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Biology 490S: Genetics of Interactions
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Cryptic Camouflage in Different Types of Mice: a Look into Adaptive Genetics

Crypsis, when the prey uses some aspect of their environment in order to avoid predation, is highly important for field mice. For many species of mouse, coat color is important in avoiding predation, as many species camouflage with their environments in order to survive. Two genes, *MC1R* and *Agouti*, are responsible for many of the variation in coat color, especially in *Chaetopidus intermedius* and *Peromyscus maniculatus,* respectively (Hoekstra & Nachman, 2003; Linnen et al. 2013).

In pocket mice, *C. intermedius*, the gene of importance is *MC1R*, or melanocortin-1-receptor, which is most important in pigmentation. *MC1R* codes for a transmembrane G-coupled protein that is prevalent in melanocytes, or pigment producing cells (Hoekstra & Nachman, 2006). Melanocyte-stimulating hormone activates MC1R and results in higher production of eumelanin, producing black or brown pigments (Hoekstra & Nachman, 2006). This association of *MC1R* with coat color has been studied at length. Hoekstra and Nachman took samples of pocket mice from four different regions in the Pinacate lava bed in southern Arizona; each of the regions had a lava flow and an adjacent light rock region, so that similar samples could be taken across regions (Hoekstra & Nachman, 2006). They found that several *MC1R* SNPs were perfectly associated with coat color types (Hoekstra & Nachman, 2006). Furthermore, four amino acid polymorphisms were found to control coat color, and as they are in complete linkage disequilibrium, mice with one or two copies of this allele are termed melanic, while mice without this allele are light colored (Hoekstra & Nachman, 2006). The *MC1R* D allele is

distinguished from the d allele by four amino acid substitutions and one synonymous substitution (Nachman, 2004). Mice with the DD and Dd polymorphisms have dark, melanic hairs, while mice with the dd genotype have light coloration; further, the D allele is dominant over the d allele (Nachman, 2004).

The coloration of mice is an extremely important type of clinal variation because it allows for predator avoidance. Previous work has shown that in some species of mice—for example, *Peromyscus maniculatus*—dark coloration on a dark substrate leads to decreased risk of predation by owls and other visual predators as compared to light coloration on a dark substrate, and that dark colored *P. manisculatus* have decreased fitness on light substrate (Dice 1947). Although a similar test has not been done on *C. intermedius*, it is expected that their coloration also serves as an antipredator adaptation because the degree of substrate matching is so much higher than that of *P. manisculatus* (Hoekstra et al, 2004). Hoekstra et al demonstrated that strong selection acts on *MC1R* allele frequencies in order to match coat and substrate color by comparing the distribution of alleles at *MC1R* to alleles at two neutral DNA and mtDNA loci, as well as estimating *MC1R* allele frequencies and migration rates between sites to find a nonrandom distribution of alleles across different-colored substrates in *C. intermedius*, suggesting that selection has acted upon these alleles to increase fitness on a given substrate (Hoekstra et al, 2004). Through phenotypic data collection, a high degree of substrate matching was found: melanic mice were most abundant on dark substrate and light mice more on light rock; however, there was a deficiency of light mice on dark rock, suggesting a very high association of color-substrate matching to avoid predation (Hoekstra et al, 2004). Survival of dark mice on light substrate was influenced by the

proximity of the light substrate to the closest dark substrate (Hoekstra et al, 2004). All these studies point to the idea that cryptic coloration in *C. intermedius* is paramount for survival and that this substrate-matching coloration, caused by the *MC1R* D and d alleles, has been highly selected for to ensure survival.

