

predicts an increase in high-frequency spike bursts and asymmetric experiential plasticity in mEC. Unlike CA1, CA3 pyramidal neurons have little HCN1. Thus, HCN1 deletion in the forebrain would impact CA3 indirectly due to changes in the upstream mEC neurons but would influence CA1 both directly and indirectly. This may be the reason for the greater enhancement of place field size, and complex spike bursts, in CA1 than CA3 with HCN1 deletion (Hussaini et al., 2011).

Finally, this mechanism of boosting of LTP by suppression of I_h could also explain why the ventral grid fields are bigger in both control and HCN1-deficient mice: the effective strength of HCN may be weaker in the more ventral mEC, resulting in greater summation of inputs, boosted LTP, and larger grid fields. In this scenario, the ventral grid fields should

be more bursty, stable, and spatially asymmetric than the dorsal ones and exhibit greater experience-dependent asymmetric expansion, but recurrent inhibition could limit these processes.

Although much remains to be clarified, the recent studies on place cells and grid cells in the HCN1 provide significant insights into the underlying cellular mechanisms and elucidate their contribution to behavioral learning.

ACKNOWLEDGMENTS

M.R.M. was supported by grants from the NSF Career #0969034, NIH/CRCNS #1-R01-MH-092925-01, and the W.M. Keck Foundation.

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A Genome Befitting a Monarch

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DOI 10.1016/j.cell.2011.11.009

The monarch butterfly is famous for its annual fall migration from eastern North America to central Mexico, but it has also been an important model for studies in long-distance migration. Now, Zhang et al. present the genome of the monarch, opening up the detailed characterization of the butterfly's navigational system and unique social life.

The annual migration of the eastern North American monarch butterfly (*Danaus plexippus*; Figure 1) is one of the more astonishing feats of the insect world. As summer draws to a close each year, a special generation of monarchs is born, who will perform a southward bound migration of up to 4,000 km. Not only do these fragile animals cover a remarkable distance, but they also display impressive accuracy in navigation. The migration is not simply directed southward, but it has a very precise goal, namely a handful of mountaintops in central Mexico where the butterflies spend the winter. Once in their winter habitat, the monarchs halt re-

production until spring arrives, when they mate and begin their fluttering journey north in search of milkweed plants, the sole plant used for egg-laying of the species. Whereas the southbound journey is completed within one generation, the northward migration involves a succession of short-lived generations.

Considerable research has been focused on understanding the monarch itself, its intrepid migration, and the means by which it localizes to its wintering grounds (Brower, 1995). Now, with this issue of *Cell*, monarch research finally enters the genomic era, as Steven Reppert and his research team provide

a draft genome of the monarch using next-generation sequencing technologies (Zhan et al., 2011). Their results pave the way for an increased understanding of long-distance migration, in particular, and the evolution of the Lepidoptera (i.e., butterflies and moths) and insects, in general.

The monarch genome comprises 273 megabases with 16,866 protein-coding genes, and it shows considerable similarities with that of the silk moth *Bombyx mori*. These similarities extend to the size of protein families and to the colocalization of genes on chromosomes. Comparing the monarch's genome with that



Figure 1. The Monarch—A King among Butterflies

The monarch butterfly (*Danaus plexippus*), illustrated here by Johann Friedrich Wilhelm Herbst in 1795, has long fascinated scientists and the general public, and it is an important model system for studies in long-distance migration. Now, research on the monarch enters the genomic era with the draft genome presented by Zhang et al. (2011). Image courtesy of the Göttinger Digitalisierungszentrum (GDZ, <http://gdz.sub.uni-goettingen.de/>).

of the silk moth indicates that Lepidoptera is a fast-evolving insect order, at least relative to Diptera (flies) and Hymenoptera (bees, ants, and wasps). This finding is in line with the large size of the Lepidoptera, which comprises > 174,000 species, and with the notion that moths and butterflies constitute the most recently radiated insect order, having expanded in the Cretaceous and the early Tertiary (i.e., ~140–60 million years ago) in conjunction with the expansion of flowering plants (Grimaldi and Engel, 2005).

