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Research on Stem Cell Properties being Potentially Therapeutic for Patients with Pancreatic Cancer

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ABSTRACT

According to the World Health Organization (WHO), in 2020 cancer reached 19.3 million people and claimed ten million lives worldwide, becoming the second most common cause of death. The WHO has warned that the cases would rise to be almost 50% higher by 2040. Nonetheless, pancreatic cancer has more than 330,000 new cases a year; it is hard to detect early. The pancreas is in a deep region of the body. Therefore, tumours in their early stages cannot be seen or felt during routine physical exams. Resultantly, the mortality rate is high. However, it is one of the least studied types of cancer (United Nations, 2021). Stem cells' properties show significant potential as a treatment for pancreatic cancer due to their potency characteristics because of which they can differentiate into pancreatic islets. This research has been carried out with the advice of a board of five doctors from the National Institute of Neoplastic Diseases alongside the President of the Peruvian Society of Medical Oncology - Dr. Montenegro, who is currently researching stem cells to find new efficient treatments to attack cancer.

Keywords: Cancer, stem cells, differentiation, regeneration, and treatment

Subject: Oncology

Research Question: To what extent stem cell properties could provide a potential treatment for patients with pancreatic cancer?

Cancer

According to the National Cancer Institute (2021), cancer is a disease in which certain cells multiply uncontrollably and disseminate to organs. Under normal conditions, human cells form and multiply (through cell division) to form new cells as the body needs them. Cells die when they become old or damaged and are replaced by new cells. When the process deviates from this order, abnormal or damaged cells form and multiply when they should not. These cells, if accumulated, may produce tumours. These can be malignant or benign. Malignant tumours spread to nearby tissues. They could also travel further to other parts of the body and form tumours, a process called metastasis.

Normal cells are only formed when they receive signals that they should form. Cancer cells ignore signals that indicate the cells to stop dividing or to be destroyed. This process is called apoptosis. The immune system usually destroys damaged or abnormal cells. Cancerous cells get to deceive the immune system to stay alive and multiply. Some cancer cells even get immune cells to protect the tumour instead of attacking it.

Cancer is a hereditary disease. Cancer is caused by mutations in the genes that control how cells function, particularly how they form and multiply. In general, cells with damaged DNA are killed by the body before they become cancerous. However, as people age, their bodies' capacity decreases. As a result, the risk of cancer rises with age (National Cancer Institute, 2021).

Pancreatic Cancer

Pancreatic cancer begins in tissues of the pancreas, which is an organ that secretes enzymes that aid digestion and produces hormones that help control blood glucose levels. Pancreatic cancer develops when cells of the pancreas develop mutations in their DNA. A cell's DNA contains instructions that stipulate the cell what to do. In the case of mutations, DNA codes for uncontrollable cell growth, and these cells live on after normal cells die. These accumulating

cells can form a tumor. When left untreated, cancerous cells in the pancreas can disseminate to nearby organs and blood vessels and to distant parts of the body (Mayo Clinic, 2022).

The most common type of cancer that forms in the pancreas begins in the cells that line the tubes that transport digestive enzymes out of the pancreas. Pancreatic cancer is rarely detected in its early stages, when it is most curable. This is because it frequently does not cause symptoms until it has spread to other organs.

Surgery is the only existent cure. Yet, most patients are not candidates due to the tumor's location in the pancreas or because the cancer itself often has no symptoms until it has spread and reached an advanced stage. Also, most people who have surgery relapse and subsequently die of pancreatic cancer. Therefore, the five-year survival rate is no more than 5% (American Cancer Society, 2019).

Stem Cells

Stem cells are undifferentiated, immature, self-renewing cells capable of generating one or more types of differentiated cells. They are distinguished by two essential properties: their capacity for self-renewal, which is based on unlimited proliferation and their preservation as undifferentiated cells, and their ability to generate (differentiate) different cell types including bone, blood, epidermal, skin, neurons. They are classified into embryonic stem cells and adult stem cells (ASC) or mesenchymal stem cells (MSCs), which are located in the connective tissue of various organs, in peripheral blood, the umbilical cord, and in some foetal tissues (Pimentel & Murcia-Ordoñez, 2017).

Currently, stem cells are one of the most debated topics due to their scientific and social importance, as their implementation in the field of medicine offers alternatives for treating countless diseases, in addition to the fact that in a future they could become the source for the solution to treat innumerable diseases ranging from neurodegenerative, cardiac, endocrinological, immunological diseases, transplants, and even organ and tissue reconstruction (Centre de Cultura Contemporanea de Barcelona, 2014).

Stem cells are divided into four major categories based on their differentiation capacity: totipotent stem cells, pluripotent stem cells, multipotent stem cells, and unipotent stem cells. This study will focus on pluripotent and multipotent stem cells:

Pluripotent stem cells: Capable of differentiating into any of the tissues or cell types corresponding to the three embryonic lineages (endoderm, ectoderm and mesoderm), as well as the sexual or germ cells that comprise an adult organism; therefore, they cannot form a complete organism. Pluripotent stem cells are located at the embryonic pole of the blastocyst; the most researched are ESCs or blastemas, which form seven days after fertilization, although we also find other types of pluripotent stem cells such as foetal stem cells, which can be collected after eight weeks of development, when the embryo has become a foetus.

