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RESEARCH ARTICLE

REGENERATIVE ABILITIES OF PLANARIANS AND ITS INFLUENCE ON THE FUTURE OF REGENERATIVE MEDICINE

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Abstract

The regenerative abilities of a particular species of flatworm, the planarian, have been a topic of discussion and interest among scientists. These animals can regenerate parts of their body that have been cut off. This review includes the general introduction of planarians, the types of stem cells in its body, its basic anatomy and physiology, behavior, regeneration process, and applications to the medical field. We also predict the future of regenerative medicine that could be achieved by studying this particular animal model.

Introduction:-

Planarians are a type of flatworm in the kingdom of Animalia, phylum of Platyhelminthes, and class of Turbellaria. This specific species of animal is unique to others in the way that it can regenerate or regrow any part of its body when it has been cut off or amputated. For instance, if the planarian is cut transversely between the head and the tail, the part with the head will grow a tail and the part with the tail will grow a head. On the other hand, if the planarian is cut sagittally, the left side will grow the right side and the right side will grow the left. Scientists and researchers have been studying this phenomenon in hopes that humans too can regenerate certain parts of our bodies whenever we need it to. Planarians have the ability to regrow their parts due to a special type of stem cell they acquire: pluripotent stem cells.

Types of Stem Cells According to Potency

Totipotent (or Omnipotent) Stem Cells

Totipotent (or omnipotent) stem cells can differentiate into embryonic and extraembryonic tissues. In other words, these types of stem cells can differentiate into all types of tissue and "[t]he most important characteristic of a totipotent cell is that it can generate a fully-functional, living organism" (Hildreth, 2022). In humans, as well as other animals with placentas, these stem cells form the placenta. A newly fertilized egg (not longer than 4 days old) in an organism is a type of totipotent stem cell.

Pluripotent Stem Cells

Pluripotent stem cells can differentiate into the three germ layers: ectoderm, endoderm, and mesoderm. These types of stem cells can form different types of tissues and organs but only with a human being. Embryonic stem cells are a type of pluripotent stem cell that is in early-stage embryonic development. Since this type of stem cells can differentiate into a number of different tissues and organs, it is often used for cellular therapy and regenerative medicine.

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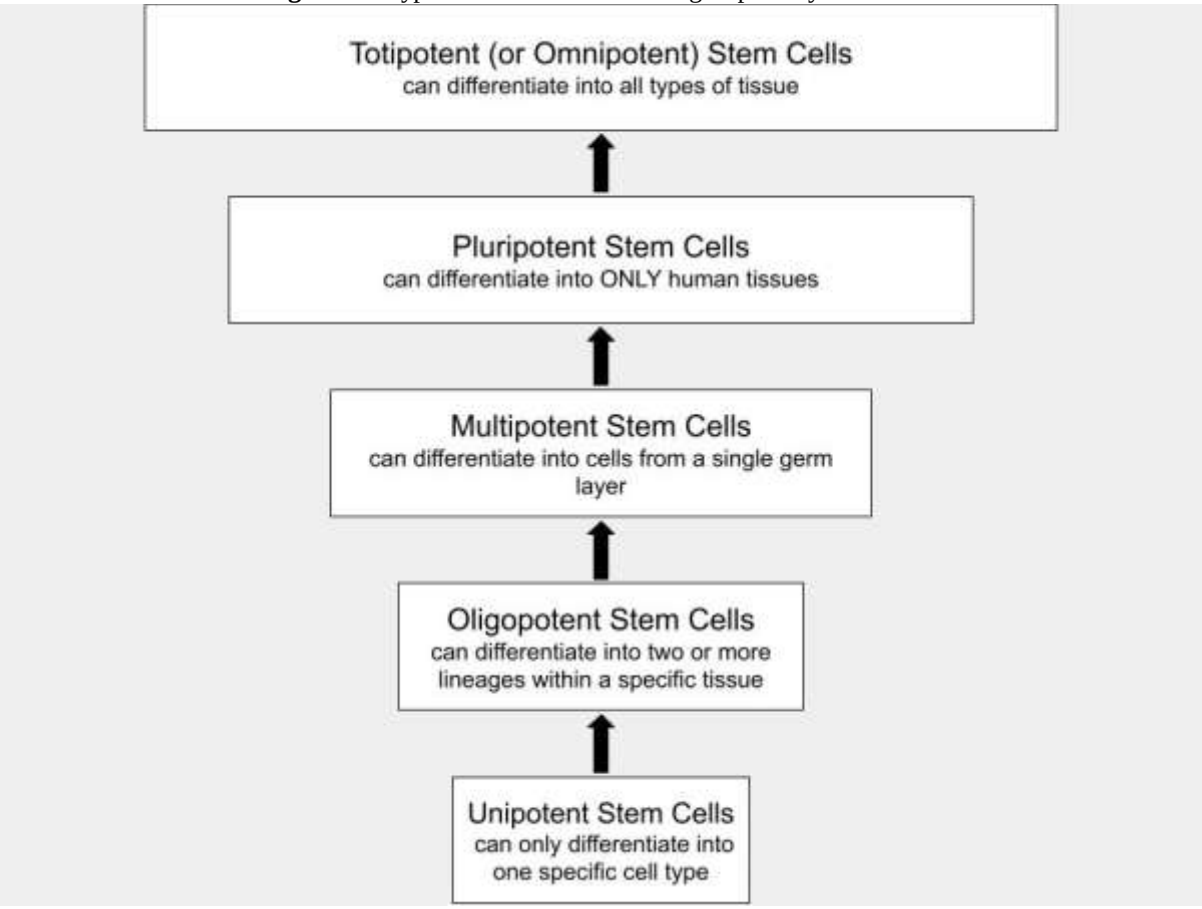
Multipotent Stem Cells
Multipotent stem cells are a type of stem cell that have the ability to differentiate into a smaller range of tissue types and they "differentiate into cells from a single germ layer" (Kolios & Moodley, 2012). An example of a multipotent stem cell is a mesenchymal stem cell which is partially diverse since "[they] can differentiate into osteoblasts (a type of bone cell), myocytes (muscle cells), adipocytes (fat cells), and chondrocytes (cartilage cells)" (Hildreth, 2022).

