

The blue whale is the largest animal to ever exist on Earth, even surpassing dinosaur species and other massive land animals at about 100 feet in length and having a mass of 190 metric tons (Incorvaia, 2023). The gigantism in whales first evolved from 5 to 10 million years ago (Incorvaia, 2023). The gigantism in whales today is a stark contrast to the first whales that were similar in size to sea lions today (Incorvaia, 2023). The evolution of gigantism in whales can be attributed to an exponential growth of ocean nutrients in the geological record and the properties of water without the influence of gravity (Incorvaia, 2023). However, the genetics underlying this evolution remains a research question; this research question led to results published in the journal *Scientific Reports* that reason that whale genes influencing growth hormone and insulin pathways directed the growth of whales (Incorvaia, 2023). Further comparative genome analysis of body size of whales in that study with closely related phylogenetic relatives such as horses, sheep, and cows found positive adaptations in four genes selecting for a larger body size (Incorvaia, 2023). The selective pressures of an aquatic environment and positive selection for GHSR, IGFBP7, PLAG1, and NCAPG genes increased body size in cetaceans (André Silva, Souza, Ramos, Freitas, and Nery, 2023). The study also found that the EGF gene or epidermal growth factor in baleen whales was a pseudogene over evolutionary time as it did not influence the evolution of a larger body size (Incorvaia, 2023). EGF may have become a pseudogene in baleen whales due to being toothless and lunge-feeding plankton (Incorvaia, 2023). Stop codons in the EGF gene indicate pseudogenization (André Silva, Souza, Ramos, Freitas, and Nery, 2023). The evidence of pseudogenization of EGF in baleen whales is presented in the loss of teeth and baleen development (André Silva, Souza, Ramos, Freitas, and Nery, 2023). The baleen in the baleen whales became an evolutionary innovation that led to filtration feeding and consequently brought about gigantism evolution (André Silva, Souza, Ramos, Freitas, and Nery, 2023). Future studies on this subject matter would examine regulatory DNA sequences that control the genes of positive natural selection for a larger body size in whales through evolutionary time (Incorvaia, 2023).

The enormous size of whales has other subjects of interest in genetics; the increased number of cells and cell divisions would be presumed to have an increased cancer risk, but this presumption is defied in whales (Incorvaia, 2023). The four genes positively selecting for a larger body size in whales also are involved in tumor suppression (Incorvaia, 2023). Whales could help in the study of genetics for inhibiting cancer or disease progression and the understanding of their evolution (Incorvaia, 2023). A study examined the evolution of 1,077 tumor suppressor genes in cetaceans with comparative genome analysis (Tejada-Martinez, Pedro de Magalhães, and Opazo, 2021). The study found positive selection in the ancestor of cetaceans in the CXCR2 gene that regulates DNA damage, tumor invasion and migration, and the immune system (Tejada-Martinez, Pedro de Magalhães, and Opazo, 2021). The study also found seven tumor suppressor genes like the CXCR2 gene in cetaceans of the 362 orthologous genes selected that are positively selected for inhibiting genes related to multiple human disorders and cancers such as lung neoplasm (ADAMTS8), leukemia (ANXA1), teratocarcinoma (DAB2), DSC3, EPHA2, and TMPRSS11A (Tejada-Martinez, Pedro de Magalhães, and Opazo, 2021). One or more cetaceans have 71 genes with duplications associated with multiple human disorders, so this study of natural selection of genes affecting human health can lead to developments in genetics and disease resistance in humans and other animals (Tejada-Martinez, Pedro de

Magalhães, and Opazo, 2021). The study concluded that the positive selection of tumor suppression genes in the ancestor of baleen whales and its lineages evolved anti-cancer and anti-aging molecular mechanisms that select for larger body mass and greater longevity in cetaceans (Tejada-Martinez, Pedro de Magalhães, and Opazo, 2021).

The references page is on page 3.

References

1. Incorvaia, D. Unlocking the genes that made whales into giants. *The New York Times*; <https://www.nytimes.com/2023/01/19/science/whale-gene-giant.html?searchResultPosition=14> (2023).
2. André Silva, F., Souza, É.M.S., Ramos, E., Freitas, L., and Nery, M.F. The molecular evolution of genes previously associated with large sizes reveals possible pathways to cetacean gigantism. *Sci Rep* **13**, 67 (2023).
3. Tejada-Martinez, D., Pedro de Magalhães, J., and Opazo, J.C. Positive selection and gene duplications in tumour suppressor genes reveal clues about how cetaceans resist cancer. *Proc. R. Soc. B.*; <https://doi.org/10.1098/rspb.2020.2592> (2021).