Scientist Shin Kubota expresses his vision in the New York Times: "*Turritopsis application for human beings is the most wonderful dream of mankind," he told me the first time I called him. "Once we determine how the jellyfish rejuvenates itself, we should achieve very great things. My opinion is that we will evolve and become immortal ourselves."*." (November 28, 2012)

Theme of the month : Longevity records of living organisms

How to understand the longest lifespan? And why?
The maximum lifespan of living things is extremely variable depending on the species. Overall, for animals, the maximum lifespan is longer with one or more of the following favorable factors:

- Predators are rare
- The metabolism is slow
- Size is large

The differences in lifespan can be enormous between species that are biologically quite close. This is one of the reasons to consider gene therapy or other medical treatment to dramatically increase the maximum lifespan of humans.

This letter includes known cases of extreme longevity. Obviously, in these cases of very long lifespans, only indirect and sometimes questionable measures are possible.

The naked mole rat and the bat, exceptional longevity and no cancer! (35-40 years)

The longevity of naked mole rats is especially surprising when compared to other captive rodents of similar size. Naked mole rats are not expected to live more than six years. However, the oldest naked mole rat known in the laboratory is... 35 years old! And, among some of its fellow rats that are over 30 years old, some females are still fertile.

Researchers have discovered why naked mole rats are cancer-free. It is thanks to hyaluronic acid, a molecule that is thought to prevent the formation of tumors in the body. According to researchers Vera Gorbunova and Andrei Seluanov, who published their results in the journal Nature, the molecular weight of hyaluronic acid in the naked mole rat is five times greater than in mice.

The tiny Brand's bat, at seven grams, lives for almost forty years. It is the same for the great mouse (*Myotis myotis*), which is five times heavier. An international team undertook a longitudinal study over eight years. Their results, published in the journal Nature Ecology & Evolution, open up promising avenues for research on aging.

Longest-lived insect: the termite queen (50 years)

Insects are normally thought of as living less than a year as adults. However, termite queens, protected from predators, can reach 50 years.

Birds: The albatross can live up to 80 years

Albatrosses are the largest seabirds in the world: the howler albatross reaches a wingspan of 3.50 meters! Their longevity is also remarkable, as they can live up to 80 years. Wisdom, a 70 years old albatross has laid eggs again. A parrot (cockatoo) has also reached a similar age (82 years).

Oldest amphibian: the cave salamander (100 years)

Naturalists attribute the longevity of the blind salamander *Proteus anguinus* to its unusually slow metabolism. Tthis salamander takes 15 years to mature, mates and lays eggs only about every 12 years, and barely moves except when foraging for food. In addition, the damp caves of southern Europe where it lives are virtually free of predators, allowing *P. anguinus* to live beyond 100 years in the wild.

Reptiles: The famous Galapagos tortoises

In 2012, "Lonesome George" died at over 100 years old. Six years after his passing, the centenarian has made a comeback thanks to the revelations of Yale researchers studying his genome! George was the last representative of a species endemic to a Galapagos island. He always shunned any mating in captivity. The scientists who had sequenced his genome during his lifetime as well as that of another species of giant tortoise, revealed the results in the journal *Nature*.

The biologists detailed 891 genes in these turtles, involved in the function of the immune system. They show that these animals have developed extra copies of genes that allow them to better respond to oxidative stress, known to be a major factor in aging. They also discovered a gene that allows cells to better defend themselves against foreign cells, as well as tumor suppressor genes that are more numerous than in most vertebrates, and others that are involved in DNA repair.

The study of aging in animals is a source of knowledge for humans. Researchers have found some similarities between the genomes of turtles and centenarians.

Jeanne Calment with her 122 years is the person who lived the longest in the history of humanity..., but certainly not enough to impress an old turtle. The longest living turtle seems to have reached 189 years of age.

Sphenodons are other reptiles that can live past a century.

Fish: 150 years for the orange roughy (*Hoplostethus atlanticus*)

Hoplostethus atlanticus is called "watchfish". The animal lives in the world's oceans at depths between 900 and 1,800 meters, especially in submarine canyons.

The species only reaches sexual maturity between 20 and 30 years of age, which could be explained by a low predation rate and the scarcity of prey in the abysses. Adults can measure 75 cm long and weigh 7 kg and the age of the oldest known specimen, determined by radiometric radiation of the mineral accumulations in its internal ears, is said to be 149 years.

