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News and Views

A rod cell marker of nocturnal ancestry

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In a recent *Cell* article, Solovei et al. (2009) have shown that the rod cell nuclei of nocturnal and diurnal mammals (including primates) are organized in distinct patterns, and that the nocturnal-associated pattern likely facilitates efficient photon capture by the photoreceptors. Their research underscores the exceptional selective pressures placed on the visual system in low light environments and provides a new marker of nocturnal ancestry. This marker can be used to advance our understanding of activity pattern evolution, potentially including the behavioral ecology of ancestral primates.

Distinct rod nuclear architectures of diurnal and nocturnal mammals

In the interphase cell, DNA is organized at multiple inter-related levels. At one level there are two principal types of chromatin, the structural combination of DNA and proteins (especially histones) of which chromosomes are composed. Gene-poor regions are packed densely as heterochromatin, and gene-rich regions are decondensed as euchromatin. The relative openness of euchromatin may facilitate regulatory transcription factor binding and gene expression, although in heterochromatin these processes are not inhibited completely (Misteli, 2007). At another organizational level, euchromatin typically occupies the nuclear interior while heterochromatin is distributed primarily at the nuclear periphery (Kosak et al., 2007; Misteli, 2007). This particular spatial organization – hereafter referred to as the 'conventional architecture' – is nearly universal among eukaryotic cells (Habermann et al., 2001; Tanabe et al., 2002; Alexandrova et al., 2003; Postberg et al., 2005) and is considered important for the precise control of complex gene expression programs (Schneider and Grosschedl, 2007; Sexton et al., 2007; Finlan et al., 2008; Reddy et al., 2008).

A striking exception to the conventional architecture is found in the mouse rod photoreceptor (Carter-Dawson and LaVail, 1979). In these cells, heterochromatin occupies the center of the nucleus and euchromatin is relegated to the periphery. Solovei et al. (2009) characterized in detail this 'inverted architecture' of mouse rod cells and performed comparisons with a diversity of other mammals. The inverted architecture was observed in the rod cells of other nocturnal species, while the conventional pattern was associated with diurnal activity (Fig. 1a). Among primates, the rod nuclei of the nocturnal pygmy mouse lemur (*Microcebus myoxinus*) and the diurnal long-tailed macaque (*Macaca fascicularis*) are organized in the inverted and conventional architectures, respectively.

What might explain the association of the inverted architecture with nocturnality? Solovei et al. (2009) used quantitative phase contrast microscopy and computer simulations to show that the mouse rod nuclei with dense heterochromatic centers act as converging lenses, achieving a more efficient light transmission (note that photons must pass through the nucleus to the rhodopsin-containing segment of the rod cell), compared to the conventional architecture (Fig. 1b). Therefore, the inverted architecture that characterizes the rod cell nuclei of nocturnal mammals is likely an adaptation that maximizes photon capture in low light environments. The inverted architecture is unique to mammals and probably evolved in a common (nocturnal) mammalian ancestor, followed by independent reversions to the conventional architecture in multiple lineages that have shifted to diurnal activity patterns (Solovei et al., 2009). Absent the intense selective pressures imposed by night vision, the conventional pattern of nuclear architecture is likely advantageous.

Implications for current debates about primate origins

A number of hard and soft tissue phenotypes, now including rod nuclear architecture, are potential indicators of activity pattern in mammals (Table 1). Generally, the primate common ancestor is reconstructed to have been nocturnal (e.g., Martin, 1990; Sussman, 1991; Heesy and Ross, 2001; Ravosa and Savakova, 2004; Ravosa and Dagosto, 2007; Ross et al., 2007; Ross and Kirk, 2007). Recently,