In deer mice, *Peromyscus maniculatus*, the gene of interest is not *MC1R*, but *Agouti*, which codes for a paracrine-signaling molecule that normally regulates pigmentation in mice by antagonizing the effects of melanocyte stimulating hormones (Linnen et al, 2013; Ollmann et al, 1998). Production of Agouti in the dermis of mice causes follicular melanocytes to produce pheomelanin, which gives rise to yellow and red pigments, as opposed to the brown and black pigments produced by eumelanin that is activated by MC1R (Ollmann et al, 1998). This distinction in coloring is especially important in deer mice that colonize the light-colored soils of the Nebraska Sand Hills because it allows predation avoidance of visually hunting predators, such as owls (Linnen et al, 2013). As compared to the wild type *P. maniculatus*, Sand Hills deer mice have a significantly lighter dorsum, a lighter ventrum, and an upward shift of the dorsal-ventral boundary, all of which suggest that selection has acted upon these mice in order to ensure survival through cryptic camouflage (Linnen et al, 2013). These coloring patterns were mapped to a serine deletion in Agouti in exon 2, which is a conserved residue in an area that interacts with Attractin, another pigment protein (Linnen et al, 2009; Linnen et al, 2013). The banding patterns of hairs are extremely important in conferring survival; melanocytes at the base of follicles can switch between producing eumelanin and pheomelanin (Linnen et al, 2009). The pheomelanic band on Sand Hills deer mice in Nebraska is markedly wider than in their darker relatives, which has been dubbed the

"wideband" phenotype (Linnen et al, 2009). *Agouti* is known as being responsible for this coloration and phenotype. After performing an adrenalectomy on deer mice, dark coloration occurs in one to three months, especially in the extremely light ventral areas, going from light tan to almost black (Bronson & Clarke, 1966). In deer mice, contrary to the previously discussed pocket mice, the light phenotype is dominant over dark; however, it was found that there was no correlation of coloration phenotype with geography, suggesting that deer mice do not mate solely based on color and that a good amount of recombination occurs in order to maintain color variation based on background (Linnen et al, 2009). Additionally, it was observed that a significant amount of positive selection was acting on the wideband haplotype but not the surrounding chromosomes, meaning that selection is most likely happening on the wideband haplotype in order to avoid predation (Linnen et al, 2009).

Overall, both these mice models use cryptic coloration as a means of survival; although the genes and coloration they use are different, there is some overlap. Agouti is the antagonist of MC1R, acting directly against the coloration patterns employed by *MC1R*. As previously discussed, *Agouti* acts by inhibiting melanocyte stimulating hormones, leading to a cis-acting increase in the duration and magnitude of *Agouti* expression to give rise to light coloration; however, *Agouti* also binds to *MC1R* in order to inhibit it and increase *Agouti* expression (Ollmann et al, 1998; Linnen et al, 2013). As such, these two genes and their subsequent proteins are always working in tandem to provide coloration in different species of mice, it just depends which phenotype is the more dominant; in pocket mice, the dark phenotype is dominant, causing *MC1R* to play a larger role, and in deer mice, the light phenotype is dominant, causing a greater

expression of *Agouti*. It remains, though, that cryptic coloration is paramount for survival in mouse population to avoid predation, and that this coloration has been strongly selected for in order to ensure this survival.

Works Cited

Bronson, F. H., and S. H. Clarke. “Adrenalectomy and Coat Color in Deer Mice.” *Science (New York, N.Y.)* 154, no. 3754 (December 9, 1966): 1349–50.

Hoekstra, H. E., and M. W. Nachman. “Different Genes Underlie Adaptive Melanism in Different Populations of Rock Pocket Mice.”*Molecular Ecology* 12, no. 5 (May 2003): 1185–94.

Linnen, Catherine R., Evan P. Kingsley, Jeffrey D. Jensen, and Hopi E. Hoekstra. “On The Origin and Spread Of an Adaptive Allele In Deer Mice.” *Science (New York, N.Y.)* 325, no. 5944 (August 28, 2009): 1095–98. doi:10.1126/science.1175826.

Linnen, Catherine R., Yu-Ping Poh, Brant K. Peterson, Rowan D. H. Barrett, Joanna G. Larson, Jeffrey D. Jensen, and Hopi E. Hoekstra. “Adaptive Evolution of Multiple Traits Through Multiple Mutations at a Single Gene.” *Science (New York, N.Y.)* 339, no. 6125 (March 15, 2013). doi:10.1126/science.1233213.

Nachman, Michael W. “The Genetic Basis of Adaptation: Lessons from Concealing Coloration in Pocket Mice.” *Genetica* 123, no. 1–2 (February 2005): 125–36.

Ollmann, Michael M., M. Lynn Lamoreux, Brent D. Wilson, and Gregory S. Barsh. “Interaction of Agouti Protein with the Melanocortin 1 Receptor in Vitro and in Vivo.” *Genes & Development* 12, no. 3 (February 1, 1998): 316–30.http://www.ncbi.nlm.nih.gov/pmc/articles/PMC316484/.