

Therapeutic Potential of Umbilical Cord Derived Mesenchymal Stem Cells Conditioned Media in Induced Chronic Pancreatitis

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Abstract:

Chronic pancreatitis is a one of serious health problem characterized by impaired general health with persistent or intermitant abdominal pain, affection of exocrine acini as impaired digestion and endocrine as diabetes. Pancreatic duct ligation is common rodent experimental model for studing the effect of chronic pancreatitis on the pancreats. Stem cells are unique cells as they can differentiate into many specialized cells but there are challenges for their use including ethical concern and risk of tumor transformation. Stem cells conditioned media is liquid obtained after stem cells culturing and is rich in nutrients as growth factors and exosomes. Studies highlight its benefits in treating chronic inflammatory conditions such as chronic pancreatitis as well as neurodegenerative diseases, cardiac, tissue repair and immune disorders through its anti-inflammatory, antiapoptotic and anti-necrotic effects. It offers advantages such as easier storage and decrease tumorigenicity risk.

Keywords: Pancreatitis ; Stem cells ; Conditioned media ; Histology.

Introduction:

An inflammatory disease that affects the pancreas is pancreatitis which may be either acute or chronic [1].

The degenerative condition known as chronic pancreatitis causes irreversible pancreatic damage, fibrosis, and loss of function [2]. Abdominal pain, digestive problems, and diabetes are signs of the condition, which is characterized by persistent inflammation that progressively damages the pancreatic exocrine and endocrine components. Recurrent episodes of acute pancreatitis, chemical assaults, and hereditary factors can all lead to chronic pancreatitis, which gradually causes the pancreatic parenchyma to fibrose [3].

Pancreatic duct ligation:

A common experimental technique for researching pancreatic damage and related disorders, such as pancreatitis, fibrosis, and regeneration, is pancreatic duct ligation (PDL). PDL causes ductal hypertension and pancreatic secretory stasis by blocking the passage of pancreatic enzymes. Inflammation, damage to acinar cells, and the start of fibrotic processes are among the pathogenic events that are brought on by this. PDL is a crucial model for investigating pancreatic disorders and evaluating regeneration treatments [4]. **(Figure 1).**

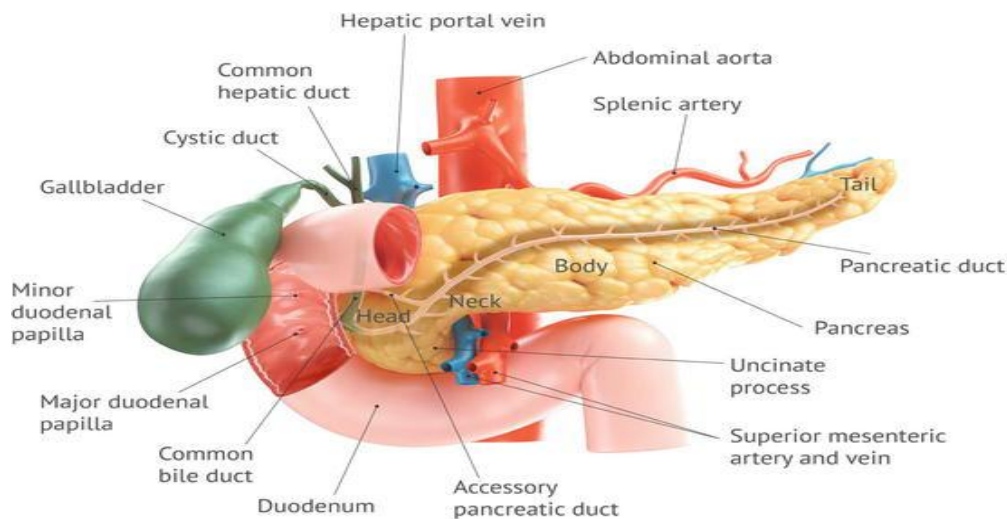


Figure (1): Anterior vision of the pancreas with duodenum section and vision of pancreatic ducts [5].

Pancreatic stellate cells (PSCs), the main source of pancreatic fibrosis, are activated by PDL-induced damage. Both endocrine dysfunction and exocrine insufficiency may result from this fibrosis's blockage of the residual ductal system [6].

Stem cells:

Stem cells have great potential for regenerative medicine and disease modeling since they are undifferentiated cells with the ability to self-renew and differentiate into specialized cell types. They are divided into three categories: induced pluripotent stem cells (iPSCs), adult stem cells (such as mesenchymal stem cells), and embryonic stem cells (ESCs). Through somatic cell reprogramming, iPSCs offer an alternative to ESCs, which are pluripotent yet controversial from an ethical standpoint. Using their multipotency and paracrine actions, adult stem cells such as hematopoietic and mesenchymal stem cells have shown therapeutic success in treating blood diseases and tissue repair [7].

One of the major obstacles to stem cell therapies is the ethical dilemma of ESC derivation, which involves the death of embryos. Immune rejection in allogeneic transplants and tumorigenic hazards such as teratoma formation from pluripotent cells continue to be major safety concerns. High prices, unpredictable trial outcomes (such as in cardiovascular repair), and technological challenges in managing differentiation further restrict clinical use. These difficulties were exacerbated by unregulated clinics and complicated regulations [8].

