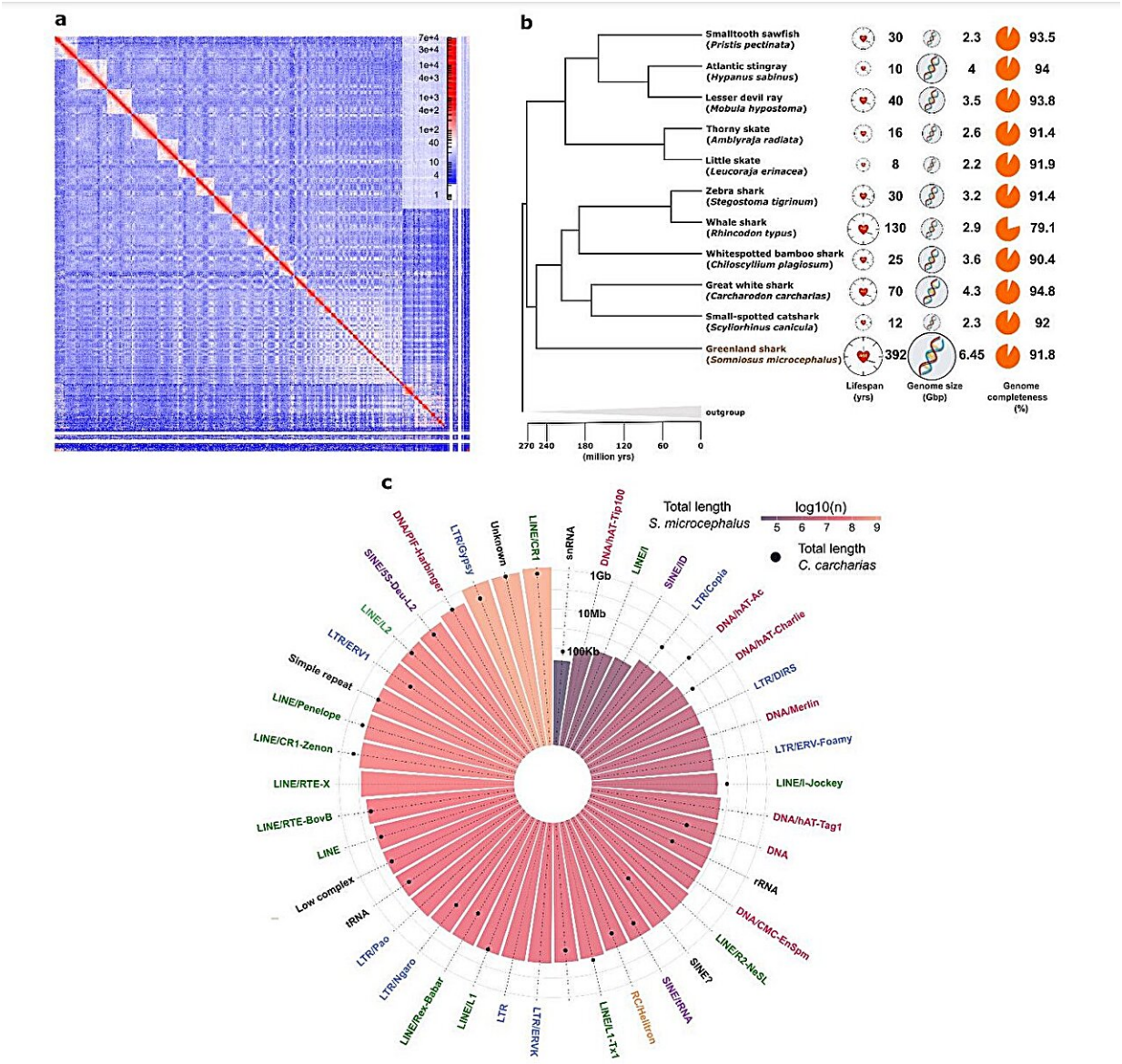
International team decodes the genome of the Greenland shark

September 11 2024, by Sylvia Kreyssel-Minar



Characteristics of the Greenland shark genome assembly. a) Intensity signal heat

map of HiC contacts. Credit: *Genomics* (2024). DOI: 10.1101/2024.09.09.611499

The Greenland Shark (Somniosus microcephalus), an elusive dweller of the depths of the northern Atlantic and the Arctic Ocean, is the world's longest-living vertebrate, with an estimated lifespan of about 400 years.

An international team of scientists at the Leibniz Institute on Aging—Fritz Lipmann Institute (FLI) in Jena, Ruhr University Bochum, SNS, University of Copenhagen, and CNR-IBF Pisa, in collaboration with other institutions, have now sequenced this iconic species' genome. They published their first results on the *bioRxiv* preprint server and made the genome sequence accessible. The data suggest that this animal's toolbox for repairing its own DNA may explain its extreme longevity—and that of other animals.

