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Evolution: Out of the shadows and into the light

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While many species are active during specific time periods throughout the day, there is significant variation across species in preferred daily temporal niche. A new study investigates the molecular changes that occurred in a mammal that has evolved diurnality.

Daily cycles, which include alternations between daylight and the darkness of night, are one of the defining ecological features of habitats on Earth's surface. Multiple factors, including presence of other individuals competing for the same resources, type of predators, and availability of sensory cues, vary over the course of a day[1,2]. Thus, many animals have evolved to be active at defined times. As day and night present different ecological challenges, a number of morphological, physiological, and behavioral traits vary in accordance with diel niche, the time period during which an organism is active[3,4]. However, while diel niche preference varies widely across species, the molecular mechanisms underlying adaptations to diel niches remain largely unknown. A study published in a recent issue of *Current Biology* by Richardson *et al.* uses genomic approaches to identify molecular variation in diel niche-associated traits in the African striped mouse, *Rhabdomys pumilio*[5] (Figure 1).

Extant mammals are hypothesized to have evolved from nocturnal ancestors, which, because they evolved to be endothermic, could be active at night and reduce predation from and competition with diurnal species of dinosaurs that could not occupy the nocturnal niche due to their need for the sun to temperature regulate[1,6]. Following this early bottleneck, different species of mammals have expanded into different temporal niches multiple times. For example, analysis of activity patterns of 700 species from the order Rodentia suggests that at least seven shifts from nocturnal to diurnal or both nocturnal and diurnal activity occurred at the family level within Rodentia alone[7]. Understanding these transitions and the mechanisms that contribute to adaptation to a temporal niche are critical to understanding diversity. However, identifying the molecular mechanisms underlying adaptations in response to a shift in preferred diel niche is challenging when comparing distantly related species with limited genetic and genomic resources.

The African striped mouse is a small rodent from the family *Muridae*, which diverged from species commonly used in laboratories, *Mus* and *Rattus*, about 5–6 million years ago[8]. Similar to its relative the laboratory mouse, the striped mouse can live and breed in laboratory colonies and is amenable to many developmental and molecular techniques[8], allowing for investigation into the genetic and developmental mechanisms underlying morphology and behavior. However, unlike lab mice and many other muroid rodents, striped mice are diurnal[8]. Thus, striped mice provide an excellent model to investigate how traits associated with a diel niche shift have evolved.

To investigate this question, Richardson *et al.*[5] first sequenced and annotated the striped mouse genome. The assembled genome is high quality and near chromosome level: 24 scaffolds contain ~95% of the assembled genome[5]. This genome will serve as a valuable resource for comparative genomic and functional genetic work in the future. For example, striped mice have a number of interesting traits that can be investigated from a genetic perspective, including dorsal stripes[9] and paternal care[10]. In their recent study, Richardson *et al.*[5] leverage this genome to investigate the evolutionary shift from nocturnality to diurnality.

Activity throughout the day is regulated by internal biological clocks. Thus, understanding if and how the molecular components of the biological clock vary between organisms is critical to understanding the mechanisms underlying evolution of diel niche preference. In mammals,

Figure 1. The African striped mouse, *Rhabdomys pumilio*.
Image from Bernard Dupont/Wikimedia Commons (CC BY-SA 2.0).

circadian timekeeping is composed of multiple clocks organized in a hierarchical fashion, with neurons in the suprachiasmatic nucleus (SCN), located within the hypothalamus, functioning as the master circadian clock which directs circadian clocks throughout other regions of the brain and peripheral tissues[11]. While only the oscillator within the SCN can be entrained to light, rhythmic expression of clock genes, which form positive and negative feedback loops that interact to generate circadian oscillations, is found within cells of both the SCN and peripheral tissues[11].

Expression of clock genes has been studied in nocturnal and diurnal mammals. These studies have revealed that the oscillation of expression of the majority of the core clock genes within the SCN is similar relative to the light:dark cycle in both nocturnal and diurnal mammals, suggesting that changes in preferred time of activity are due to downstream mechanisms[12]. Comparisons of clock gene expression in peripheral tissues between multiple diurnal and nocturnal mammals have found that rhythmic expression of these genes in peripheral tissues is often reversed in diurnal mammals compared to nocturnal mammals[12]. Thus, changes in phase of rhythmic expression of clock genes between the central and peripheral clocks may be an important component of the evolution of diel niche preferences.