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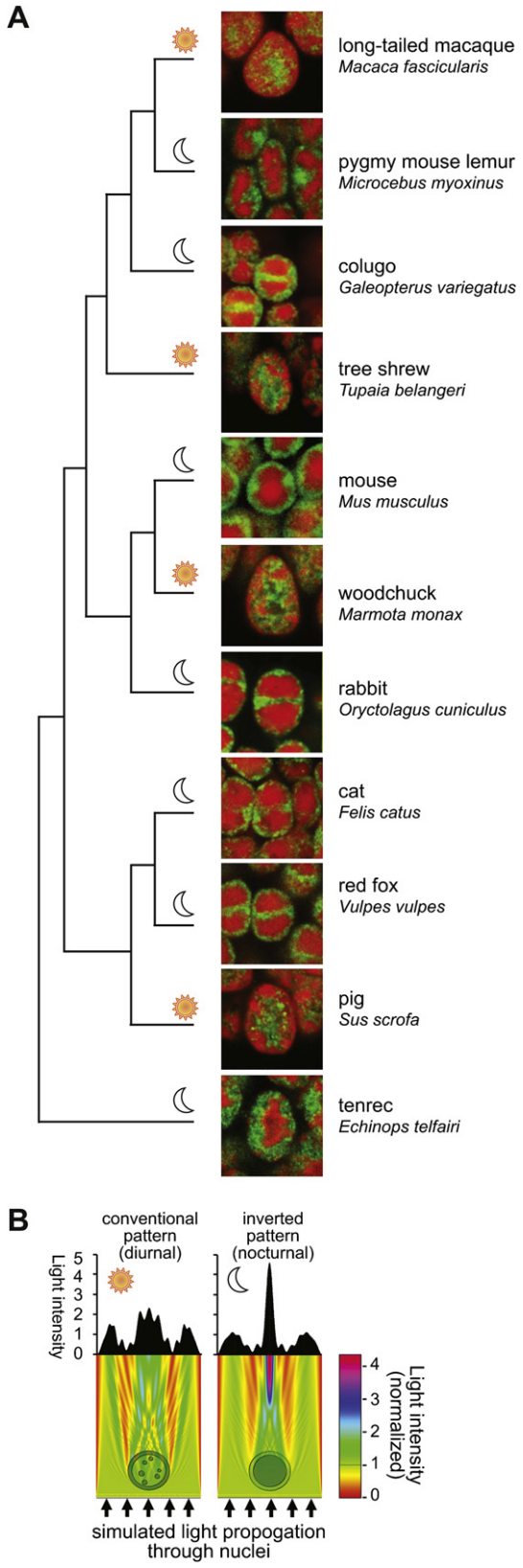

however, this standard view has been questioned (Tan et al., 2005; Lucas et al., 2007; Ankel-Simons and Rasmussen, 2008), in part based on a new appreciation of visual system diversity among extant nocturnal primates. Specifically, some taxa – dwarf lemurs, lorisoids, and night monkeys – probably have monochromatic vision resulting from functional loss of the blue-sensitive opsin gene (Jacobs et al., 1996; Tan et al., 2005). Yet in other lineages – mouse lemurs, *Avahi*, *Lepilemur*, aye-ayes, and tarsiers – both the blue and the green/red-sensitive opsin genes are intact (Tan et al., 2005). The corresponding cone types are present in the retina of at least two of these taxa (Hendrickson et al., 2000; Dkhissi-Benyahya et al., 2001), signifying the functional viability of both opsins and the capacity for dichromacy, which is likely the ancestral mammalian state. Assuming that nocturnality would necessarily lead to monochromacy, Tan et al. (2005) concluded that the primate common ancestor was either diurnal or cathemeral, followed by at least seven independent shifts to nocturnality. Some of these shifts must have been relatively recent, so that mutations that otherwise would disable the blue opsin gene have not had sufficient opportunity to occur and accumulate by genetic drift (Tan et al., 2005).

Based on a population analysis of aye-aye opsin gene sequences, the assumption underlying Tan et al.'s conclusion (2005) has been questioned by the suggestion that color vision may be adaptive for some primates even under nocturnal conditions (Perry et al., 2007). This possibility is supported by recent research on nocturnal bats. While the blue opsin gene has been lost in some lineages, two opsins have been maintained intact over many millions of years in others (Wang et al., 2004; Zhao et al., 2009a; Zhao et al., 2009b), echoing the diversity observed among nocturnal primates. Moreover, if tarsier activity pattern continuity can be inferred from morphological similarities with the middle Eocene fossil *Tarsius eocaenus* (Rossie et al., 2006), then this implies the maintenance of two opsins (and likely dichromacy) in a nocturnal lineage for >45 M.yr.

