The role of stem cells in treatment of gastrointestinal diseases

An essay
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بسم الله الرحمن الرحيم

قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيم

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Abbreviations

(5-ASA)	5-Aminosalicylate
(ASCs)	Adult stem cells
(AF)	Amniotic fluid
(BAL)	Bronchoalveolar lavage
(CNS-SCs)	Central nervous system stem cells
(CD)	Chron's disease
(CS)	Cyclosporine
(CK)	Cytokeratin
(CK-9)	Cytokeratin-9
(CMV)	Cytomegalovirus
(DM)	Diabetes mellitus
(DAH)	Diffuse alveolar haemorrhage
(ESCs)	Embryonic stem cells
(ERC)	Endometrial regenerative cells
(FACS)	Fluorescence activated cell sorting
(GVHD)	Gastrointestinal Graft-versus-Host Disease
(GFP)	Green fluorescent protein
(HSCs)	Haematopoietic stem cells
(HAPC)	Human activated protein C
(HHV-6)	Human herpes virus-6
(IBD)	Inflammatory bowel disease
(ICM)	Inner cell mass

(IBL)	Interpapillary basal layer
(ICCs)	Intestinal crypt cells
(IVF)	InVitro fertilization
(LIF)	Leukemia inhibitory factor
(MIBE)	Measles inclusion body encephalitis
(MSCs)	Mesenchymal stem cells
(MAPCs)	Multipotent adult progenitor cells
(ngn-3)	Neurogenin-3-positive cells
(Pdx-1)	Pancreatic duodenal homeobox factor
(PP)	Pancreatic polypeptide
(PBL)	Papillary basal layer
(RSV)	Respiratory syncytial virus
(TS-SCs)	Tissue specific stem cells
(TBI)	Total body irradiation
(TSC)	Totipotent stem cells
(TNF)	Tumor necrosis factor
(UACL)	Ulcer associated cell lineage
(UC)	Ulcerative colitis
(VOD)	Veno-occlusive disease

Contents

Introduction

Stem cells differ from other kinds of cells in the body. All stem cells-regardless of their source-have three general properties: they are capable of dividing and renewing themselves for long periods, they are unspecialized, and they can give rise to specialized cell type. ***(Campli, et al., 2003)***

Now it's possible to isolate and culture stem cells from embryo and adult tissue of many species, including human. Because of their unique combined abilities of unlimited expansion and pluripotency, embryonic stem cells are a potential source for regenerative medicine and tissue replacement. Stem cell plasticity is the ability of adult tissue-specific stem cells to switch to new identities; it also means stem cell phenotypic potential, which is broader than phenotypes of differentiated cells in their original tissues. ***(Korbling et al., 2002)***

Stem cells play a key role in tissue homeostasis and in renewal after damage, so a knowledge of stem cell biology may become a sort of Pandora's box ,which when opened will make it possible to clarify the nature and the pathphysiology of several human diseases and to find new therapies for those pathologies, such as cancers, degenerative, autoimmune and genetic disorders, that at present cannot be successfully prevented and resolutely cured, Stem cell research could be

particularly promising in gastroenterology for the specific characteristics of gut genesis and regeneration processes.
(A.C. Piscaglia, 2003)

Despite the numerous efforts mad during the last 20 years, the knowledge acquired on gastrointestinal stem cells appears fragmentary, incomplete and sometimes contradictory, and many questions thus remain to be solved: do intestinal stem cells really exist? What are their molecular and phenotypic characteristics? Where do they come from and where do they go? What are the mechanisms that regulate their proliferation and differentiation? What is their true potential? What is their role in homeostasis maintenance and in the genesis of diseases? How can we use them for prevention and / or for cure in gastroenterology*?* ***(A.Gasbarrini, 2003)***

Aim of the work

The aim of this Thesis is to review the role of stem cells transplantation as a treatment for gastrointestinal diseases in the present and the future.

