Jellyfish, aging and cancer research

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Abstract. This paper is an overview of interesting research on the perspectives that jellyfish offer as model organisms in understanding the aging and regeneration of animal tissues. *Turritopsis dohrnii* jellyfish are small, bell-shaped creatures that have the ability to transform their mature cells into young cells. After reaching maturity and mating, jellyfish give back their biological clock and become young again. This process is called transdifferentiation and is the closest phenomenon to immortality on the planet. Research on this narrow topic is just beginning, but the immortal jellyfish, both gorgeous and fascinating, could one day cure aging effects and cancer.
Key Words: aging, cancer, immortal jellyfish, *Turritopsis dohrnii*.

Aging as a fact of life. Aging is a natural process that all living organisms on the planet go through. But the secret of eternal youth was one of the great challenges of our species (Petrescu-Mag & Papuc 2019), since ancient times (Popescu & Scarlat 2017). We have been looking for and we are constantly looking for ways in which we can delay this aging process, so that the signs of the passage of time do not affect our quality of life (Shiovitz-Ezra et al 2009; doc.ro).

When does the human body begin to age? Some of us would say: as soon as we are born. But the reality is that after we reach adulthood, around the age of 20, the changes in our body are no longer about growth and development, but about aging. At the cellular level, aging begins around the age of 25. The first signs are seen on the skin: wrinkles, dry skin, changes in texture, all appear when we approach 30 years (doc.ro). Also around the age of 30, the brain begins to age (doc.ro). Although it is a slow process, the human brain loses neurons as it ages, hence the changes related to memory loss, difficulty concentrating (Matthews et al 2017).

The heart begins to age around the age of 40, which is why cardiovascular disease becomes more common after this age (Kajstura et al 2010). The elasticity of blood vessels decreases and the first deposits of lipid compounds appear on the walls of the arteries, if we have a genetic predisposition or we had an unhealthy diet during youth (doc.ro). Also at the age of 35-40, the lung capacity is reduced, reaching only 50% by the age of 70. Similar to the lungs, the kidneys lose about 50% of their ability to filter waste by the age of 70 (doc.ro).

The liver is the strongest organ in terms of age (Anantharaju et al 2002). Because of the excellent ability of the hepatocyte to regenerate (Anantharaju et al 2002), as long as it is not affected by infections, excess alcohol, sugar or drugs, the liver remains young until 60-70 years (Le Couteur & McLean 1998; Horvath et al et al 2014; Tammen et al 2014; Taddei et al 2016).

This paper is an overview of interesting research on the perspectives that jellyfish offer as model organisms in understanding the aging and regeneration of animal tissues.

Immortal jellyfish (*Turritopsis dohrnii*) - a model organism for understanding the regeneration process. *T. dohrnii* was discovered in the 19th century, but scientists have only recently noticed the incredible ability of this species in the 1990s. The myth of immortality is one of the oldest fantasies of mankind. Long ago, expeditions were organized to discover the source of eternal youth, because people have always been attracted to the idea of living forever (Incredibila.ro 2021).

There are species with incredibly long lives, such as turtle species, which live 150 years, or Greenland sharks (*Somniosus microcephalus*), which can reach 400 years of age. But no creature is immortal. In fact, today we are convinced that immortality is a myth. What if that is not the case? We searched the Earth for evidence of immortality, or we imagined creatures like vampires, but we did not search the depths of the sea. It seems that the proof of immortality is just below the waves (Incredibila.ro 2021).

In the depths of the seas lives a species of jellyfish that, biologically, is immortal (the passage of time does not trigger the aging process and does not lead to death) (Bavestrello et al 1992). *T. dohrnii* jellyfish are small, bell-shaped creatures that have the ability to transform their mature cells into young cells (Kubota 2009). After reaching maturity and mating, jellyfish give back their biological clock and become young again (Piraino et al 1996, 2004). This process is called transdifferentiation (Schmid et al 1982; Piraino et al 1996) and is the closest phenomenon to immortality on the planet (Incredibila.ro 2021).