While the possibility of adaptive color vision for some nocturnal primates may be exciting, this would not necessarily help us to answer questions about primate origins, because the opsin evidence would be compatible with any possible ancestral state: nocturnal, cathemeral, or diurnal. Other soft tissue activity pattern markers are subject to convergence (e.g., Martin and Ross, 2005; Peichl, 2005) and thus may not be useful for ancestral inference based on extant taxa observations, and we lack recognizable fossils from appropriate time periods (Tavare et al., 2002) to address this issue more directly with hard tissue markers.

Can we now use rod cell nuclear architecture to retrodict the likely activity pattern of the primate common ancestor as nocturnal or cathemeral, given that the inverted architecture is observed in

Fig. 1. Phylogenetic and functional analyses of rod cell nuclear organization. Images adapted from Solovei et al. (2009) with permission from Elsevier and the authors. (A) Immunostaining of rod nuclei from retinal sections. Heterochromatin is stained with DAPI (red). An antibody against histone 3 tri-methylated lysine 4 (H3K4me3; green) marks euchromatin (Litt et al., 2001; Noma et al., 2001; Bernstein et al., 2005). Conventionally, heterochromatin localizes predominantly to the nuclear periphery while euchromatin is in the nuclear interior. Such an architecture is observed in the rod cells of diurnal mammals (as well as the nuclei of non-rod cell types, not shown). The inverted architecture is observed in the rod cell nuclei of nocturnal mammals. Depicted phylogenetic relationships are based on the recent literature (Janecka et al., 2007; Murphy et al., 2007). Sun and moon symbols identify diurnal and nocturnal taxa, respectively. (B) Simulated light transmission (wavelength=500 nm, the peak sensitivity of rod photoreceptors) through conventional- and inverted-architecture nuclei. In the illustrated nuclei, darker shading represents heterochromatin (corresponding to the red-stained regions in part A of the figure) while unshaded regions represent euchromatin (green-stained regions in part A). Heatmaps depict light intensities at points beyond the nuclei (arrows indicate light direction), with intensities from the top margin of the heatmap plotted above. Light must pass through the nucleus to reach the rhodopsin-containing segment of the rod cell. Inverted-architecture nuclei act as converging lenses to focus light at relatively increased intensity.

Table 1
Phenotypes reportedly associated with nocturnal activity pattern in mammals.

Phenotype	Comments
Tapetum lucidum (Nicol, 1981)	While diurnal lemurs have tapeta (Martin and Ross, 2005) there is uncertainty about this for cathemeral lemurs (Kirk, 2006b). The absence of tapeta in secondarily nocturnal tarsiers and night monkeys may partly explain their hypertrophied orbits and eyes (Kay and Kirk, 2000). Structural and chemical variation of tapeta among different mammalian orders suggests convergence (Martin and Ross, 2005).
Relatively large cornea to eye size (Kirk, 2004)	Cathemeral lemurs have intermediate morphology (Kirk, 2006b).
Relatively large orbital aperture size (Kay and Cartmill, 1977)	May distinguish only smaller-sized primates (Kay and Cartmill, 1977). Cathemeral lemurs have intermediate morphology (Kay and Kirk, 2000). Not strictly correlated with eye size (Kirk, 2006a).
Relatively high rod:cone ratio (Wikler and Rakic, 1990)	To our knowledge, a comprehensive, comparative analysis of this trait among nocturnal, diurnal, and cathemeral lemurs has not yet been conducted.
Relatively high summation of photoreceptors to ganglion cells (Kay and Kirk, 2000)	Sensitivity in low light conditions requires neuronal input summed from multiple photoreceptors. Acuity is higher with less retinal summation, when there is closer to a 1:1 ratio between rod/cone photoreceptors and ganglion cells. Excepting the haplorhine fovea, the rods and cones of all mammals have at least some degree of summation (Peichl, 2005).
Relatively narrow optic foramen compared to orbit diameter, body-size adjusted (Kay and Kirk, 2000)	Optic foramen area is strongly correlated with optic nerve area and fiber number and thus may be a proxy for retinal summation (Kirk and Kay, 2004). Cathemeral lemurs have intermediate morphology with some overlap of both diurnal and nocturnal strepsirrhines (Kay and Kirk, 2000). To our knowledge, there has not yet been a comprehensive comparison of this trait between nocturnal and diurnal non-primate mammals. Therefore, extrapolations to the primate fossil record are still tentative (Martin, 2004; Martin and Ross, 2005).
Monochromacy - functional loss of blue opsin (Tan et al., 2005)	This phenotype is a characteristic of some nocturnal mammals (Bowmaker and Hunt, 2006), yet multiple nocturnal primates and bats maintain an intact blue opsin gene (Wang et al., 2004; Tan et al., 2005; Zhao et al., 2009a; Zhao et al., 2009b). Therefore, this trait is likely not a definitive marker of nocturnal ancestry.
Rod inverted nuclear architecture (Solovei et al., 2009)	Rod nuclear architecture is not yet known for tarsiers, cathemeral and diurnal lemurs, or in detail for night monkeys.

