

## Great white shark genome decoded

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Great white shark. Credit: Byron Dilkes, Danah Divers

The great white shark is one of the most recognized marine creatures on Earth, generating widespread public fascination and media attention, including spawning one of the most successful movies in Hollywood history. This shark possesses notable characteristics, including its massive size (up to 20 feet and 7,000 pounds) and diving to nearly 4,000 foot depths. Great whites are also a big conservation concern given their relatively low numbers in the world's oceans.

In a major scientific step to understand the biology of this iconic apex predator and sharks in general, the entire <u>genome</u> of the white shark has now been decoded in detail.

A team led by scientists from Nova Southeastern University's (NSU) Save Our Seas Foundation Shark Research Center and Guy Harvey Research Institute (GHRI), Cornell University College of Veterinary Medicine, and Monterey Bay Aquarium, completed the white shark genome and compared it to genomes from a variety of other vertebrates, including the giant whale shark and humans.

The findings are reported in the 'Latest Articles' section of the journal *Proceedings of the National Academy of Sciences*, USA.

Decoding the white shark's genome revealed not only its huge size—oneand-a-half times the size of the human genome—but also a plethora of genetic changes that could be behind the evolutionary success of largebodied and long-lived sharks.



The researchers found striking occurrences of specific DNA sequence changes indicating molecular adaptation (also known as positive selection) in numerous genes with important roles in maintaining genome stability ¬¬- the genetic defense mechanisms that counteract the accumulation of damage to a species' DNA, thereby preserving the integrity of the genome.

These adaptive sequence changes were found in genes intimately tied to DNA repair, DNA damage response, and DNA damage tolerance, among other genes. The opposite phenomenon, genome instability, which results from accumulated DNA damage, is well known to predispose humans to numerous cancers and age-related diseases.



Great white shark. Credit: Byron Dilkes, Danah Divers



"Not only were there a surprisingly high number of genome stability genes that contained these adaptive changes, but there was also an enrichment of several of these genes, highlighting the importance of this genetic fine-tuning in the white shark," said Mahmood Shivji, Ph.D., director of NSU's Save Our Seas Foundation Shark Research Center and GHRI. Shivji co-led the study with Michael Stanhope, Ph.D., of Cornell University College of Veterinary Medicine.

Also notable was that the white shark genome contained a very high number of "jumping genes" or transposons, and in this case a specific type, known as LINEs. In fact this is one of the highest proportions of LINEs (nearly 30%) discovered in vertebrates so far.

"These LINEs are known to cause genome instability by creating double stranded breaks in DNA," said Stanhope. "It's plausible that this proliferation of LINEs in the white shark genome could represent a strong selective agent for the evolution of efficient DNA repair mechanisms, and is reflected in the positive selection and enrichment of so many genome stability genes."

The international research team, which also included scientists from California State University, Monterey Bay, Clemson University, University of Porto, Portugal, and the Theodosius Dobzhansky Center for Genome Bioinformatics, Russia, also found that many of the same genome stability genes in the white shark were also under positive selection and enriched in the huge-bodied, long-lived whale shark.

The discovery that the whale shark also had these key genome stability adaptations was significant because theoretically, the risk of developing cancer should increase with both the number of cells (<u>large bodies</u>) and an organism's lifespan—there is statistical support for a positive relationship of body size and cancer risk within a species. Interestingly, this does not tend to hold up across species.



Contrary to expectations, very large-bodied animals do not get cancer more often than humans, suggesting they have evolved superior cancerprotective abilities. The genetic innovations discovered in genome stability genes in the white and whale shark could be adaptations facilitating the evolution of their large bodies and long lifespans.

"Decoding the white shark genome is providing science with a new set of keys to unlock lingering mysteries about these feared and misunderstood predators—why sharks have thrived for some 500 million years, longer than almost any vertebrate on earth" said Dr. Salvador Jorgensen, a Senior Research Scientist at the Monterey Bay Aquarium, who co-authored the study.







Great white shark close up. Credit: Byron Dilkes, Danah Divers

But the innovations did not end there.

The shark genomes revealed other intriguing evolutionary adaptations in genes linked to wound healing pathways. Sharks are known for their impressively rapid wound healing.

"We found positive selection and gene content enrichments involving several genes tied to some of the most fundamental pathways in wound healing, including in a key blood clotting gene," said Stanhope. "These adaptations involving wound healing genes may underlie the vaunted ability of sharks to heal efficiently from even large wounds."

The researchers say they have just explored the "tip of the iceberg" with respect to the white shark genome.

"Genome instability is a very important issue in many serious human diseases; now we find that nature has developed clever strategies to maintain the stability of genomes in these large-bodied, long-lived sharks," said Shivji. "There's still tons to be learned from these evolutionary marvels, including information that will potentially be useful to fight cancer and age-related diseases, and improve wound healing treatments in humans, as we uncover how these animals do it."

Decoding the white shark genome will also assist with the conservation of this and related sharks, many of which have rapidly declining populations due to overfishing," said Steven O'Brien, a conservation geneticist at NSU, who co-conceived this study. "The genome data will



be a great asset for understanding white shark population dynamics to better conserve this amazing species that has captured the imagination of so many."

**More information:** Nicholas J. Marra el al., "White shark genome reveals ancient elasmobranch adaptations associated with wound healing and the maintenance of genome stability," *PNAS* (2019). <u>www.pnas.org/cgi/doi/10.1073/pnas.1819778116</u>

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