Normally, a mere mortal jellyfish passes through five stages of life (Boero et al 2014; sciencefocus.com; see Figure 1):

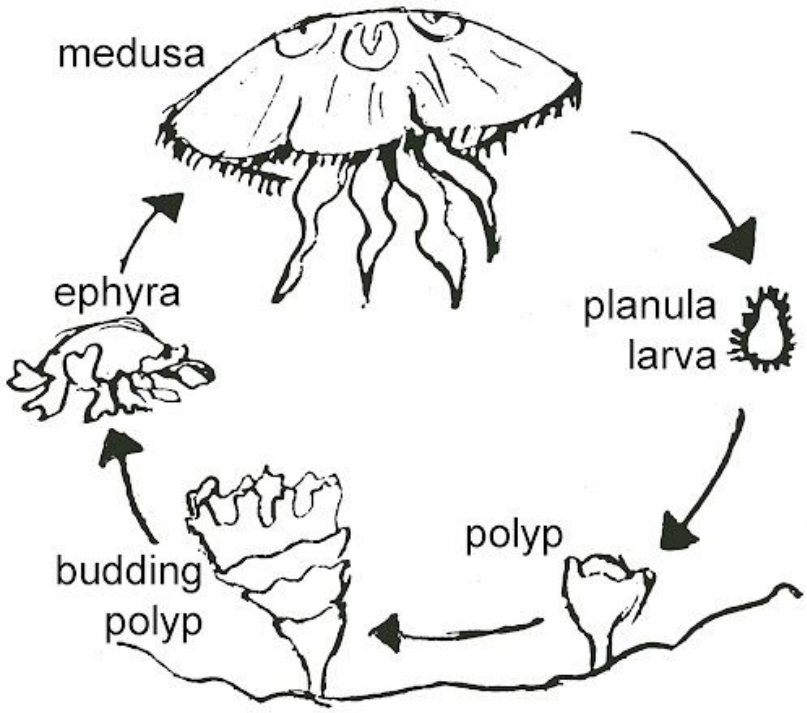

Figure 1. Life cycle in Hidrozoans (source: tolweb.org).

Stage 1. Fertilised egg: an adult jellyfish (i.e. a medusa) will spawn eggs and sperm into the water, with these two types of cells joining up to create fertilized eggs (Boero et al 2014);
Stage 2. Planula: fertilized eggs grow into small larvae, which are called planulae (Boero et al 2014; Matsumoto et al 2019). Planula looks something like a microscopic worm and can swim about freely (sciencefocus.com);
Stage 3. Polyp: the planula will swim down to find a solid surface, where it will develop a digestive system and this way it will be able to feed itself (Boero et al 2014). When the environment parameters, such as temperature, become suitable, the polyp will reproduce asexually, creating a small colony of identical individuals (clones);

Stage 4. Ephyra: after forming a new set of muscles and nerves, a section of a polyp (either the original polyp or one of the clones) becomes an ephyra, an organism that in this stage can swim independently, feed and grow (Dipper 2021; sciencefocus.com);
Stage 5. Medusa: this is a fully-grown adult jellyfish, which can reproduce sexually with another jellyfish (usually dying shortly afterwards) (sciencefocus.com). Sexual reproduction provides the species with the genetic variability necessary to adapt to various environmental factors, which are constantly changing.

As with other hydrozoans, there are two parts in the life cycle of the immortal jellyfish: the polyp stage and the jellyfish stage (Figure 1). However, a more specific life cycle is presented in Figure 2.

