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Genetic Marvels: Exploring the Genetics Behind Heterochromia in Companion Animals

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Introduction:

Heterochromia, also known as heterochromia iridum, is a fascinating condition characterized by a contrast in the colors of the irises, resulting in multicolored eyes (Azad *et al.*, 2024). This phenomenon can affect the entire iris or just a part of it. Eye color is an example of structural coloration, where lighter-colored eyes result from Rayleigh scattering of light in the stroma. The variation in eye color is due to the amount, type, and distribution of melanin pigment produced by melanocyte cells and deposited in melanosomes. Genetics play a crucial role in determining eye color, with up to 150 genes involved. Two primary genes, OCA2 and HERC2, located on chromosome 15, are particularly significant. The OCA2 gene produces "P protein," which is essential for melanosome maturation, while the HERC2 gene regulates OCA2. Additionally, the EYCL1 (gey gene) and EYCL3 (bey2 gene) also influence iris color inheritance, with various alleles (green, blue, and brown) interacting to create a range of eye colors. Heterochromia can noticeable in numerous forms: (1) Complete Heterochromia (each eye has a completely different color), (2) Sectoral Heterochromia (portion of the iris being non-pigmented while another part is pigmented), (3) Central Heterochromia (center of the iris having a different color than the outer ring). Heterochromia is more common in animals than in humans and is usually genetic (Rahman, 2008). However, it can also result from injury or illness. Although heterochromia is still considered uncommon to rare among all animals it occurs in. Occurrence of heterochromia in cat estimated to be around 0.6% of the feline population and in dog population it varies by breed.

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Genetic Basis:

Genetic mutations can influence eye color by altering melanin levels in the iris. While many genes impact eye color, the OCA2 gene is particularly significant, influencing nearly 75% of the blue-brown color range. Various single nucleotide polymorphisms (SNPs) within the OCA2 gene are closely linked to eye color variation. Polymorphisms in the regulatory sequence of OCA2 can sometimes affect gene expression and, consequently, pigmentation. The HERC2 gene regulates OCA2 expression, and a specific mutation within HERC2 contributes to the presence of blue eyes. In addition to that polymorphisms in the OCA2 gene can reduce the production of P protein, resulting in lower melanin levels and lighter eye colors. Other genes contributing to eye color include HERC2, ASIP, IRF4, SLC24A4, SLC24A5, SLC45A2, TPCN2, TYR, and TYRP1. Genetic expression can also cause variations such as heterochromia, where an individual has different colors in each eye, or ocular albinism, characterized by a complete lack of pigmentation.

Breeds and Species Affected:

Cat breeds commonly exhibiting heterochromia include British Shorthairs, Cornish and Devon Rex, Japanese Bobtails, Munchkins, Persians, Scottish Folds, Siamese, Sphynxes, Turkish Angoras, and Turkish Vans. In dogs, heterochromia is often seen in Australian Cattle Dogs, Australian Shepherds, Border Collies, Chihuahuas, Dachshunds, Dalmatians, Great Danes, Shetland Sheepdogs, Siberian Huskies, and Shih Tzus.

Clinical Manifestation:

Eye color in animals typically changes from lighter to darker shades within the first year of life, predominantly between 3 and 6 months of age, influenced by adrenergic innervation. Animals with heterochromia generally have a good prognosis and typically do not experience visual issues. If an animal does have associated vision problems, treating the underlying condition usually resolves the issue. Heterochromia can be classified by onset as either congenital or acquired. Congenital heterochromia is often inherited as an autosomal dominant trait, while acquired heterochromia can result from injury, inflammation, certain eye medications, or tumors that damage the iris. Congenital heterochromia, present in animals from birth, is not inherently dangerous and is not typically linked to any health conditions. The exception is Dalmatians with partial or sectoral heterochromia, who may have an increased risk of deafness. Acquired heterochromia mainly associated with eye injury, glaucoma, swelling, neuroblastoma, eye cancer and certain medicines, including glaucoma drugs such as bimatoprost and latanoprost in animals.

Diagnostic evaluation:

Heterochromia in dogs and cat can be diagnosed by following methods, Physical examination (Visual inspection & Light examination), Medical history (Genetic background & Health history), Ophthalmic examination (Slit lamp examination & Fundoscopy), Genetic testing

