STEM CELL POTENTIAL USES IN RETINAL DYSTROPHIES

UTILIZACIÓN POTENCIAL DE CÉLULAS MADRE EN ENFERMEDADES DEGENERATIVAS RETINIANAS

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The way to obtain and maintain a culture of mice embryo stem cells has been known for about 25 years (1). In late 1998, after intense experimentation work, a group of Wisconsin University researchers obtained the first culture of human embryo stem cells (2). As of that time, stem cells have been presented as the great therapeutic hope of the new century. The human embryo stem cells are immortal and have almost unlimited development potential. After remaining months in a culture, said cells maintain the ability to differentiate into any type of cell. This proliferation and differentiation capacity carries the promise of supplying specific cell types for basic research or therapeutic transplant for application to various types of pathologies such as heart disorders, leukemia, diabetes, Parkinson's or retinal degenerative diseases.

The main applications in stem cell research are: the identification of action mechanisms of various drugs and the assessment of their therapeutic potential, the understanding, prevention and treatment of congenital diseases, the study of cell differentiation at the basic research level and the obtainment of tissues and cells for transplants. After achieving the differentiation of stem cells in a specific type of precursor or mature cell, it could be utilized for some human diseases caused by the death or dysfunction of a specific cell type (dopaminergic neurons in Parkinson's, insulin-producing cells in diabetes, photoreceptors in pigmentary retinosis or retinal pigmentary epithelium) in ARMD.

The lines of human embryo stem cells are not the only source of cells for therapeutic use. For instance, neuronal precursors for the retina can be obtained from the eyes of fetus which did not complete their development, from hematopoietic cells and the umbilical cord. The literature has also described the possibility of multipotential retinal cells in the pars plana of the ciliar body in human adults (3), as is the case in other vertebrate species such as amphibians or fish.

The use of human embryo and fetal cells in cell therapy has given rise to ethical and social issues, in addition to the technical difficulties involves in obtaining the effective integration of said cells in the recipient tissue at the morphological and functional level.

Many questions remain to be answered about controlled differentiation of stem cells to form a given cell type. It is known that stem and progenitor cells receive instructions from specific regulatory genes as well as obtaining information from their environment. These signals determine the destiny of said cells and the type of tissue they will originate. Embryo stem cells can form embryoid bodies in culture and can be directed towards neural differentiation by adding retinoic acid of FGF2 to the culture medium after a proliferation phase in the presence of various factors. The subsequent differentiation into retinal neurons can be achieve by a joint culture with retinal cells or overexposure of some regulatory gene (such as Crx).

Stem cells which differentiate into various neuronal types o retinal pigmentary epithelium have been utilized in cell therapy on various animal models of pigmentary retinosis, generally obtaining an improvement in functional response and anatomic preservation (4). Recently, researchers have observed the establishment of correct synaptic connections after transplanting rod-precursor postnatal cells in blind

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mice (5). Even though numerous problems remain to be solved for effectively applying said cells in patients, including ethical and legal barriers, substitution therapy with stem cells holds a promising outlook for treating a large number of retinal neurodegenerative diseases.

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