To find their way en route to Mexico, monarchs rely on a sun compass, located in their eyes, where the horizontal position of the sun and the derived pattern of polarized skylight provide the directional information. The compass is also adjusted for time by circadian clocks in the antennae and brain, which help the monarchs maintain a southbound flight direction (Perez et al., 1997; Heinze and Reppert, 2011). With the genome in place, deciphering the molecular machinery underlying the monarch's navigational prowess can now begin in earnest. Reppert and colleagues also provide a detailed annotation of genes potentially involved in the sun compass and associated processes. These include clock genes, as well as opsins and transcription factors involved in the development of the eyes and the central complex (i.e., the processing site of the compass input). To accomplish the long journey south, migratory mon-

archs also undergo multiple physiological changes, which include an increase in life span and a pause in reproductive activity. Many of these traits are regulated or influenced by the endocrine system, including the juvenile hormone pathway (Herman and Tatar, 2001), which regulates (among several things) growth and metamorphosis in insects. In short, elucidating the functional role of the highlighted genes, especially those being differentially expressed in migratory animals, is obviously a top priority.

The monarch genome also opens up the ability to identify candidate migratory-specific genes by comparative genomics approaches. The whole-genome sequencing of nonmigratory members of the genus *Danaus*, such as the Southern monarch (*D. erippus*) and the Jamaican monarch (*D. cleophile*), would now require only moderate efforts because de novo assembly is theoretically not necessary. Instead, reads from the other species can be mapped onto the monarch scaffolds and thus drastically reduce the sequence cover needed. Likewise, resequencing and comparison of gene expression from migratory and stationary populations of monarchs could also be instrumental in identifying critical molecular components enabling the migration.

In line with their diurnal lifestyle, monarchs and other butterflies are assumed to rely primarily on vision. In contrast, their nocturnal relatives, the moths,

chiefly use olfactory cues. This dichotomy in sensory reliance is not reflected in the repertoire of chemosensory genes because the monarch surprisingly displays similar numbers of chemosensory receptors as found in the moths investigated to date (e.g., Grosse-Wilde et al., 2011; Wanner et al., 2007). Thus, the monarch's sense of smell is an interesting topic.

As opposed to most if not all other insects, the olfactory system of the migratory monarch needs to function in two distinctly different environments: in meadows and gardens during the summer and in alpine forests of coniferous sacred firs (*Abies religiosa*) during the winter. The monarch's nose could therefore be an amalgamation of a summer and a winter nose, each adapted to the different volatile chemicals that make up the respective habitats. In addition, one could also envision that subsets of the chemosensory repertoire are differently expressed in migratory versus summer animals, such that receptors for sacred fir volatiles are upregulated in the former and downregulated in the latter, and vice versa for the receptors tuned to milkweed host odors. Although the genome gives no answers as to whether this is the case and, if so, how such a nose would be configured, the genome is a necessary prerequisite for future functional dissections aiming at solving this type of question.

Most interestingly, the monarch shows a number of odorant receptors clustering within the male-specific pheromone receptor subgroup of the silk moth. This is surprising because the monarch supposedly does not use long-range pheromones. A pheromone system of some type in the monarch is also hinted at by the observation that the monarch has even more pheromone-binding proteins than the silk moth. Zhang and colleagues speculate that this potential pheromone system may be involved in building social interactions among the migrating monarchs, rather than mediating long-distance attraction. In contrast to the summer monarchs, the migrants are highly gregarious, and the hinted at pheromone system could be the molecular substrate for an aggregation pheromone system triggered during the fall migration.

Olfaction could also play a more direct part in the monarch's migratory

orientation, as has been shown for birds (Holland et al., 2009). Volatiles emitted from the sacred fir forest habitat at their wintering site could act as a “destination beacon” guiding the butterflies (Reppert et al., 2010). One could also envision other volatile cues guiding the monarchs on their way south, being detected by specific odorant receptors.

That it took so long for a butterfly to be fully sequenced is rather peculiar given the popularity of butterflies and their prominent place in human culture. That the honor of being first has befallen the monarch is fitting, as few butterflies embody the elegance and marvel like this stately lepidopteran. With the genome at hand, a new era of monarch research has

begun, allowing detailed dissection of all of the intricate mechanisms involved in the amazing life history of this beautiful insect. The North American monarch butterfly has supplied us with several surprises before, and many more are very likely awaiting us now.

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