the rod cells of the pygmy mouse lemur? The answer depends on the plasticity of the character. Solovei et al. (2009) favor a single-origin model for the inverted architecture; however, this hypothesis is difficult to test. Assuming that other platyrrhines share the conventional rod nuclear architecture with catarrhines (e.g., long-tailed macaques), it will be informative to discern the rod nuclear architecture of night monkeys (and other secondarily nocturnal mammals, including tarsiers, though we could not assume *a priori* a conventional architecture for the haplorhine common ancestor). In their supplementary information, Solovei et al. (2009) write that the pattern in night monkeys appears unlike those of other nocturnal mammals, but a comprehensive study has yet to be undertaken. An accounting of the genetic and developmental bases underlying the inverted architecture would make homology assessments even more definitive. This aim may not be unrealistic given the intense interest in the role of nuclear organization on gene regulatory processes (Misteli, 2007; Sutherland and Bickmore, 2009) and the availability of the mouse as a model organism for this trait. Continuing investigations will thus represent an intersection among the fields of cellular biology, molecular genetics, and evolutionary anthropology.

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References

Alexandrova, O., Solovei, I., Cremer, T., David, C.N., 2003. Replication labeling patterns and chromosome territories typical of mammalian nuclei are conserved in the early metazoan Hydra. Chromosoma 112, 190–200.
Ankel-Simons, F., Rasmussen, D.T., 2008. Diurnality, nocturnality, and the evolution of primatevisual systems. Yearb. Phys. Anthropol. 47, 100–117.
Bernstein, B.E., Kamal, M., Lindblad-Toh, K., Bekiranov, S., Bailey, D.K., Huebert, D.J., McMahon, S., Karlsson, E.K., Kulbokas 3rd, E.J., Gingeras, T.R., Schreiber, S.L., Lander, E.S., 2005. Genomic maps and comparative analysis of histone modifications in human and mouse. Cell 120, 169–181.
Bowmaker, J.K., Hunt, D.M., 2006. Evolution of vertebrate visual pigments. Curr. Biol. 16, R484–489.
Carter-Dawson, L.D., LaVail, M.M., 1979. Rods and cones in the mouse retina. I. Structural analysis using light and electron microscopy. J. Comp. Neurol. 188, 245–262.
Dkhissi-Benyahya, O., Szel, A., Degrip, W.J., Cooper, H.M., 2001. Short and mid-wavelength cone distribution in a nocturnal Strepsirrhine primate (*Microcebus murinus*). J. Comp. Neurol. 438, 490–504.
Finlan, L.E., Sproul, D., Thomson, I., Boyle, S., Kerr, E., Perry, P., Ylstra, B., Chubb, J.R., Bickmore, W.A., 2008. Recruitment to the nuclear periphery can alter expression of genes in human cells. PLoS Genet. 4, e1000039.
Habermann, F.A., Cremer, M., Walter, J., Kreth, G., von Hase, J., Bauer, K., Wienberg, J., Cremer, C., Cremer, T., Solovei, I., 2001. Arrangements of macro- and microchromosomes in chicken cells. Chromosome Res. 9, 569–584.
Heesy, C.P., Ross, C.F., 2001. Evolution of activity patterns and chromatic vision in primates: morphometrics, genetics and cladistics. J. Hum. Evol. 40, 111–149.
Hendrickson, A., Djajadi, H.R., Nakamura, L., Possin, D.E., Sajuthi, D., 2000. Nocturnal tarsier retina has both short and long/medium-wavelength cones in an unusual topography. J. Comp. Neurol. 424, 718–730.
