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Induced pluripotent (iPSCs) and mesenchymal stem cells: Potential therapeutic role in glomerular repair: What we know and what we need to find out

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The study of stem cells is a growing field in which these are used to repopulate, therefore, repair damaged tissues. Many studies have been performed in several organ systems. In the kidney, studies of stem cell repair have been conducted for repair of the tubules but very little has been published about glomerular repair.

Our laboratory has been engaged in the study of mesangial repair after injury induced by using mesenchymal stem cells (MSC) to repopulate the damaged mesangium and differentiate into mesangial cells. Mesangial injury produced by glomerulopathic monoclonal immunoglobulin light chains can produce damage either by lysis of the mesangial matrix with replacement of the damaged matrix by amyloid (AL-amyloidosis) or increased matrix by deposition of abnormal light chains (light chain deposition disease) depending upon the physicochemical abnormality of the light chain utilized in the experiments, and corresponding interactions with mesangial cells.

Our unique experimental model of mesangial injury has allowed us to explore the use of exogenous stem cells for mesangial repair of the damage produced by two different physicochemically and, therefore, conformationally (stoichiometrically abnormal) different light chains.

In vivo and *In vitro* platforms have been used to observe mesangial damage and repair from the In vitro and In vivo aspects. The sequence of events that leads to mesenchymal stem cells identifying the site of glomerular damage, eliminating the remnants of the damaged mesangium such as apoptotic cells and extraneous matrix (LCDDD and AL-amyloid) and to differentiating into mature mesangial cells which then lay down new mesangial matrix has been elucidated. Part of our in vitro studies includes our observations utilizing a six Dimensional (6 D) live cell culture system by which the actual glomerular repair was observed and digitally recorded for up to approximately 14 days. By this method the process of mesenchymal stem cells clearing mesangial debris and differentiation into mesangial cells can be analyzed in detail.

Each of the platforms will be presented to show their advantages and limitations. By studying the information obtained by each model system we have been able to better understand how exogenous mesenchymal stem cells can participate in the repair of the glomerular mesangium.

The use of induced pluripotential stem cells (iPSC) in the kidney has a scant representation in the literature. A review of what is available will be presented. iPSC are a type of pluripotent stem cells that can be generated from adult stem cells.

Dr. Shinya Yamanaka is the pioneer of this revolutionary technology that allows experimentation and ultimate repair and treatment of different conditions without the use of embryonic stem cells and the controversial method of obtaining them. Yamanaka, in 2006 showed that the introduction of four specific genes that encode transcription factors into the genome of mature/committed cells, leads to the reprogramming of these cells into pluripotent stem cells. Advantages of iPSCs (besides not being necessary to destroy or manipulate embryos), is that these can be made patient-specific making it useful in the treatment of genetic diseases and others.

Methods of reprogramming mature cells can range from Yamanaka's method of virally introducing the four specific genes: OCT4, SOX2, KLF4 and c-Myc to a variety of other methods are still in evolution. Concerns of oncogenic transformation due to tampering with the cellular genome brought about in 2008 a technique for removal of the oncogenes introduced after inducing pluripotency and in 2009 scientists found a way to induce pluripotency without the necessity to tamper with the genome by the exposure of mature cells to recombinant proteins or protein induced pluripotent stem cells (iPSC). Recombinant proteins are also about 100-200 times more efficient than retroviral methods in inducing regression of mature cells into pluripotency.

The evaluation and experimentation to develop new methods of inducing pluripotentiality avoiding those that could be potentially harmful to patients is ongoing and it is our hope that it will develop into efficient methods by which stem cells can be produced and used for the repair and healing of damaged kidneys as well as other organs.

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