Multipotent stem cells: Capable of generating cells from their own embryogenesis layer, which includes, endoderm, ectoderm and mesoderm tissues. They are also denominated organ-specific stem cells and can generate an entire organ, either in the embryo or in the adult individual. This type of cells can be obtained from a broad range of variety of sources, among which, bone marrow and umbilical cord blood stand out; however, in humans they are found in numerous regions such as the brain, skin, heart muscle and skeletal, retina and pancreas.

Aside from their potency, stem cells can be categorized based on their provenance. Currently, different types of classification exist for this parameter, depending on the author being studied. They generally fall into two categories: embryonic stem cells (ESC) and adult stem cells (ASC).

Embryonic stem cells: Found in the early stages of the embryo's development and possess the ability to produce any type of cell; in other words, they are pluripotent cells since they have the ability to morph into any functional type of the three embryonic lineages. From the endoderm forms the pancreas, liver, thyroid, lung, bladder, and urethra. The mesoderm gives rise to the development of bone marrow, skeleton, striated muscle, myocardium, blood vessels, and renal tubules. Skin, neurons, the pituitary gland, the eyes, and the ears all develop from the ectoderm.

Adult stem cells: Divided into multipotent and unipotent stem cells, where cellular differentiation is irreversible, since the three embryonic layers have formed. This cell population can be obtained without harming the embryo because it is found in adult tissues and the umbilical cord. These cells allow adult cells of the tissue in which they are found, their proliferation occurs through asymmetric cell division, granting a progenitor cell and a transient amplification cell. These cells' role is to preserve and restore the tissue in which they are found; all tissues have a population of ASC that do not divide but enable tissue preservation. The best known are those belonging to the bone marrow and skin, which do tend to divide constantly (Pimentel & Murcia-Ordoñez, 2017).

Application of Stem Cells as A Potential Therapeutic

As pancreatic cancer progresses, it can cause complications such as weight loss, also known as cancer-associated cachexia. This is a complex problem. Pancreatic tumourssecretes compounds into the blood referred to as cytokines. These alter nutrient metabolism, causing the organism to burn calories faster than normal. It also breaks down muscle protein, decreases appetite, and makes nutrient digestion difficult because the pancreas lacks the ability to produce enough digestive hormones, including insulin (Pancreatic Cancer Action Network, 2022).

Stem cells have the ability to resolve this labyrinthine sequel and optimize treatment outcomes. A research team headed by Timo Otonkoski at the University of Helsinki, in collaboration with postdoctoral researcher Diego Balboa at the Center for Genomic Regulation (CGR), has pioneered efforts to optimize the functionality of pancreatic cells derived from stem cells.

The researchers demonstrated in an article published in Nature Biotechnology that stem cells can differentiate into cells that closely resemble pancreatic islets, both structurally and functionally. "Insulin secretion is properly regulated in cells, and cells respond to changes in glucose level," says VäinöLithovius, a University of Helsinki group member.

The physicians team displayed the function of these cells in cell culture as well as in mouse studies. Researchers confirmed in rodents that beta cells derived from transplanted stem cells began to effectively control glucose metabolism.

“After cell transplantation, blood glucose levels dropped to that seen in humans, to approximately 4 to 5 millimolar in mice. It was maintained at this level, demonstrating that stem cell-derived transplantation was capable of regulating blood glucose levels in these animals in the long-term," says Jonna Saarimäki-Vire, director of stem cell transplantation and also a researcher at the University of Helsinki.

Aside from insulin secretion, the researchers analysed the functionality of the mechanisms that regulate insulin secretion, including metabolism and ion channels, and linked their findings to gene expression in individual cells (Creative Commons SINC, 2022).

In this regard, the production of these cells, which are similar to pancreatic islets, would counteract the negative effects of cytokine secretion in relation to metabolism, the breakdown of proteins, carbohydrates and fats faster than normal. This would reduce the risk of cancer-associated cachexia and malnutrition, which affect quality of life, daily activities, response to treatment, and lead to longer hospitalizations and complications such as infections (Salud y Medicina, 2022).

Ethical Considerations

A main factor to take into consideration is the type of stem cells involved. The controversy over stem cell research and medical applications can be reduced to a single issue: their origin. When stem cells are derived from embryos, some ethical issues arise. It is argued that using human embryonic stem cells implies the destruction of embryos; however, life is thought to begin with the union of the spermatozoon and the ovum. This would imply the annihilation of a human life, which is unjustifiable (Ramírez, 2007).

Factors To Consider

Forbye from ethical considerations, embryonic stem cells have a proclivity for excessive proliferation and tumour formation (when obtained from embryonic teratomas), whereas adult stem cells do not suffer from this type of problem and new research shows that they have the same plasticity of ESCs, which is of great importance because the cell differentiation factor is key to the proposed treatment.

Another important consideration in stem cell research is the possibility that the patient's immune system could reject the treatment. ASCs present this issue because they have the genetic configuration of the individual to be treated, which ESCs do not have (Wadington, 2022).

CONCLUSION

Even though pancreatic cancer continues to increase its number of deaths, it has not been possible to find a method to optimize the results of treatment. However, since stem cells have the ability to differentiate into cells similar to pancreatic islets, thus I credit them competent to cope with one of the most complex complications, cachexia associated with cancer, due to their ability of producing insulin and regulating insulin secretion. In that vein, stem cells could reduce the risk of cancer-associated cachexia and malnutrition, improving quality of life, response to treatment, and avoid long hospital stays and complications such as infections.

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