Echinoderms: 200 years for the giant red sea urchin (*Astropyga radiata*)

Quite common in the Indian Ocean and in part of the Pacific Ocean, this echinoderm owes its name to its color and its size, which can reach nearly 20 cm in diameter, the largest known among sea urchin species. Some individuals have reached the age of 200 years.

Mammals: 200 years for the bowhead whale (*Balaena mysticetus*)

Living in Arctic waters, the bowhead whale is a cetacean measuring up to 20 meters and weighing around 100 tons. Its longevity has been estimated at more than 200 years thanks to scars left by old wounds caused by whale

hunters. This exceptional longevity could be explained by certain genes. For example, analysis of the whale genome shows unique mutations in the ERCC1 gene involved in the repair of damaged DNA. Another gene, called PCNA and associated with cell growth and DNA repair, contains a duplicate section of DNA. This duplication could slow down cetacean aging.

Sharks: 400 years for the Greenland shark (*Somniosus microcephalus*)

This rather plump grey shark, measuring five meters, lives in the waters of the Arctic Ocean and is the champion of longevity among vertebrates. Its growth is estimated at about 1 cm per year.

In an article published in *Science*, an international team of researchers describes how they managed to measure the age of 28 Greenland sharks. The results revealed that the largest shark, a female over five meters long, was 392 years old, although there is a significant margin of error of plus or minus 120 years. The sexual maturity of females is thought to be reached at the age of about 150 years.

According to this research by Julius Nielsen at the University of Copenhagen, published in August 2016, the Greenland shark would therefore be the longest-living vertebrate.

Oldest Mollusc: The Ocean Quahog (500 years)

Scientists have determined that the ocean quahog, *Arctica islandica* , can literally survive for centuries, as demonstrated by one individual, Ming, which has surpassed the 500-year mark (you can determine a mollusk's age by counting the growth rings in its shell).

Trees. The Giant Sequoia: over 3000 years old!

Some trees seem to have no senescence mechanism. They remain as fertile at the age of several centuries as in their youth.

The Giant Sequoia is characterized by its longevity since it can reach more than 3000 years.

Many other species of trees can live for centuries: olive trees, oaks. The absolute record seems to be held by a 5,000 year old Bristlecone pine.

Finally, trees, like other plants, can multiply clonally and form a collective organism. In this sense, the clonal colony of aspen Pando is, at 80,000

years, one of the oldest organisms on the planet.

Microscopic organisms: endoliths (10,000 years)

Determining the lifespan of a microscopic organism is a tricky question: in a sense, all bacteria are immortal, as they propagate their genetic information by constantly dividing (rather than having sex and dying of age).

The term "endoliths" refers to bacteria, fungi, amoebas, or algae that live deep underground in cracks in rocks.

Studies have shown that individuals in some of these colonies undergo cell division only once every hundred years and can have a lifespan of about 10,000 years.

Technically, this differs from the ability of some microorganisms to recover from stasis or freezing after tens of thousands of years; in a significant sense. Endoliths are continuously "alive", though not very active. Perhaps most importantly, endoliths are autotrophic, meaning that they fuel their metabolism not with oxygen or sunlight, but with inorganic chemicals, which are virtually inexhaustible in their underground habitats.

Biological immortality in lobsters, hydras, sponges and corals

A small number of multicellular animals seem to have no mechanism of senescence. They do not degrade as they age. For example, their fertility remains constant or even increases.

Hydras, like all cnidarians, can regenerate, which allows them to recover from an injury and reproduce asexually. All hydra cells divide continuously. It has been suggested that hydras do not undergo senescence and, as such, are biologically immortal. In a four-year study, three cohorts of hydras showed no increase in mortality with age.

One species of sponge can live up to 11,000 years, namely *Monorhaphis chuni*, according to a U.S. study published in the journal *Aging Research Reviews* in 2014.

Some colonial animals, such as corals, can live more than 4,000 years.
Research suggests that lobsters may not slow down, weaken or lose fertility with age, and that older lobsters may be more fertile than younger lobsters. This does not, however, make them immortal in the sense of no impact of

senescence, as they are much more likely to die in a shell molt with advancing age due to their increasing size.

Their longevity may be due to telomerase, an enzyme that repairs long repetitive sections of DNA sequences at the ends of chromosomes, called telomeres. Unlike vertebrates, lobsters express telomerase in adulthood throughout most tissues, which has been suggested to be related to their longevity.