General features of stem cells

1-Introduction

2-Definition

3-History of stem cells

4-Ethics of stem cells

5-Properties of stem cells

6- Potency definitions

A- Totipotent stem cells

B- Pluripotent stem cells

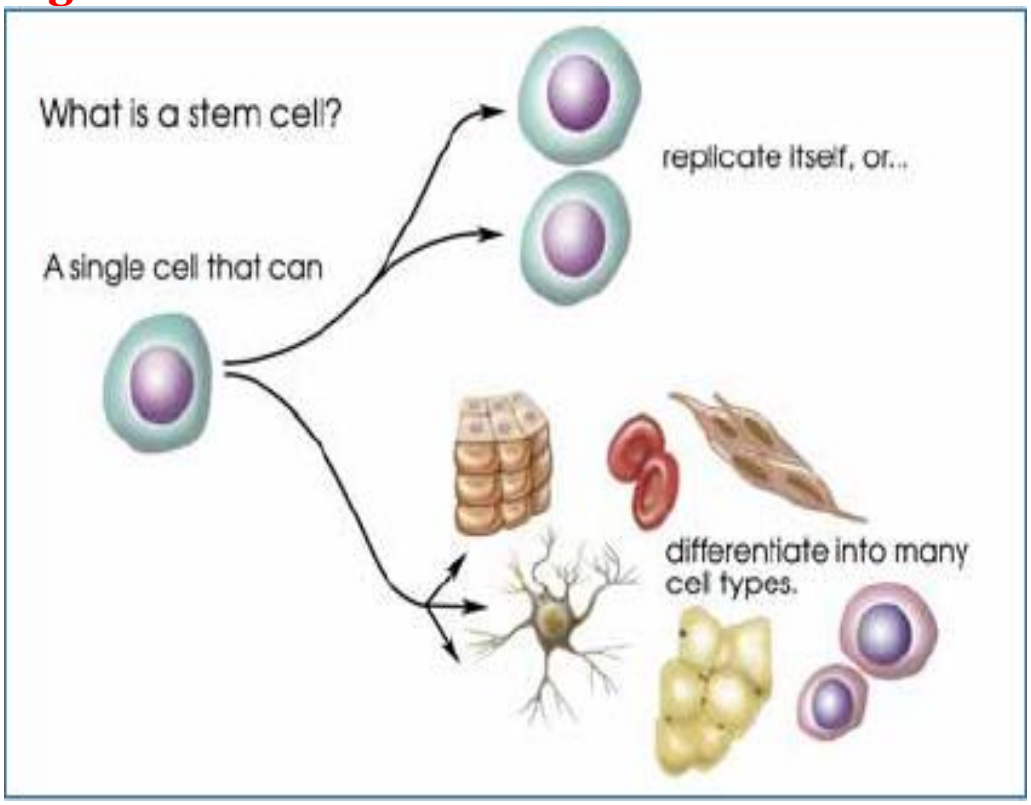
C- Multipotent stem cells

D- Unipotent stem cells

1- Introduction

A stem cell is a special kind of cell that has a unique capacity to renew itself and to give rise to specialized cell types. Although most cells of the body, such as heart cells or skin cells, are committed to conduct a specific function, a stem cell is uncommitted and remains uncommitted, until it receives a signal to develop into a specialized cell. Their proliferative capacity combined with the ability to become specialized makes stem cells unique ***(Slack, 2000)***. Stem cells play a key role in tissue homeostasis and renewal after damage. Stem cells clarify the nature and the pathophysiology of several human diseases and can find new treatments for pathologies, such as cancers, degenerative, autoimmune and genetic disorders, that are currently untreatable ***(Weissman, 2002).***

Figure 1: what is stem cell?



(Chandross, 2001)

2-Definition of stem cell

A stem cell is a cell that has the ability to divide (self replicate) for indefinite periods, often throughout the life of the organism. Under the right conditions, or given the right signals, stem cells can give rise (differentiate) to the many different cell types that make up the organism (Figure 1). Stem cells have the potential to develop into mature cells that have characteristic shapes and specialized functions, such as heart cells, skin cells, or nerve cells. ***(Chandross, 2001)***

3-History of Stem cells

- ***The beginnings: teratocarcinomas in mice***

The late 1960s and early 1970s was the first era of stem cell research. The first stem cells to be recognized in differentiated tissues were in teratocarcinomas, a cancerous tumour. The teratocaricomas were isolated from rats, and found to contain "embryonic carcinoma" cells. These cells were noted to respond to stimulation by differentiation both in vitro and in vivo ***(Stevens, 1967).***

Inserting these embryonic carcinoma cells into other sites in the mice caused either teratomas or teratocarcinomas in those areas of transplantation ***(Evans, 1972)***.However; the behavior of these embryonic carcinoma cells was similar enough to embryonic stem cells that they were used as a model to derive similar cells from actual embryos.

- ***Embryonic stem cells are isolated from animals***

The 1980s the first embryonic stem cells, were isolated from mice ***(Evans, 1981).***Whereas the earlier teratocarcinomas-derived embryonic carcinoma cells lost their ability to differentiate over time, the embryonic stem cells continued to maintain differentiation. When introduced into blastocysts. ***(Bradley, 1984).***

- ***Embryonic stem cells differentiating to somatic tissues***

The 1980s also saw the advances in research into the ability of the stem cells to become end somatic tissues. The cells were cultured to tissues ranging from neural to skeletal to cardiac***. (Doetschman, 1985).***

- ***Human embryonic stem cells are isolated***

The next step was isolation of stem cells from humans. This was first performed using embryos collected from patients enrolled in an in vitro fertilization (IVF) program, who volunteered some embryos for stem cell research ***(Bongso, 1994).*** The embryos were cultured to produce blastocysts. The inner cell mass (ICM) of each blastocyst was separated into individual stem cells.

- ***Animal dependency is fully removed from the equation***

Originally, stem cells were grown on animal mediums such as murine embryonic fibroblasts. However, there is an inherent risk to using such growth media in a therapeutic scenario, since could one could theoretically pass diseases from animal to the human one is trying to treat.