The Immortality of *Turritopsis nutricula*

**Tyler Kaplan**  
Department of Biology  
Lake Forest College  
Lake Forest, Illinois 60045

**Introduction to Sexual Selection**  
The Fountain of Youth is a mythical spring that grants youth to anyone who drinks its magical elixir. Many have attempted to find the location of the Fountain, but its whereabouts continue to be a mystery. Despite the countless endeavors, there have been no reports of anyone actually drinking from the Spring’s contents, thus casting a shadow of doubt on its existence. However, a cnidarian, *Turritopsis nutricula*, has discovered its own fountain of youth due to its unique ability to change from its adult state, a medusa, back into a polyp, which is the stage it is normally in for only a few months until it reproduces. This hydrozoan was discovered more than one-hundred thirty years ago, but its unique genetic capabilities were not discovered until 1992. Pia Miglietta, a Pennsylvania State University biology researcher says, *T. nutricula* is “like a butterfly, but instead of dying it turns back into a caterpillar”(Henleffer, 2010). Rather than dying like all other organisms, *T. nutricula* is able to avoid the inevitability of death due to a variety of molecular alterations that allow it to revert back to an earlier stage in its life cycle.

The life cycle of *T. nutricula* is similar to many other hydrozoans, but differences in its medusa state make it unique to other hydrozoans. Hydrozoans, which are in phylum Cnidaria, have multiple variations in their life cycles (See Figure 1). Typically, hydrozoans begin as larvae, which then develop into polyps, which are small and cylindrically shaped. These polyps then bud other polyps through asexual reproduction and form colonies. Once the polyps reach reproductive maturity, the polyps bud medusae, which form gametes. Medusae are similar to a typical jellyfish with an umbrella like dome with multiple tentacles protruding from underneath(Cartwright & Nawrocki, 2010) After medusae produce gametes multiple times they die, but *T. nutricula* has developed a unique adaptation that protects itself from death.

![Metamorphosis Diagram](image)

1This author wrote the paper as a part of FYST121: Making Sense of Aging under the direction of Dr. Smith

*T. nutricula* is unique because of its ability to revert to an earlier stage in its life cycle by reactivating specific genes that were only used for that stage. This reverse metamorphosis is produced by a variety of cell processes such as transdifferentiation and apoptosis(Piraino et al., 2004). Transdifferentiation is when an already mature, specialized cell redifferentiates into another type of differentiated cell without going through an intermediate stage (Piraino et al., 2004). Ontogeny reversal has been observed in multiple Cnidarians, but this is always before maturation and sexual reproduction can occur (Piraino et al., 2004). *T. nutricula* is the only organism that is able to perform ontogeny reversal even after sexual reproduction occurs. In addition, *T. nutricula* exhibits the rare ability to have potential immortality in its solitary state, which is a medusa. Many colonial organisms have a potentially unlimited lifespan because even though individual organisms within the colony die, the entire group as a whole continues on. All the stages of a medusa have the ability to transform back into a stolon or polyp, allowing it to have a potentially unlimited lifespan Therefore, transdifferentiation plays a key role in the transformation process.

Selective excision experiments were conducted by removing specific tissues from medusae to see how it would affect medusae transformation. Results showed that in order for medusae to revert to the stolon or polyp form, differentiated cells of the epidermis and the gastrovascular cavity were required(Piraino et al., 2004). Interestingly, medusae have special muscle cells, nerve rings, and sensory organs that are not present in polyps. These anatomical differences between the forms of *T. nutricula* demonstrate that tissue substitution, regeneration, and reorganization must occur, and epidermal and cells of the gastrovascular cavity play a crucial role in this process. This is done through the process of transdifferentiation, where previously differentiated cells return to an undifferentiated state or spontaneously change their specialization through gene expression alterations(Piraino et al., 2004). Although stem cells most likely are involved in the process, it was initially thought that stem cells were responsible for ontogeny reversal. However, other hydrozoans that contain large amounts of replicating stem cells cannot revert back to their polyp stage(Piraino et al., 2004). Based on the data, it appears that transdifferentiation is the main process in which ontogeny reversal is accomplished, not stem cells.

Another experiment was conducted where groups of medusae in various stages of their development were exposed to a variety of stressors to trigger ontogeny reversal (See Figure 2). The factors were starvation, reduction in the salinity of the environment, change in the temperature of water, or mechanical damage to the bell structure of the medusae. All immature medusae, when subject to these different variables, regressed to the polyp or stolon stage after going into a cyst-like stage. The control group that was exposed to no abnormal conditions did not transform. When medusae were exposed to all of the stressors during sexual maturation, 20-40% of medusae reverted into the stolon or polyp stage without entering a cyst-like stage that immature medusae reverted to(Piraino et al., 2004). This most likely means medusae that spontaneously transformed into a polyp stage were already sexually mature because all of the mature medusae skipped the cyst stage as well(Piraino et al., 2004). Reverse metamorphosis is a defense mechanism used when the organism is not in an optimal environment. By reverting to an earlier state, *T. nutricula* is able to wait longer to reproduce in expectation that the environment will be better...
suited for reproduction. Although it is not completely understood how *T. nutricula* reacts in this manner, studies have revealed the conditions that trigger physical changes in the hydrozoan.

The 12-Tentacle stage is when the medusa is sexually immature. The 14-Tentacle stage is while the medusa is sexually maturing. The medusa is not fully mature until it contains 16 tentacles. (Schmich et al., 2007)

*T. nutricula* avoids death because of molecular changes in its cells allowing for ontogeny reversal. Through the process of transdifferentiation, cell substitution occurs in medusae that allow sexually matured organisms to revert back to an immature polyp stage. Studies have revealed that *T. nutricula*’s cells have a unique ability to alter their gene expression even after cell differentiation occurs. Although the process in which *T. nutricula* transforms is understood, it is not known how it is able to alter RNA expression and the specific genes involved in the process. In addition, due to the role of stem cells in the process, scientists are specifically interested in studying *T. nutricula* to hopefully one day develop human applications based on the function of stem cells in the hydrozoan.

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References

