1008536. https://doi.org.10.1371/journal.pgen.1008536

Kokiattrakool, W., Saengcharatuaong, N., Luapan, J., Sroykham, W., Kumsiri, R., & Kanchanaphum, P. (2024). Differentiation between wild type and heterozygous albino ball pythons (Python regius) by PCR and qPCR. *Brazilian Journal of Biology,* 84, e286676. https://doi.org.10.1590/1519-6984.286676

Kulathunga, K., Wakimoto, A., Hiraishi, Y., Yadav, M.K., Gentleman, K., Warabi, E., Sakasai, T., Miwa, Y., Mizuno, S., Takahashi, S., & Hamada, M. (2021). Albino mice with the point mutation at the tyrosinase locus show high cholesterol diet-induced NASH susceptibility. *Scientific Report*, 11(1), 21827. http://doi.org.10.1038/s41598-021-00501-5

Kumsiri, R., Yin, N.N. & Kanchanaphum, P. (2025). Discrimination between wild type and heterozygous piebald ball pythons (Python regius) by PCR and qPCR. *Brazilian Journal of Biology*, 85, e293718. https://doi.org/10.1590/1519-6984.293718

Kwon, B.S., Halaban, R., & Chintamaneni, C. (1989). Molecular basis of the mouse Himalayan mutation. *Biochemical and Biophysical Research Communications*, 161(1), 252-260. https://doi.org.10.1016/0006-291x(89)91588-x

Lai, X., Wichers, H.J., Soler-Lopez, M., & Dijkstra, B.W. (2018). Structure and Function of Human Tyrosinase and Tyrosinase-Related Proteins. *Chemistry*, 24(1), 47-55. https://doi.org.10.1002/chem.201704410

Lamoreux, M.L., Wakamatsu, K., & Ito, S. (2001). Interaction of major coat color gene functions in mice as studied by chemical analysis of eumelanin and pheomelanin. *Pigment Cell & Melanoma Research,* 14(1), 23-31. https://doi.org.10.1034/j.1600-0749.2001.140105.x

Lauer, S. & Gresham, D. (2019). An evolving view of copy number variants. *Current Genetics*, 65(6), 1287-1295. https://doi.org.10.1007/s00294-019-00980-0

Lavoro, A., Falzone, L., Tomasello, B., Conti, G.N., Libra, M., & Candido, S. (2023). *In silico* analysis of the solute carrier (SLC) family in cancer indicates a link among DNA methylation, metabolic adaptation, drug response, and immune reactivity. *Frontier in Pharmacology*, 14, 1191262. http://doi.org.10.3389/fphar.2023.1191262

Liu, Y., Wang, L., Li, Z., Li, L., Ding, T., Chen, S., Duan, P., Wang, X., Qiu, Y., Ding, X., & Tian, Y. (2025). DNA methylation and transcriptome profiling reveal the role of the antioxidant pathway and lipid metabolism in *Plectropomus leopardus* skin color formation. *Antioxidants (Basel),* 14(1), 93. https://doi.org.10.3390/antiox14010093

López, S., García, I., Smith, I., Sevilla, A., Izagirre, N., de la Rúa, C., & Alonso, S. (2015). Discovery of copy number variants by multiplex amplifiable probe hybridization (MAPH) in candidate pigmentation genes. *Annals of Human Biology*, 42(5), 485-493. https://doi.org.10.3109/03014460.2014.965202

Lyons, L.A., Imes, D.L., Rah, H.C., & Grahn, R.A. (2005). Tyrosinase mutations associated with Siamese and Burmese patterns in the domestic cat (Felis catus). *Animal Genetics*, 36(2), 119-126. https://doi.org/10.1111/j.1365-2052.2005.01253.x

Miura, I., Tagami, M., Fujitani, T., & Ogata, M. (2018). Spontaneous tyrosinase mutations identified in albinos of three wild frog species. *Genes & Genetics System,* 92(4), 189-196. https://doi:org.10.1266/ggs.16-00061

Nicholas, W.B., Iliana, E.E., Ariel, J.L., & Michael, S.M. (2014). An intracellular anion channel critical for pigmentation. *eLife,* 3, e04543. https://doi.org.10.7554/eLife.04543