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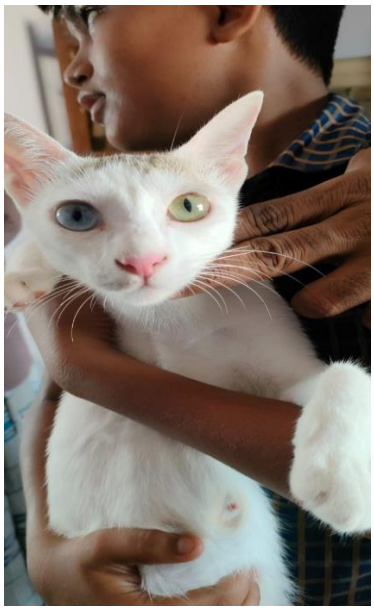
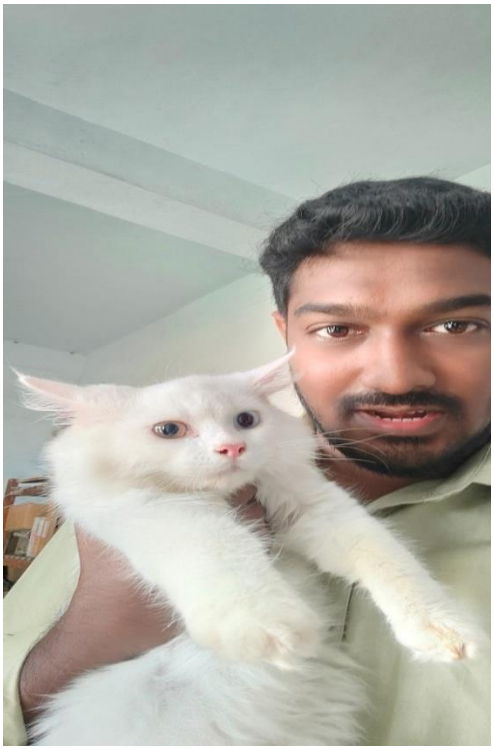
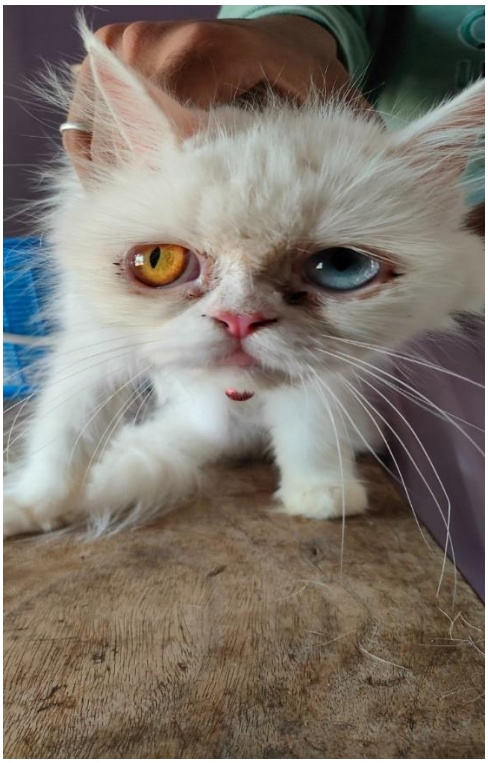
(DNA analysis & breed specific testing), Imaging technique (Ultrasound & MRI/CT scan), Laboratory tests (Blood tests & Biopsy) and Neurological examination (Pupil reflex testing & Neurological history) (Wolfs *et al.*, 2024).







Management and care:

Regular veterinary check-ups are essential for pets with heterochromia, including annual visits and ophthalmic examinations to monitor overall health and eye condition. Maintaining eye hygiene involves regularly cleaning around the eyes and inspecting for redness, swelling, or

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discharge, which could signal infection or irritation. To protect their eyes, pets should be kept away from smoke, dust, and other potential irritants and their exposure to bright sunlight should be limited by providing shaded areas. A balanced diet rich in essential vitamins and minerals, along with supplements such as omega-3 fatty acids, supports eye health (Oluwole *et al.*, 2011). Monitoring for behavioral changes, which are often linked to vision problems, as well as changes in eye color, helps in the early detection of issues. Addressing underlying conditions like eye infections or injuries and managing chronic eye diseases can prevent complications. Ensuring a safe living environment, free from hazards, and encouraging gentle play can help prevent eye injuries and trauma. By adhering to these routine care guidelines, pet owners can effectively ensure the health and well-being of their pets with heterochromia, addressing any potential issues promptly

Conclusion and Future Prospects:

Heterochromia, a condition characterized by contrasting iris colors, is a fascinating phenomenon observed more frequently in animals than humans. The variation in eye color, determined by the amount and distribution of melanin, is influenced by genetic factors, particularly the OCA2 and HERC2 genes. This condition, which can be congenital or acquired, generally does not pose health risks to animals. Regular veterinary care, including eye examinations and maintaining a safe, clean environment, is crucial for the health and well-being of pets with heterochromia.

Future research into the genetic markers associated with heterochromia will likely provide deeper insights into the complex interplay of genes involved in eye color variation. Advancements in genetic testing and diagnostic techniques will improve the ability to identify and manage heterochromia and related ocular conditions. Additionally, further studies on the impact of environmental factors and potential treatments for acquired heterochromia could lead to better preventative measures and therapeutic options. Continued exploration in this field holds the promise of enhancing our understanding and care of animals with this unique condition, ensuring they lead healthy, fulfilling lives.

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