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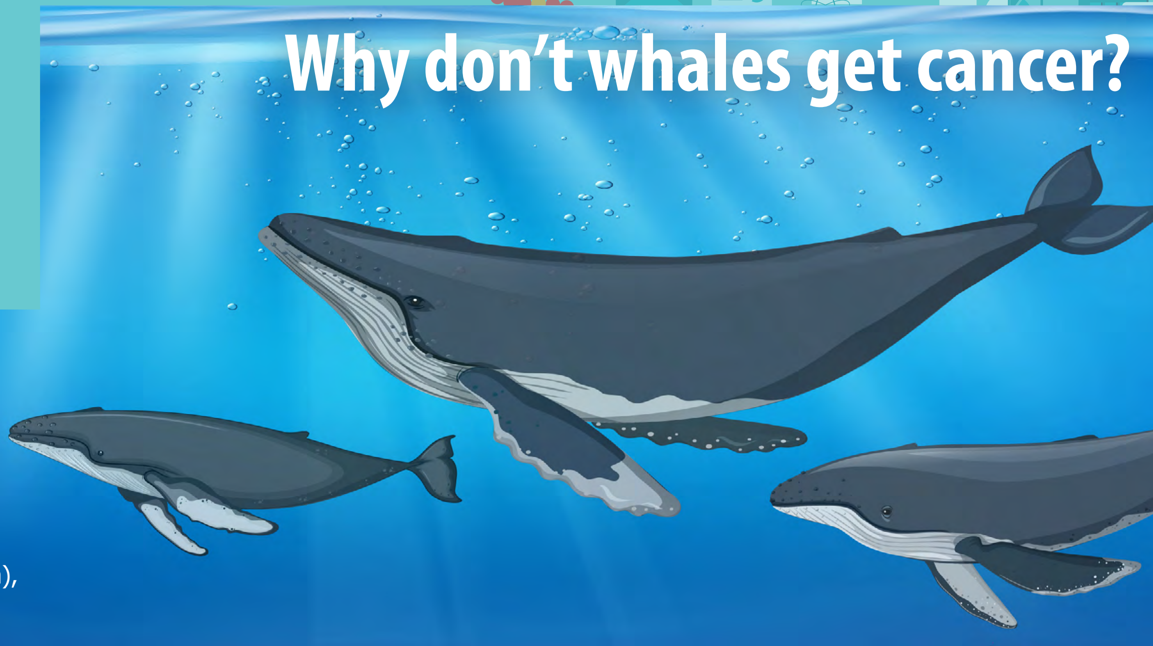
Why don't whales get cancer?



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Abstract

Every day, the cells in your body are super busy growing and dividing. When something goes wrong, mutations appear. Our immune system usually detects cells with mistakes and kills them before they become a problem. But sometimes they go undetected and the rogue cell multiplies, turning into cancer. So, if an animal has more cells and a longer life, it should get more cancer. Whales have up to 1,000 times more cells than humans and some live for over 200 years. But their cancer rates are no higher than ours! To figure out why this is, we compared the humpback whale and other whale genomes to other mammal genomes. Our DNA analysis showed that in whales there was duplication of cancer-suppressing genes. We also found that whales have the slowest rate of genetic changes. Our findings help us understand the role of DNA in preventing cancer. It could also help us fight cancer in humans!

Introduction

Our cells contain lots of information, collectively referred to as our **genome**. A genome is an organism's complete set of **DNA**. The DNA found in our cells forms a molecular instruction book. It's organized into little chunks of information that we call **genes**. Each gene carries a specific set of instructions for how to make a certain aspect of you. Scientists think our genetic code contains around 23,000 genes!

Some genes tell cells how to make proteins involved in cell growth and division. They do so by creating "photocopies" of DNA for new cells. But errors or **mutations** can occur, causing a misprint in the order of these sequences. This could be positive and lead to new traits for adaptation through evolution. But it could also lead to negative consequences, such as the development of **cancer**.

So, larger animals with many cells and longer life spans should have more opportunities for mutations to occur. This should mean a greater chance of getting cancer. But this is not the reality! Scientists have spent so much time researching this problem that it has a name: **Peto's paradox**. It suggests that larger animals have developed mechanisms that help to control cell replication – and thus prevent the development of cancer.

Humpback whales are famous for breaching (jumping out the water) and showing their tails when they dive. This makes them very popular with whale watchers as it's a dramatic sight!
Photo: NOAA Fisheries

Humpback whales (*Megaptera novaeangliae*) can live for up to 95 years and grow to over 13 meters long. Scientists have already produced the entire genomes of 13 **cetacean** species (whales, dolphins, and porpoises). But so far, no one has compared these genomes to ask how cetaceans beat cancer. We did this for the first time, comparing the humpback whale to other cetaceans and mammals. We wanted to understand exactly how their genomes work.

Methods

Step 1: Collecting tissue and extracting DNA

We extracted DNA from a humpback whale tissue sample. We used a specialized toolkit to make sure the DNA was of high quality and not damaged. We could then figure out the structure of each section of DNA in a process called **sequencing**.

Step 2: Creating the assembly

Next we used supercomputers to piece together the humpback whale genome. It's a bit like making sure all the pages of the book are in the correct order. After editing the damaged ones, we could form a complete story.

Step 3: Reading and identifying the genes within the genome

We compared whole genome alignments of 12 different mammals including other cetaceans. We looked at specific sites along these strands to identify differences and similarities in their genes. Next we calculated the number of mutations over time in each species. This gave us their **substitution rate**.