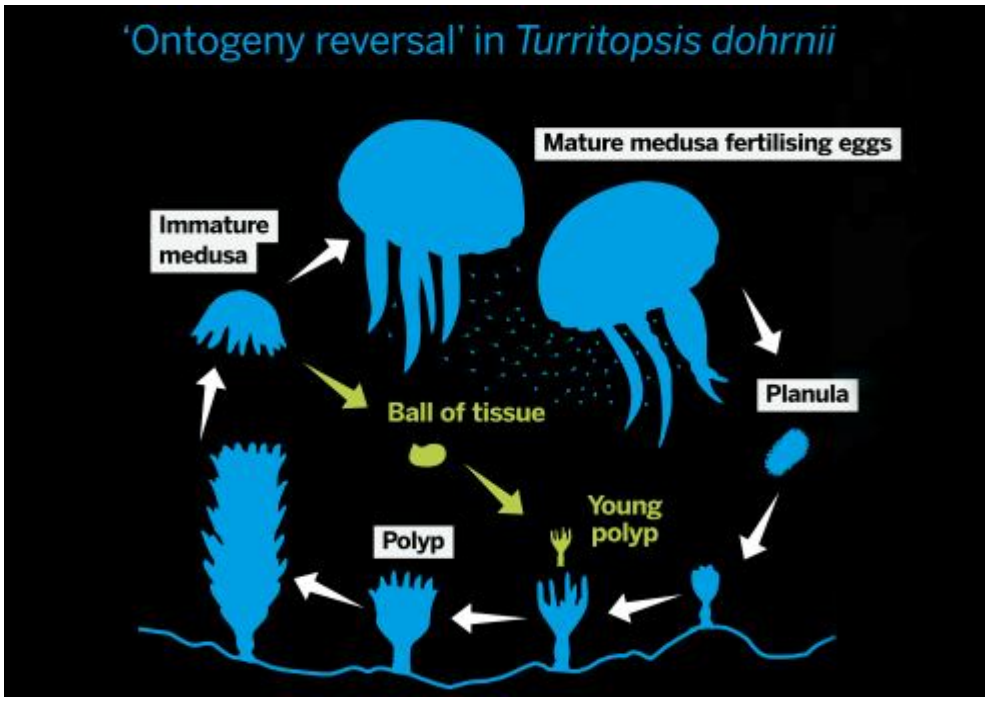

Figure 2. Life cycle of *T. dohrnii* (source: thebiologist.rsb.org.uk).

The immortal adult jellyfish is 4.5 mm wide when it reaches the right age for mating. When it is threatened or seriously injured, it turns into a ball (see Figure 2), and its cells begin to turn into other types of cells (Piraino et al 1996, 2004). Muscle cells can turn into sperm, and nerve cells can turn into muscle cells (Incredibila.ro 2021).

As a general description, we can say that young specimens have eight tentacles, and adults can have up to 90 tentacles. The stomach region is bright red, which contrasts with the bluish hue of the rest of the body. They are a truly magnificent view (Incredibila.ro 2021).

Immortal jellyfish feed on small mollusks, plankton and the eggs of some fish species. Can these jellyfish die? Yes, they can. These jellyfish are very fragile and tiny creatures. If eaten by predators, or affected by a deadly disease, jellyfish die. Because nature is intelligent, this phenomenon would certainly not occur in species at the top of the trophic pyramid.

***T. dohrnii* jellyfish, a solution in the fight against cancer?** Nature has found a way to provide such abilities to creatures that thus integrate into a diverse and balanced world. What does this mean for people? Will scientists find a way to help mankind by studying these jellyfish? There have been some links between the special ability of jellyfish and cancer (Matsumoto & Miglietta 2021; Mikuła-Pietrasik et al 2021). Micro-RNA is the genetic material that controls genes and is why immortal jellyfish can transform one cell type into another (Incredibila.ro 2021).

It has been found that cancer cells also have changes in micro-RNA (Pan et al 2018) and so, if scientists can control the micro-RNA, then they will probably be able to

transform tumor cells into other types, such as nerve or muscle cells (Piraino et al 1996, 2004; Incredibila.ro 2021). Research on this narrow topic is just beginning, but the immortal jellyfish, both gorgeous and fascinating, could one day cure cancer (Matsumoto & Miglietta 2021; Mikuła-Pietrasik et al 2021).

Conclusions. *T. dohrnii* jellyfish are small, bell-shaped creatures that have the ability to transform their mature cells into young cells. After reaching maturity and mating, jellyfish give back their biological clock and become young again. This process is called transdifferentiation and is the closest phenomenon to immortality on the planet. Research on this narrow topic is just beginning, but the immortal jellyfish, both gorgeous and fascinating, could one day cure aging effects and cancer.

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