Oligopotent Stem Cells
Oligopotent cells are a type of stem cell that has an even smaller range of types of tissues that they can differentiate into than multipotent stem cells. "Oligopotent stem cells are able to self-renew and form 2 or more lineages within a specific tissue" (Kolios & Moodley, 2012). An example of oligopotent cells are hematopoietic stem cells that can differentiate into myeloid and lymphoid cells.

Unipotent Stem Cells
Unipotent stem cells are stem cells that can differentiate into the most restricted range of tissues. These types of stem cells can only differentiate into one specific cell type. An example of unipotent stem cells are muscle stem cells. Muscle stem cells can renew and differentiate only into muscle cells.

Figure 1:- Types of stem cells according to potency flowchart.

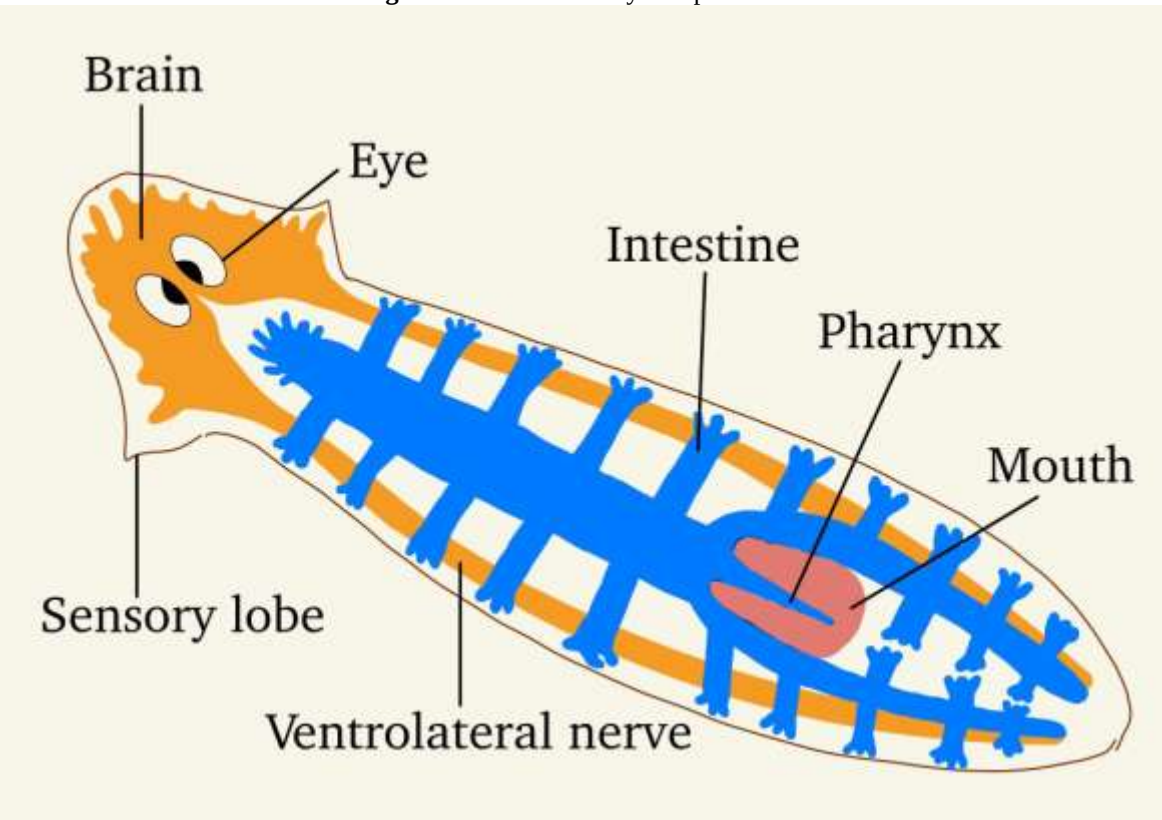


Anatomy of a Planarian
A planarian is a type of flatworm and all flatworms are acoelomates, "which is a fancy way of saying their bodies are so flat there isn't room for internal body cavities" (Planaria: Facts & Anatomy, 2015). These planarians are solid all throughout their body. They "inhale" oxygen and "exhale" carbon dioxide through their skin since they do not have lungs. These animals are composed of a body wall, head, pharynx, mouth, intestines, and eyes.