We then used genetic software to compare 10 cetacean genomes and our humpback genome. This identified areas of **large segmental duplications** (LSDs). It also showed the number of times these patterns occurred. We used a reference genome database to label the gene functions.

Results

We found that cetacean genomes contain an average of 318 large segmental duplications (LSDs). 51 of these are shared across all 11 cetacean genomes. The reason for shared LSDs could be that they hold an important function for all whales.

We identified 426 genes within these LSD components. Many were anti-cancer defending genes. These LSDs were also found to be species specific. So, each cetacean has their own unique associated genes and duplications (Figure 1).

Which species of whale has the highest number of LSDs?

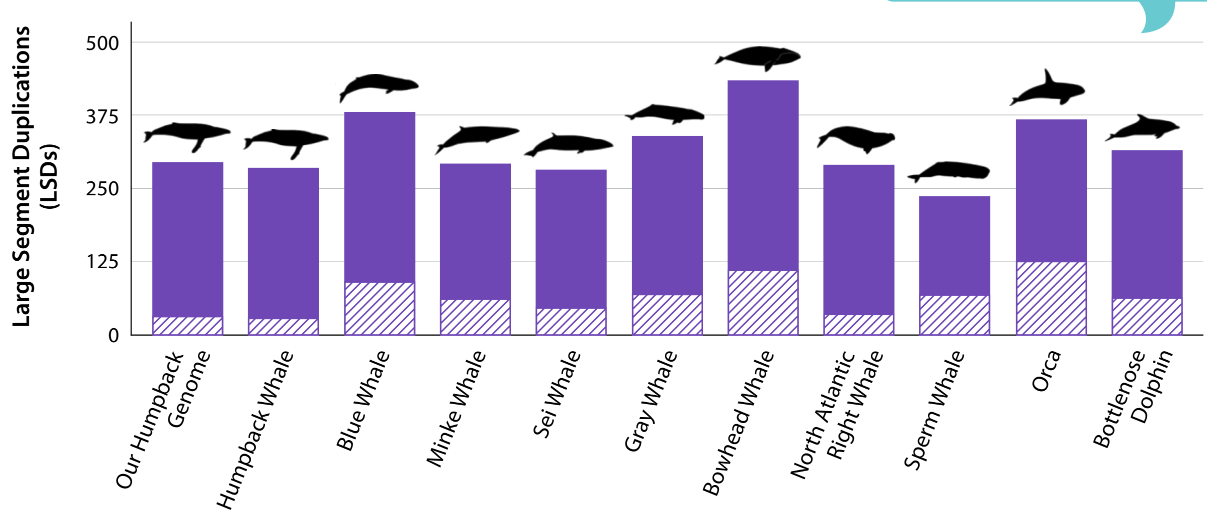

Figure 1: Cetaceans labeled with their total number of large segmental duplications. The hatched part of each bar represents the quantity of the total LSDs that are species specific ("unique").

Cetaceans showed the lowest number of DNA substitutions per site in mammals (per million years). Mice had the highest substitution rate. This suggests there is a potential link between mutation occurrence and lifespan.

Discussion

Our expected genome size was larger than the genome we put together. This might be because whale genomes have so many large segmental duplications. So, it's easy to miss regions when fitting our puzzle pieces together.

We found a lot of duplicated genes related to cancer suppression. We also saw evidence of more white blood cell function and DNA repair in whales. So, humpback immune systems might have adapted to fight cancer! Studying substitution rates helps scientists understand the pace of evolution between species. We worked out that cetaceans have one of the slowest rates of genetic change. This could be due to their long lives and longer generation times. This means they have fewer opportunities for mutations to build up between generations.

Our research helps to identify genes responsible for particular cell functions. This means we can understand more about the genetic basis of diseases. This could help us to develop new ways to target cancer in humans.

Conclusion

It's important to remember that whales do still get cancer sometimes. In fact, it can occasionally be because of us. We have found tumors in whales' skin, tongue, and lymph nodes. Large populations of belugas also developed high cancer rates. This may have been due to the regular release of some oil nearby. Whales, dolphins, and porpoises depend on a healthy environment to survive. Even small actions can make a difference!

- Try to buy fish from only sustainable fisheries.
- Make sure you put all used plastics in the bin and nowhere near waterways. Organize or take part in a beach or river clean-up.
- Look up your nearest marine protection organization and help to spread the word!

Glossary of Key Terms

Cancer - when cell division goes wrong and the uncontrolled growth results in tumors.

Cetacean - an aquatic lineage that includes whale, dolphin, or porpoise.

DNA - the genetic information inside the body's cells that helps make people who they are. It's the instructions for how to make the body.

Gene - a section of DNA that codes for a protein.

Genome - all of the genetic material of an organism.

Large segmental duplications (LSDs) - blocks of DNA that typically share more than 90% sequence identity and occur at more than one site within the genome.

Mutation - a rare, random change in the structure of an organism's genetic material. Some can be inherited.

Peto's paradox - the lack of correlation between body size and cancer risk.

Sequencing - a process used to figure out the exact structure and composition of an organism's DNA.

Substitution rate - the rate at which mutations are accepted. So, the rate at which "mistakes" become incorporated into a genome. This helps us estimate the speed of evolution.

Check your understanding

1 What are gene mutations? What is an example of a positive outcome of a gene mutation? What about an example of a negative one?

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2 Why do animals like whales have a lower likelihood of developing cancer?

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3 What are large segmental duplications (LSDs), and what is their function?

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4 Why did we think our actual genome size was shorter than our predicted genome size?

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5 With a partner, create a poster to explain Peto's paradox. Look up and include other large animals that have lower cancer rates.

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