Stem cells conditioned media :

Conditioned medium (CM) is a nutrient-rich liquid that is collected after stem cells are cultured. It contains bioactive molecules that the cells produce during growth, such as growth factors, cytokines, and exosomes; these components are collectively referred to as the secretome. By encouraging tissue repair, angiogenesis, and immunomodulation, CM and exosomes provide cell-free therapeutic advantages [9] (Figure 2).

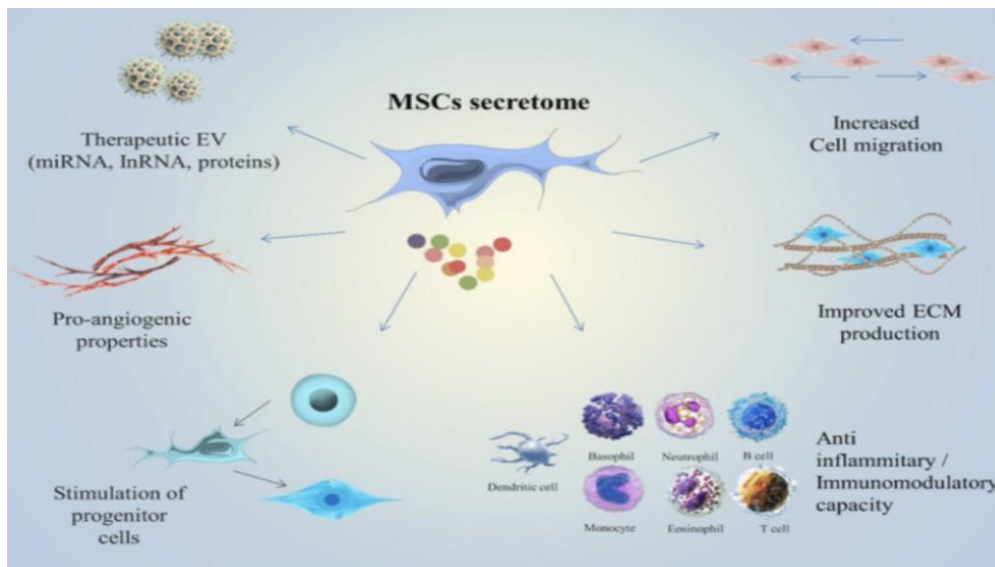


Figure (2) : stem cell bioactive molecules [10].

CM preserves the regenerative effects of cell transplantation while avoiding hazards like immunological rejection. Research demonstrates its effectiveness in wound healing, corneal restoration, and skin rejuvenation; standardized production techniques are developing as a focus for future therapies that eliminate the hazards associated with stem cell therapies, providing a more accessible and safe alternative [11].

CM has advantages over direct stem cell therapy, including easier storage, a longer shelf life, and a lesser risk of tumorigenicity or immunological reaction. Furthermore, CM avoids the ethical and legal issues surrounding stem cell treatments, which increases its viability for widespread clinical application [12].

MSCs derived from tissues such as bone marrow, adipose tissue, umbilical cord blood, Wharton's jello, and dental pulp can produce conditioned medium (CM). The characteristics of the CM are influenced by the source of MSCs; umbilical cord MSCs, for example, have improved immunomodulatory and regenerative activities [13].

Cytokines, chemokines, and growth factors like Vascular Endothelial Growth Factor (VEGF), Transforming Growth Factor-beta (TGF-beta), and Epidermal Growth Factor (EGF) are among the components of CM that support angiogenesis, tissue repair, inflammation regulation, and cell migration, among other biological processes. The therapeutic potential of CM is largely dependent on these characteristics [14].

Because of its anti-inflammatory qualities, conditioned media is especially helpful in the treatment of long-term inflammatory conditions such inflammatory bowel disease and rheumatoid arthritis. By encouraging neuronal survival and regeneration, it also exhibits promise for treating neurodegenerative illnesses like Alzheimer's [15].

Among the many advantages of mesenchymal stem cell conditioned medium (MSC-CM) are the promotion of wound healing, the reduction of inflammation, and the assistance of tissue restoration. This cell-free treatment reduces the possibility of tumor development or immunological rejection, making it a safer option than stem cell-based methods [16].

MSC-CM has many uses, such as wound healing, heart repair, immunological modulation, neurodegenerative disease treatment, and anti-aging treatments. As a less intrusive option to stem cell-based treatments, CM is also showing promise in the treatment of gastrointestinal and musculoskeletal disorders [7].

Mesenchymal stem cell-conditioned media has been pushed as a novel therapeutic agent in the treatment of numerous disorders, including induced fatty liver disease through its anti-inflammatory, anti-necrotic and anti-apoptotic. Additionally, the use of MSCs-CM protects recipients from potential risks of

infection, tumorigenicity, and immunogenicity, among other significant safety concerns including thyroid illness [17].

Additionally, MSC-CM is crucial for heart repair and wound healing in regenerative medicine. It provides a cell-free substitute for stem cell therapies without the concerns of immunological rejection by stimulating angiogenesis, decreasing scarring, and promoting tissue regeneration [18].

Understanding MSC-CM is essential for physicians since it provides a secure and efficient substitute for treating long-term illnesses. Doctors who are familiar with CM can investigate novel, minimally invasive treatment alternatives and contribute to the development of standardized, clinical-grade CM therapies [19].

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