It has been claimed that some fish, notably the bigmouth buffalo, do not have measurable senescence. However, with the exception of the Greenland shark, no captured fish whose age was measured exceeded 200 years.

Why no biological immortality in vertebrates, even those without predators?

Natural selection, at least for vertebrates, always results in species with limited lifespans. This can be explained by the fact that an animal species without aging would lose its genetic diversity and be eliminated by any environmental change. This also explains sexual reproduction: more genetic mixing means more adaptability to the environment.

But in a certain sense, systematic aging remains an evolutionary mystery. Indeed, even salamanders or cave fish in an extremely stable environment (hundreds of thousands of years) and without predators do not seem to live much beyond a century.

Cnidaria: biological immortality and rejuvenation for the jellyfish *Turritopsis nutricula*

Small in size, but long in life expectancy. The jellyfish *Turritopsis nutricula* measures only 5 mm in diameter, but could live ad vitam æternam. Native to the Caribbean Sea, the species is nowadays very widespread. Several specialists are worried about its proliferation over the whole globe.

Thanks to a particular cellular process called transdifferentiation, the animal is able to stop its aging and even to become younger. It is already known that the best way to push a *Turritopsis Nutricula* to regenerate is to stress it. For example, in case of an injury, the process starts immediately and within a few days, the jellyfish returns to its juvenile stage and starts a new life.

This makes it an exceptional subject of study for biologists and geneticists, and a subject of interest for some pharmaceutical groups who are already

considering the production of a rejuvenating cream containing Turritopsis DNA. "*It's as if a butterfly were able to go back to the caterpillar stage*," says Stefano Piraino, a professor at the University of Salento in Italy.

Dormancy as a longevity strategy

Dormancy is a term that covers all forms of slowed life.

It is the period in the life cycle of an organism when growth, development and/or physical activity (in animals) are temporarily stopped. This reduces metabolic activity and thus helps the organism to conserve energy.

Especially in extreme environments, or ones of a very seasonal nature, dormancy can only be an adaptive strategy if a stimulus for the seed to move from a "dormant" to a "non-dormant" state is made possible at the "right time". And indeed, dormancy often does indeed cease when environmental conditions permit.

The longevity of a seed (the length of time it can remain in a dormant state without losing its ability to germinate) is highly variable. In plants, all the intermediaries exist, between the seed of the lotus which holds the record of longevity (about1000 years) and the seeds of cocoa tree, little dehydrated, which must, under pain of death, find, in the few days following their maturation, conditions allowing their germination. Scientists have even managed to germinate seeds of silence (a plant with white flowers) frozen for nearly 32,000 years in the Siberian subsoil!

Although costly, the dormancy strategy prevents all individuals carrying the same genotype from simultaneously encountering an environment not conducive to their survival or reproduction.

A rotifer survived 24,000 years of freezing in the Arctic permafrost.

Bdelloid rotifers generally live in aquatic environments and have an incredible ability to survive. Russian scientists discovered these creatures in a core of frozen soil extracted from the Siberian permafrost using a drill.

In a study published recently in the journal *Current Biology*, the Russian researchers used radiocarbon dating to determine that the creatures they recovered from the permafrost (ground that is frozen year-round, except for a thin layer near the surface) were about 24,000 years old.

This is not the first time ancient life has been "revived" from a permanently frozen habitat.

Antarctic moss stems were successfully regenerated from a 1,000-year-old sample and a living campion flower was regenerated from seed tissue, probably stored by an Arctic squirrel, that had been preserved in 32,000-year-old permafrost. Simple worms, called nematodes, were "resurrected" from permafrost at two locations in northeastern Siberia in sediments more than 30,000 years old.

This month's good news: Private investments for longevity. The European Union announces widespread health data sharing for its citizens by 2025.

- Vitalik Buterin donates over $2 million to the Methuselah Foundation.
- Michael Greve, founder of Forever Healthy, pledges 300 million to advance rejuvenation startups.
- In an unfortunately poorly circulated document, the European Commission announces that it aims to have EU citizens able to share their health data with the healthcare providers and authorities of their choice by 2025. This would mean, if followed through, that European citizens will be able to easily share their data for scientific research, including healthy longevity.

For more information:

- *See in particular:* heales.org, sens.org, longevityalliance.org *and* longecity.org.
- Source of image