Jacobs, G.H., Neitz, M., Neitz, J., 1996. Mutations in S-cone pigment genes and the absence of colour vision in two species of nocturnal primate. Proc. Biol. Sci. 263, 705–710.
Janecka, J.E., Miller, W., Pringle, T.H., Wiens, F., Zitzmann, A., Helgen, K.M., Springer, M.S., Murphy, W.J., 2007. Molecular and genomic data identify the closest living relative of primates. Science 318, 792–794.
Kay, R.F., Cartmill, M., 1977. Cranial morphology and adaptations of *Palaechthon nacimienti* and other Paromomyidae (Plesiadapoidea, ? Primates), with a description of a new genus and species. J. Hum. Evol. 6, 19–53.
Kay, R.F., Kirk, E.C., 2000. Osteological evidence for the evolution of activity pattern and visual acuity in primates. Am. J. Phys. Anthropol. 113, 235–262.
Kirk, E.C., 2004. Comparative morphology of the eye in primates. Anat. Rec. A 281A, 1095–1103.
Kirk, E.C., 2006a. Effects of activity pattern on eye size and orbital aperture size in primates. J. Hum. Evol. 51, 159–170.
Kirk, E.C., 2006b. Eye morphology in cathemeral lemurids and other mammals. Folia Primatol. 77, 27–49.
Kirk, E.C., Kay, R.F., 2004. The evolution of high visual acuity in the Anthropoidea. In: Ross, C.F., Kay, R.F. (Eds.), Anthropoid Origins: New Visions. Kluwer Academic / Plenum Publishers, New York, pp. 539–602.
Kosak, S.T., Scalzo, D., Alworth, S.V., Li, F., Palmer, S., Enver, T., Lee, J.S., Groudine, M., 2007. Coordinate gene regulation during hematopoiesis is related to genomic organization. PLoS Biol. 5, e309.

Litt, M.D., Simpson, M., Gaszner, M., Allis, C.D., Felsenfeld, G., 2001. Correlation between histone lysine methylation and developmental changes at the chicken beta-globin locus. Science 293, 2453–2455.

Lucas, P.W., Dominy, N.J., Osorio, D., Peterson-Pereira, W., Riba-Hernandez, P., Solis-Madrigal, S., Stoner, K.E., Yamashita, N., 2007. Perspectives on primate color vision. In: Ravosa, M.J., Dagosto, M. (Eds.), Primate origins: Adaptations and Evolution. Springer, New York, pp. 805–819.

Martin, R.D., 1990. Primate Origins and Evolution: A Phylogenetic Reconstruction. Princeton University Press, Princeton.

Martin, R.D., 2004. Palaeontology: Chinese lantern for early primates. Nature 427, 22–23.

Martin, R.D., Ross, C.F., 2005. The evolutionary and ecological context of primate vision. In: Kremers, J., Silveira, L., Martin, P. (Eds.), Structure, Function, and Evolution of the Primate Visual System. John Wiley, New York, pp. 1–36.

Misteli, T., 2007. Beyond the sequence: cellular organization of genome function. Cell 128, 787–800.

Murphy, W.J., Pringle, T.H., Crider, T.A., Springer, M.S., Miller, W., 2007. Using genomic data to unravel the root of the placental mammal phylogeny. Genome Res. 17, 413–421.

Nicol, J.A.C., 1981. Tapeta lucida of vertebrates. In: Enoch, J.M., Tobey, F.L. (Eds.), Vertebrate Photoreceptor Optics. Springer-Verlag, Berlin, pp. 401–431.

Noma, K., Allis, C.D., Grewal, S.I., 2001. Transitions in distinct histone H3 methylation patterns at the heterochromatin domain boundaries. Science 293, 1150–1155.

Peichl, L., 2005. Diversity of mammalian photoreceptor properties: adaptations to habitat and lifestyle? Anat. Rec. 287A, 1001–1012.