Additionally, the team's work to decode the animal's genetic makeup will shed new light on general mechanisms enabling longevity.

"The Greenland Shark's genome is a quintessential step for understanding the molecular mechanisms of aging in this exceptionally long-lived species," says Steve Hoffmann, computational biologist and research group leader at the Leibniz Institute on Aging—Fritz Lipmann Institute (FLI) in Jena, Germany. The researchers expect the Greenland Shark study to be essential for many other organisms.

"Exploring the genetic underpinnings of the huge lifespan diversity across the tree of life offers an entirely new perspective for investigating the mechanisms enabling exceptional longevity," explains Alessandro Cellerino, neurobiologist and associated group leader at FLI and a professor at the Scuola Normale Superiore (SNS) in Pisa.

Only a few complex animals can outlive humans. Astounding examples are giant tortoises, like Jonathan, a 191-year-old specimen currently residing in St. Helena. Yet, this record pales compared to the Greenland Shark.

The shark's genome size posed one of the project's early challenges. With 6.5 billion base pairs, the Greenland Shark's genetic code is twice as long as that of a human, and it is the largest among shark genome sequences to date.

"There are only a few animals sequenced thus far that have an even larger genome," says Arne Sahm, the study's first author, referring to the axolotl and recently published lungfish genome studies.

As for the axolotl and the lungfish, the massive Greenland Shark genome size is primarily due to the presence of repetitive and frequently self-replicating elements. Such transposable elements, sometimes called jumping or selfish genes and often considered genomic parasites, account for over 70% of the Greenland Shark's genome.

Interestingly, a high repeat content is often regarded as detrimental since jumping genes can destroy the integrity of other genes and reduce the genome's overall stability. In the case of the Greenland Shark, however, the high repeat content does not appear to have limited its lifespan.

On the contrary, Sahm and his colleagues suspect that the expansion of transposable elements may have even contributed to the Greenland Shark's extreme longevity. Sometimes, other more functionally relevant genes can hijack the molecular machinery encoded by transposable elements to multiply. The team suggests that several regular genes seized this opportunity during the Greenland Shark's evolution. Surprisingly, many duplicated genes are involved in repairing DNA damage.

"In each of our cells, the DNA sustains damage thousands of times every day, and specialized molecular mechanisms constantly repair it. A remarkable finding of comparative genomic studies is that long-lived mammalian species are exceptionally efficient in repairing their DNA," explains Cellerino. Thus, the team's results indicate that DNA repair may represent a general mechanism underlying the evolution of exceptional longevity.

"We are tempted to speculate that the evolution of the Greenland Shark has found a way to counterbalance the negative effects of transposable elements on DNA stability—by hijacking the very machinery of transposable elements," adds Sahm.

The researchers are also eager to learn more about the mechanisms that control the spreading of transposable elements.

"We can now start answering whether the silencing of transposable elements in Greenland Sharks is any different from that in other species," says Helene Kretzmer from the Max Planck Institute for Molecular Genetics.

The team also found a specific alteration in the protein p53—also known as the "guardian of the genome." Strikingly, p53 acts as a control hub that responds to DNA damage in humans and in many other species.

"This protein is mutated in about half of all human cancers and is the most important tumor suppressor we know. Therefore, it is an essential gene for longevity," says Steve Hoffmann. However, further studies are needed to show to which extent the observed changes in critical genes (such as p53 and molecular pathways, e.g., duplications of DNA repair genes or changes in tumor suppressors) contribute to the animals' exceptional longevity.

"Our genome project now provides a basis for many independent studies that will help us to better understand the evolution of this remarkable species," says Paolo Domenici from CNR—IBF Pisa.

"This is one of the reasons we decided to make the genome immediately available to the scientific community," adds Alessandro Cellerino. The genome sequence and the corresponding web resources provided by the team enable researchers worldwide to analyze the Greenland Shark version of their genes of interest.

"This work is a cornerstone for a better understanding of the basis of the Greenland Shark's extreme physiology. Furthermore, it helps us assess their genomic diversity and thus the population size of this vulnerable species for the first time," says John Fleng Steffensen from the University of Copenhagen, who has been studying these giant animals in the field for the last 15 years.

More information: Arne Sahm et al, The Greenland shark (Somniosus microcephalus) genome provides insights into extreme longevity, *bioRxiv* (2024). DOI: 10.1101/2024.09.09.611499

Provided by Leibniz-Institut für Alternsforschung - Fritz-Lipmann-Institut e.V. (FLI)