

Mutation rates in whales found to be much higher than previously reported

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This picture shows how a small biopsy is collected, using a hollow-point crossbow dart, from a fin whale in the Gulf of Maine. The fin whale is one of the species included in the study. Credit: Center for Coastal Studies image collected under U.S. NMFS ESA/MMPA Permit 1632

An international team of marine scientists, led by the University of



Groningen in the Netherlands and the Center for Coastal Studies in the U.S., has studied the DNA of family groups from four different whale species to estimate their mutation rates. The results revealed much higher mutation rates than previously thought, which are similar to those of smaller mammals such as humans, apes, and dolphins.

Using the newly determined rates, the group found that the number of humpback whales in the North Atlantic before whaling was 86% lower than earlier studies suggested. The study is the first proof that this method can be used to estimate mutation rates in <u>wild populations</u>. It is published in the journal *Science*.

Mutation rate is a key parameter in genetics and genomics, where it is used to determine rates of evolution and adaptation. It is also used to derive the number of whales in the oceans before they were decimated by large-scale commercial whaling. However, estimating the rate at which new mutations appear in whales, or in any wild species, is difficult.

Pedigree method

For a long time, the phylogenetic method was used to measure mutation rates. This method uses fossil data from different species to estimate when they diverged. Subsequently, DNA from those species is compared to infer how many mutations must have occurred since the divergence.

"However, the fossil record is not that exact. And some mutations may have disappeared over time," says Per Palsbøll, Professor of Marine Evolution and Conservation at the University of Groningen. He has studied whales since the late 1980s and is a corresponding author of the *Science* paper.

A more recent approach is the pedigree method, which uses the genomes

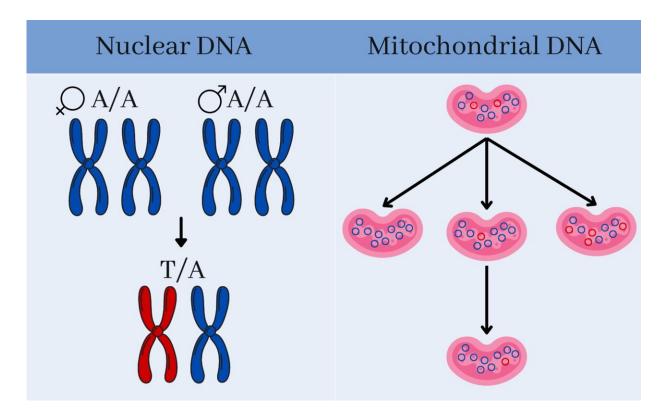


of a pair of parents and their offspring to identify new mutations in the offspring. This more direct method relies on very few assumptions and is ideal for comparing mutation rates among different species, such as whales and humans.

Especially in <u>wild species</u>, the challenge is to obtain tissue samples from both parents and their offspring. First author Marcos Suárez-Menéndez explains, "The method has only been used on a handful of animals that are living in the wild, such as a single wolf pair and their cubs. It has also been used to estimate mutation rates in zoo animals, although it is uncertain if this reflects the mutation rates in the wild where the conditions are very different."

However, the team, comprising scientists from the Netherlands, U.S., Greenland, Denmark, Canada, and the UK, were able to use skin biopsy samples collected from whales during a collaboration that has been ongoing for more than 30 years.





Nuclear mutation rates were determined through genome sequencing of whale trios (mother, father, and calf). The mutation rate was calculated by counting nucleotide base changes (i.e. mutations) exclusive to the calf and dividing them by the total number of bases. The mitochondrial mutation rate was estimated by analyzing the transmission of mitochondrial heteroplasmy (two distinct mitochondrial genomes within an individual caused by a mutation) and its frequency across hundreds of maternal lineages. Credit: Marcos Suárez-Menéndez, University of Groningen

Crossbow

Palsbøll collected his first whale biopsy samples among icebergs in the waters off West Greenland in 1988.

"To do this, we had to sail very close to a whale and then fire a dart with



a hollow point using a crossbow," he says. The dart punches out a sample and bounces back into the water from where it is collected.

Finding both parents of a whale calf is the first step in measuring the <u>mutation rate</u> using the pedigree method. This is where large-scale DNA analyses come in. Suárez-Menéndez analyzed data that were generated by the other first author, Martine Bérubé, from microsatellite markers in DNA. This DNA was extracted from a large archive of whale biopsy samples and used to create a genetic fingerprint of individuals.

"I sifted through the microsatellite data to find individuals that were related as mother and calf. Next, I looked for possible fathers in the database," says Suárez-Menéndez.

In this way, he managed to identify 212 putative parent and offspring trios in four different whale species. The DNA of eight trios was then sent off for genome sequencing. After a final paternity check, Suárez-Menéndez and his colleagues estimated the number of new mutations in the calf and the average mutation rate in whales.

Industrial whaling

The results showed that the mutation rates in whales are similar to the rates seen in pedigrees in smaller mammals such as humans, apes, and dolphins. In contrast, earlier estimates in whales using the phylogenetic method were much lower compared to these smaller mammals.

Suárez-Menéndez notes, "And just like in humans, most new <u>mutations</u> originate from the father. So, whales are very similar to us in this respect."

The team also used a slightly different maternal pedigree method to estimate the mutation rates in DNA from mitochondria, the cell's power



plants. This method has so far only been used in penguins. Mitochondria and their DNA are passed on through the maternal line and Suárez-Menéndez took advantage of four decades of sighting data of humpback cow and calf pairs in the Gulf of Maine, directed by senior author Jooke Robbins at the Center for Coastal Studies.

"Our study revealed that the mutation rate in whale mitochondrial DNA is also much higher than earlier estimates based on the phylogenetic method," explains Suárez-Menéndez.

The newly determined, higher mutation rates were used to infer that the number of whales in the North Atlantic before industrial whaling. The result was 86% lower than earlier reported estimates based on phylogenetic mutation rates.

"Our new mutation rates suggested that some 20,000 humpback whales lived in the North Atlantic before commercial whaling, in contrast to the previous estimate of 150,000," says Palsbøll. This is important information, not only for the conservation of whales but also for our understanding of the state of the oceans before whaling.

Palsbøll adds, "Another conclusion of wide-ranging consequences is that our study shows that it is entirely feasible to estimate the mutation rate in wild animals."

Cancer

The human-like <u>mutation rates</u> in whales also led the authors to reject one possible cause of Peto's paradox. This is the observation that at the species level, the incidence of cancer does not appear to correlate with the number of cells in an organism. Whales have a hundred to a thousand times more cells than—for example—humans, so if they have the same cancer rate as humans, they should get cancer very early in life.



Several mechanisms have been proposed for protecting these large sea mammals against cancer. One of those is a slower mutation rate as a consequence of whales having much lower metabolic rates. The discovery that this is not the case, implies that other mechanisms are probably at play in whales, such as an increase in the number of copies of the p53 gene which protects against cancer.

Finally, as the study relied on a large number of <u>tissue samples</u> that have been collected over several decades, the paper highlights the importance of long-term ecological research projects.

Palsbøll observes, "It is difficult to acquire sustained funding for these kinds of long-term ecological studies. However, we wouldn't have been able to do this research without the sustained commitment and dedication of the many colleagues who recorded all the sightings and collected the samples that our study relied on."

More information: Marcos Suárez-Menéndez et al, Pedigrees provide a new perspective on mutation rates and historic abundance in baleen whales, *Science* (2023). <u>DOI: 10.1126/science.adf2160</u>. <u>www.science.org/doi/10.1126/science.adf2160</u>

Provided by University of Groningen

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