

The researchers, Yim, H. et al., used methods of whole-genome sequencing and *de novo* assembly of DNA fragments of the common minke whale (*Balaenoptera acutorostrata*) genome, and they conducted a comparative genomic analysis of additional genomic sequences of three minke whales, a fin whale (*Balaenoptera physalus*), a bottlenose dolphin (*Tursiops truncatus*), and a finless porpoise (*Neophocaena phocaenoides*). The four minke whales and a finless porpoise used as specimens for this genome sequencing were accidentally killed off the coast of east Korea. The bottlenose dolphin specimen was obtained from a marine park in Jeju Island, Korea. Lastly, the fin whale specimen was deceased and stranded at the Southwest Fisheries Science Center. This research was a part of the Korea Institute of Ocean Science and Technology's whale genome project. The purpose of this research is to examine the aquatic adaptations of whales, dolphins, and porpoises in the order Cetacea, and the use of comparative genomic analysis allows for comparisons of orthologous gene families within the divergence of the Cetartiodactyla clade. The Cetartiodactyla clade includes Cetacea and Artiodactyla, which consist of even-toed ungulates or otherwise known as hoofed terrestrial mammals. Extant lineages of cetaceans and terrestrial artiodactyls diverged 54 million years ago from the extinct genus *Indohyus* that had a deer-like resemblance as a semi-aquatic ungulate mammal.

The use of eukaryotic gene mapping in the minke whale sample found of its 21 pairs of autosomes and 1 pair of sex chromosomes, a diploid number common to cetaceans, the minke whale genome contained 20,605 genes and 2,598 non-coding RNAs. The researchers found that the minke whale genome shares 12,675 orthologous gene families with 9,848 of which that are shared by minke whale, bottlenose dolphin, cow, and pig lineages within the Cetartiodactyl clade, which indicate that these orthologous genes among different species are derived from common ancestral genes before the divergence event from a common ancestor. Only 494 of the orthologous gene families are unique to the minke whale following speciation. In addition, the researchers found that the minke whale genome had 1,156 expanded and 2,048 contracted gene families that affected their specific adaptations or positively selected genes, genotypes, and amino acid changes. The whale lineage studied under the researchers' specimens had a total of 4,773 genes with unique amino acid changes and of these amino acid changes, 695 of them altered the function of those genes.

The significance of the researchers' findings lies in the adaptations conferred to the whale lineage in their changing aquatic environment. For example, orthologous gene families relating to body hair and mammalian olfactory and taste receptors were contracted in the whale lineage but expanded in the cow and pig lineages. The whole genome sequencing of the minke whale and the other specimens emphasized the importance of physiological and morphological adaptations in an aquatic environment relating to stress response to low oxygen, oxygen reactive species, blood pressure, and high salt concentrations to name a few. Regarding metabolism, there were positively selected genes for antioxidant enzymes like those in the peroxiredoxin family that reduce peroxides and regulate against oxidative stress in redox signaling. O-GlcNAc transferase that is encoded by OGT genes was found to be expanded in the whale lineage to regulate oxidative stress, hypoxic conditions, and osmotic stress. For the whale lineage to adapt to hypoxic conditions, glutathione metabolism pathway genes are positively selected as an antioxidant that prevents cellular damage by reactive oxygen species. Another adaptation that maintains homeostasis in cetaceans is haptoglobin, an antioxidant protein that regulates heme-induced reactive oxygen species and aids against the loss of iron in hemoglobin and the renal

system. When blood lactate levels in the whale lineage increases after diving in hypoxic conditions, lactate dehydrogenase is involved in the metabolism of breaking down pyruvate to lactate; the LDH gene that encodes this function has also been positively selected and expanded for whales to adapt to hypoxic conditions. The renin-angiotensin-aldosterone system in whales regulates blood pressure and osmotic balance of salt concentrations. A morphological adaptation in the whale lineage is encoded in several HOX genes that play a role in body plan and embryonic development to aid in locomotion and adapting to the physiological stresses in their aquatic environment. The whale lineage has gained many useful adaptations unique to them such as echolocation, species specific blood clotting, and oxygen transportation in hypoxic conditions. Positively selected amino acid changes and expansions in the gene families of cetaceans have conferred useful adaptations to their environment that allows for their lineage to continue to persist since their divergence from a common ancestor.

See next page for *Nature* style citation.

References

Yim, H. et al. Minke whale genome and aquatic adaptation in cetaceans. *Nature Genetics* **46**, 88-92 (2014).