Planarians have a very simple nervous system with a group of nerve cells in the dorsal side that acts as their brain. Their central nervous system is separated into two parts: the anterior brain and the ventral nerve cords. "About nine branches in each lobe elongate to the head margin to form sensory organs, such as auricles" (Agata & Umesono, 2009). These types of flatworms consist of two eyes on the side of their head. The eyes are made up of only two cell types: pigment cells and photoreceptor cells. The axons of this cell form an optic chiasma and send signals to the central main lobe of the planarian where photosensory signals are processed to allow the planarians to sense their surroundings.

The pharynx is the body part of the planarian that allows it to consume food. It is located in the center of the planarian's body and looks like a minuscule tube coming out of its body. The "mouth is a single pore in the pharyngeal cavity opening on the ventral side" (Orii, et al., 2002). The mouth secretes digestive enzymes and external digestion begins. Internal digestion occurs in the intestines of the planarian.

Figure 2:- Basic anatomy of a planarian.



Planarian's Behavior

Planarians generally avoid open spaces. When they are put in containers, such as a petri dish, they will spend most of their time near the walls of the containers. "The head region, containing the brain, is important in movement and orienting toward or away from stimuli. If the head is separated it will move away from the less mobile headless body" (Deochand, et al., 2018). After being placed in a new environment, a planarian will go through an initial exploratory phase. They will "fold" their body while observing the surroundings.

This animal can both reproduce sexually and asexually. Planarians that reproduce asexually reproduce by binary fission followed by regeneration of the missing part of their body in about one week without developing sexual organs. Planarians that reproduce sexually "have hermaphroditic reproductive organs" (Nakagawa, et al., 2018) which means they have both ovary and testis, and they reproduce by these organs. These planarians mate by exchanging sperm and each one is fertilized by the other. This causes a higher genetic variability. After development, the eggs are then generally laid near a rock in freshwater streams. The eggs will hatch and the embryo planarians will become a juvenile one.

The Regeneration Process

Neoblasts, a type of stem cell, are necessary for planarian regeneration. These cells are located throughout the body and are activated to regenerate the tissues that have been severed when a portion of the worm is removed (Rossant, 2014). Thirty percent of the planarian body cells consist of these neoblasts. This type of pluripotent stem cell is responsible for the regenerative abilities of the planarian. Since neoblasts are all throughout the body of the planarian, it could regenerate any body part that is cut off.

The pharynx of the planarian does not contain stem cells. As a result, they are unable to regenerate the rest of the body. Other portions of the planarian, however, can easily regenerate the pharynx. A gene called the FoxA gene is what codes for the regeneration of the planarian's pharynx. Both the developing and mature pharynx of the planarians contain the FoxA gene. A few neoblasts are also present and scattered around the site of the amputation. Neoblasts are still there in the absence of FoxA, but they don't migrate to the site of the amputation and start the regeneration process; instead, they are diverted to other sites (Rossant, 2014).

Application to the Medical Field

The planarian is capable of regenerating all parts of its body including its limbs, pharynx, eyes, and even its brain. This is a capability that humans do not acquire. With further research, this skill set of the planarians could possibly be adapted from planarians to humans. Humans who are brain dead could possibly regenerate their nerves and neurons and come back to be considered living again. Those who lose a limb or other parts of their body can possibly regrow the part they want with this specific technology from planarians.

Despite the benefits of this technology, there will be risks and drawbacks to scientific processes. For instance, regeneration could go wrong and regenerate a body part that wasn't planned to regenerate. This could lead to cancer and other severe physical illnesses. "Most problematic among the risks of [stem cell]-based therapies, in addition to the possible rejection or loss of function of the infused cells, is their potential neoplastic transformation. Indeed, [stem cells] may be used to cure devastating diseases, but their specific properties of self-renewal and clonogenicity may render them prone to generate cancers" (Piscaglia, 2008).

Concluding Remarks and Future of Regenerative Medicine

The science of regenerative medicine, which includes cell treatment, gene therapy, gene-modified cell therapy, and tissue engineering, has the potential to revolutionize many areas of clinical medicine. This field has begun to expand over the last few years. Many predict that it will fulfill its promise over the coming decade and start to alter clinical medicine as we currently know it (Bokkelen & Vuksanaj, 2021). Some diseases that could be cured by stem cell therapy or regenerative medicine includes "degenerative disorders associated with the loss of [adult stem cell] functions, such as hematologic, cardiovascular, muscular and neurological diseases, gastrointestinal pathologies and chronic hepatopathies" (Piscaglia, 2008). With further research and development within the topics of regenerative medicine and planarians, clinical medicine could further improve its safety and efficacy on stem cell therapy and beyond.

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