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ORIGINAL ARTICLE

Endogenous bone marrow stem cell mobilization in rats: Its potential role in homing and repair of damaged inner ear

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Abstract The stem cells are widely used in the last few years in different fields of medicine, either by external transplantation or endogenous mobilization, most of these studies are still experimental on animals; few were tried on humans as in the spinal cord injury or myocardial infarction. As regards its use in the inner ear, stem cell transplantation was examined in many previous studies, while the mobilization idea is a new method to be experimented in inner ear hair cell regeneration.

The aim of this work was to assess the use of GCSF to induce bone marrow SC mobilization to home and repair the damaged inner ear hair cells in rats after the damage had been inflicted by Amikacin injection.

First we had to develop an animal model for damaged inner ear, so we used the well known ototoxic effect of Amikacin intra-tympanic injection till we reached complete loss of hearing function. And this can be assessed by DPOAEs. Now we have an animal model of damaged inner ear hair cells and mobilization of bone marrow SCs was induced by subcutaneous injection of G-CSF for 5 days.

Clinical assessment was done using DPOAEs before and after G-CSF injection also histological assessment of the inner ear was done before and after G-CSF by two methods H&E staining and Scanning Electron Microscopy.

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The results of histological examination of the specimens showed some promising changes that may be responsible for the improvement of hearing function in some rats that was detected by OAEs.

1. Introduction

The inner ear is composed of two main parts. The auditory portion includes the cochlea, which is involved in hearing, and the vestibular system which is involved in balance. Our ability to hear and our sense of balance are critically dependent on specialized sensory receptors called hair cells, these cells have structures called stereocilia, which sense sounds by bending back and forth, converting mechanical vibrations into electrical, or neural signals that are then passed to the brain through the auditory nerve.[1,2]

Auditory hair cells, like a microphone, are designed to convert sounds into neural activity. Vestibular hair cells, those located in structures called the semicircular canals; detect head rotation, whereas other vestibular hair cells, located in structures called the utricle and saccule, sense head orientation with respect to gravity.[2,3]

Finding ways to cure deafness represent a major scientific and clinical breakthrough.[1] Recently, stem cells from the inner ear of adult mice have been identified.[4] These adult stem cells are found in the utricle of the vestibular region of the inner ear. They have the characteristic features of stem cells such as the capacity for self renewal and expansion (they divide and multiply). They form spheres, which begin to differentiate into new cell types termed as progenitor cells. Some progenitor cells differentiate into cells that express proteins and genes present in the developing inner ear and nervous system. Under appropriate conditions, some cells differentiate into cells resembling hair cells, which have stereocilia; hair bundles protruding from their surface and express specific hair cell marker proteins. The discovery of such cells is a first step toward a promising line of treatment in restoring hearing and balance function.[5,6]

Stem cells are unspecialized cells that have two defining properties: the ability to differentiate into other cells and the ability to self-regenerate. The ability to differentiate is the potential to develop into other cell types. A totipotent stem cell (e.g. fertilized egg) can develop into all cell types including the embryonic membranes. A pluripotent stem cell can develop into cells from all three germinal layers (e.g. cells from the inner cell mass). Other cells can be oligopotent, bipotent or unipotent depending on their ability to develop into few, two or one other cell type(s). Self-regeneration is the ability of stem cells to divide and produce more stem cells.[6,7]

There are two main types of stem cells: embryonic and adult stem cells. Embryonic stem cells are derived from embryos. Typically 4 or 5 days old and consist of a hollow microscopic collection of cells called the blastocyst. Unlike adult stem cells, embryonic stem cells can become all cell types because they are pluripotent.[8–11]

Adult stem cells are stem cells that can be derived from different parts of the body and, depending on where they are from, have different properties. They exist in several different tissues including the bone marrow, the blood and the brain. Some studies have suggested that adult stem cells are very versatile and can develop into many different cell types.[12,13]

Hematopoietic stem cells are adult stem cells found mainly in the bone marrow and they provide the blood cells required for daily blood turnover and for fighting infections. Compared to adult stem cells from other tissues, hematopoietic stem cells are easy to obtain, as they can be either aspirated directly out of the bone marrow or stimulated to move into the peripheral blood stream, where they can be collected easily .[14–19]

More recently, their use in treatment of breast cancer and coronary artery diseases has also been explored.[20] The potential for hematopoietic stem cells to produce cell types other than blood cells has become the subject of intense scientific controversy, and it is still not clear whether they could be used on a clinical scale to restore tissues and organs other than blood and the immune system.[21,22]

Mesenchymal stem cells are another well-characterized population of adult stem cells. These cells, also found in the bone marrow, can form a variety of cells in the laboratory, including fat cells, cartilage, bone, tendon and ligaments, muscles cells, skin cells and even nerve cells. Unlike most other human adult stem cells, mesenchymal stem cells can be obtained in quantities appropriate for clinical applications, making them good candidates for use in tissue repair.[16,23]

From a scientific perspective, scientists will first need to identify compounds and conditions that can increase the growth of stem cells and promote their differentiation into hair cells or supporting cells.[24] From a clinical perspective, surgical and technical procedures need to be developed to successfully transplant stem cells into the inner ear. The critical question to be answered is whether transplanted stem cells can migrate to the correct location, differentiate into hair cells and restore hearing or balance.[25,26]

Mobilization of endogenous stem cells provides an alternative way of replacing damaged inner ear hair cells, and correcting hearing loss.[19,22] Mobilizing host stem cells is less cumbersome than transplantation in that it avoids the logistical complexity associated with the use of embryonic as well as non embryonic stem cells, including supply, surgical trauma, and possibilities of graft rejection, uncontrolled graft cell proliferation and tumor formation.

2. Aim

The aim of this work is to assess the use of G-CSF (Granulocyte Colony Stimulating Factor) to mobilize Bone Marrow Stem Cells to reach the inner ear of rats and its ability to repair damaged inner ear after injecting Amikacin sulfate into the middle ear of rats.