To determine the phases of expression of rhythmic genes relative to the light:dark cycle in striped mice, RNA-sequencing was performed on tissue collected during the day and at night from the SCN, the retina, the lung and the liver harvested from animals entrained to a 12:12 light:dark cycle. Analysis of gene expression of core clock genes in the day compared to the night revealed that while expression of many of these genes differed depending on time of day, expression was similar in the SCN and the peripheral tissues in the striped mice[5]. This result was further supported by RNA-sequencing results obtained by sampling these tissues every hour over the course of 24 hours in constant darkness. While this analysis identified fewer genes with rhythmic gene expression, for those clock genes that showed rhythmic expression, the results were largely consistent with phased rhythmic gene expression between the SCN and the peripheral tissues[5]. These data suggest that, similar to other diurnal mammals that have been investigated, striped mice maintain the phase of gene expression of components of the circadian clock relative to nocturnal mammals in the SCN, while they change the phase of expression of these genes in peripheral tissues[5,12]. Thus, this shift in phase of expression of clock genes in peripheral tissues may represent a common mechanism by which diurnality evolves in mammalian species. Further, this work establishes striped mice as a model for studying molecular changes in circadian rhythms in response to diel niche shift and may provide insight into the mechanisms by which changes in phase of circadian gene expression in peripheral tissues occur.

One of the ways to understand how a species has adapted to an environmental change is to identify whether individual genes or groups of genes affecting certain biological processes or traits have been impacted by selection. Relative evolutionary rates were calculated for protein coding transcripts from orthologous genes across the genomes of the striped mouse and other murid species. This analysis identified genes which show faster rates of evolution relative to the background rate in the striped mouse. Pathway analysis of genes with accelerated evolutionary rates revealed enrichment for functions related to the rhodopsin-mediated phototransduction cascade, suggesting changes to selective pressure on the function of rods, the photoreceptor cells responsible for vision in low-light, in striped mice[5]. Accelerated evolution of genes could be due to positive selection for changes in rod function or, alternatively, relaxation of purifying selection. Further analysis suggested that the latter is likely the case. Thus, relaxation of purifying selection at these loci is possibly a result of reduced need for dim light vision following a shift to daytime activity in striped mice[5].

If striped mice rely less on dim-light vision than nocturnal rodents, they might be expected to perform less well in tests of visual performance under dim-light conditions. To directly examine this, visual performance was tested in striped mice and laboratory mice by electroretinography under dim- and bright-light conditions. Reduced visual performance of striped mice was found specifically under dim-light conditions[5]. While additional work is required to directly link genetic variation in the genes exhibiting accelerated evolution to functional differences in dim-light vision, these data are consistent with relaxation of purifying selection affecting vision under dim-light conditions in the diurnal striped mouse. Thus, this work adds to our understanding of the visual adaptations associated with diel niche across a wide

range of species, including ants[13], snakes[14] and birds[15].

Together, Richardson *et al.*[5] take a range of approaches to identify molecular correlates of functional changes that may contribute to a temporal niche shift in striped mice. Moreover, their work further establishes the African striped mouse as a powerful model for studying the genetic variation associated with adaptation of the visual system following a diel niche shift and a range of other phenotypes.

DECLARATION OF INTERESTS

The author declares no competing interests.

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Memory: Meet the new engram, same as the old engram

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A new study shows that while the neuronal organization of a memory changes with time, including greater cortical engagement, a core ensemble exists in the CA1 region of the dorsal hippocampus that is necessary for retrieval of both a recent and remote memory.

The concept of a stable neural correlate of memory, referred to as a *memory trace* or an *engram ensemble,* gained traction with the ability to tag and subsequently manipulate neurons active during a training event. These neurons active during training (engram ensemble neurons) are necessary for memory retrieval and sufficient to drive behavior consistent with memory retrieval in the days after the event[1,2]. However, memories are thought to reorganize over time, in a process known as systems consolidation[3]. For instance, initially hippocampal-dependent memories become increasingly dependent on the cortex, including the anterior cingulate cortex (ACC), over time such that the hippocampus may not even be necessary for the retrieval of the memory at remote time points[4,5]. How can these observations be reconciled? Are memories encoded in stable memory traces or is there a wholesale reorganization of memory? As with many findings in science that appear at first blush to be fundamentally opposed, the ground truth may lie somewhere in the middle. In this issue of *Current Biology*, Refaeli *et al.*[6] combine a variety of elegant techniques to show that neuronal circuits supporting a contextual fear memory in mice do indeed reorganize over time, with the ACC becoming increasingly important, but that a sparse population of engram ensemble neurons in the CA1