Ni-Komatsu, L. & Orlow, S.J. (2006). Heterologous expression of tyrosinase recapitulates the misprocessing and mistrafficking in oculocutaneous albinism type 2: effects of altering intracellular pH and pink-eyed dilution gene expression. *Experimental Eye Research*, 82(3), 519-528. https://doi.org.10.1016/j.exer.2005.08.013

Oetting, W.S., Fryer, J.P., & King, R.A. (1998). Mutations of the human tyrosinase gene associated with tyrosinase related oculocutaneous albinism (OCA1). Mutations in brief no. 204. Online. *Human Mutatation,* 12(6), 433-434. https://doi.org.10.1002/(SICI)1098-1004(1998)12:6

Orlow, S.J., Lamoreux, M.L., Pifko-Hirst, S., & Zhou, B.K. (1993). Pathogenesis of the platinum (cp) mutation, a model for oculocutaneous albinism. *Journal of Investigative Dermatology,* 101(2), 137-140. https://doi.org.10.1111/1523-1747.ep12363621

Pös, O., Radvanszky, J., Buglyó, G., Pös, Z., Rusnakova, D., Nagy, B., & Szemes, T. (2021). DNA copy number variation: Main characteristics, evolutionary significance, and pathological aspects. *Biomedical Journal,* 44(5), 548-559. https://doi.org.10.1016/j.bj.2021.02.003

Puri, N., Gardner, J.M., & Brilliant, M.H. (2000). Aberrant pH of melanosomes in pink-eyed dilution (p) mutant melanocytes. *Journal of Investigative Dermatology,* 115(4), 607-613. https://doi.org.10.1046/j.1523-1747.2000.00108.x

Sato, H., Tamba, M., Ishii, T., & Bannai, S. (1999). Cloning and expression of a plasma membrane cystine/glutamate exchange transporter composed of two distinct proteins. *Journal of Biological Chemistry,* 274(17), 11455-11458. https://doi.org.10.1074/jbc.274.17.11455

Simeonov, D.R., Wang, X., Wang, C., Sergeev, Y., Dolinska, M., Bower, M., Fischer, R., Winer, D., Dubrovsky, G., Balog, J.Z., Huizing, M., Hart, R., Zein, W.M., Gahl, W.A., Brooks, B.P, & Adams, D.R. (2013). DNA variations in oculocutaneous albinism: an updated mutation list and current outstanding issues in molecular diagnostics. *Human Mutation,* 34(6), 827-835. https://doi.org.10.1002/humu.22315

Vitavska, O. & Wieczorek, H. (2013). The SLC45 gene family of putative sugar transporters. *Molecular Aspects of Medicine,* 34, 655–660. https://doi.org.10.1016/j.mam.2012.05.014

Wang, Q.W., Qin, J., Chen, Y.F., Tu, Y., Xing, Y.Y., Wang, Y., Yang, L.Y., Lu, S.Y., Geng, L., Shi, W., Yang, Y., & Yao, J. (2023). 16p11.2 CNV gene Doc2α functions in neurodevelopment and social behaviors through interaction with Secretagogin. *Cell Reports*, 42(7), 112691. http://doi.org.10.1016/j.celrep.2023.112691

Wright, D., Boije, H., Meadows, J.R., Bed'hom, B., Gourichon, D., Vieaud, A., Tixier-Boichard, M., Rubin, C.J., Imsland, F., Hallböök, F., & Andersson, L. (2009). Copy number variation in intron 1 of SOX5 causes the Pea-comb phenotype in chickens. *PLoS Genetics,* 5(6), e1000512. https://doi.org.10.1371/journal.pgen.1000512

Wu, W., Wang, Y., Liu, Y., Guo, H., Li, Z., Zou, W., Liu, J., & Song, Z. (2023). TRPA1 promotes UVB-induced skin pigmentation by regulating melanosome luminal pH. *Experimental Dermatology*, 32(2), 165-176. http://doi:10.1111/exd.14693

Zhang, F., Gu, W., Hurles, M.E., & Lupski, J.R. (2009). Copy number variation in human health, disease, and evolution. *Annual Review of Genomics and Human Genetics,* 10, 451-81. https://doi.org.10.1146/annurev.genom.9.081307.164217