Perry, G.H., Martin, R.D., Verrelli, B.C., 2007. Signatures of functional constraint at aye-aye opsin genes: the potential of adaptive color vision in a nocturnal primate. Mol. Biol. Evol. 24, 1963–1970.

Postberg, J., Alexandrova, O., Cremer, T., Lipps, H.J., 2005. Exploiting nuclear duality of ciliates to analyse topological requirements for DNA replication and transcription. J. Cell Sci. 118, 3973–3983.

Ravosa, M.J., Dagosto, M. (Eds.), 2007. Primate origins: Adaptations and Evolution. Springer, New York, pp. 805–819.

Ravosa, M.J., Savakova, D.G., 2004. Euprimate origins: the eyes have it. J. Hum. Evol. 46, 357–364.

Reddy, K.L., Zullo, J.M., Bertolino, E., Singh, H., 2008. Transcriptional repression mediated by repositioning of genes to the nuclear lamina. Nature 452, 243–247.

Ross, C.F., Hall, I.M., Heesy, C.P., 2007. Were basal primates nocturnal? Evidence from eye and orbit shape. In: Ravosa, M.J., Dagosto, M. (Eds.), Primate Origins: Adaptations and Evolution. Springer, New York, pp. 233–256.

Ross, C.F., Kirk, E.C., 2007. Evolution of eye size and shape in primates. J. Hum. Evol. 52, 294–313.

Rossie, J.B., Ni, X., Beard, K.C., 2006. Cranial remains of an Eocene tarsier. Proc. Natl. Acad. Sci. 103, 4381–4385.

Schneider, R., Grosschedl, R., 2007. Dynamics and interplay of nuclear architecture, genome organization, and gene expression. Gen. Dev. 21, 3027–3043.

Sexton, T., Schober, H., Fraser, P., Gasser, S.M., 2007. Gene regulation through nuclear organization. Nat. Struct. Mol. Biol. 14, 1049–1055.

Solovei, I., Kreysing, M., Lanctot, C., Kosem, S., Peichl, L., Cremer, T., Guck, J., Joffe, B., 2009. Nuclear architecture of rod photoreceptor cells adapts to vision in mammalian evolution. Cell 137, 356–368.

Sussman, R.W., 1991. Primate origins and the evolution of angiosperms. Am. J. Primatol. 23, 209–223.

Sutherland, H., Bickmore, W.A., 2009. Transcription factories: gene expression in unions? Nat. Rev. Genet. 10, 457–466.

Tan, Y., Yoder, A.D., Yamashita, N., Li, W.H., 2005. Evidence from opsin genes rejects nocturnality in ancestral primates. Proc. Natl. Acad. Sci. 102, 14712–14716.

Tanabe, H., Muller, S., Neusser, M., von Hase, J., Calcagno, E., Cremer, M., Solovei, I., Cremer, C., Cremer, T., 2002. Evolutionary conservation of chromosome territory arrangements in cell nuclei from higher primates. Proc. Natl. Acad. Sci. 99, 4424–4429.

Tavare, S., Marshall, C.R., Will, O., Soligo, C., Martin, R.D., 2002. Using the fossil record to estimate the age of the last common ancestor of extant primates. Nature 416, 726–729.

Wang, D., Oakley, T., Mower, J., Shimmin, L.C., Yim, S., Honeycutt, R.L., Tsao, H., Li, W.H., 2004. Molecular evolution of bat color vision genes. Mol. Biol. Evol. 21, 295–302.

Wikler, K.C., Rakic, P., 1990. Distribution of photoreceptor subtypes in the retina of diurnal and nocturnal primates. J. Neurosci. 10, 3390–3401.

Zhao, H., Rossiter, S.J., Teeling, E.C., Li, C., Cotton, J.A., Zhang, S., 2009a. The evolution of color vision in nocturnal mammals. Proc. Natl. Acad. Sci. 106, 8980–8985.

Zhao, H., Xu, D., Zhou, Y., Flanders, J., Zhang, S., 2009b. Evolution of opsin genes reveals a functional role of vision in the echolocating little brown bat (*Myotis lucifugus*). Biochem. Syst. Ecol. 37, 154–161.