Gene Delivery to Mesenchymal Stem Cells

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Abstract

There is increasing trend in using recombinant stem cells as novel therapeutic candidates in different diseases. These studies encompass different applications from targeted homing of Mesenchymal Stromal (stem) Cells (MSC), to arming them with different cytokines. Resistance to transfection or transduction methods had urged researchers to look for better gene delivery alternates and optimizing them. Though chemical transfection methods are usually considered safer than viral gene delivery methods, most of these reagents suffer from low efficiency in lower concentrations and high toxicity in the higher ones. We, as well as other researchers, have reported the best efficiencies with Lipofectamin 2000^{TM} reagent, with up to 50% efficiency in some reports while we have not been able to reach this level. Theoretically low transfection efficiency could be compensated by stably transfecting a cell line followed by long term culture in a selective medium. Usually this approach is not practical for MSC since they should be used within the first few passages after isolation. Indeed, we have previously shown that long-term culture of these cells is associated with chromosomal abnormalities and profound morphological changes.

Lentiviral transduction methods have achieved the highest efficiency in delivering foreign genes to MSC (above 95%in several cases) but the safety concerns has hindered their application in clinical studies. While adeno-associated viral vectors have been used in several gene therapy studies, MSC seem to be resistant to this method. There are reports of high efficiency of adenoviral gene delivery to MSC, though in our hand it was much lower than lentiviruses. Howevere, we found pretreating these cells with valproic acid could increase transduction efficiency of adeno-associated vectors by 2.5 fold, mainly through increasing the expression of its cell surface receptor. In our lab, using lentiviral vectors, we could transduce MSC with the efficiency of more than 90%. In conclusion, we believe that chemical transfection methods such as Lipofectamin 2000^{TM} is a good choice when transduction rate is not a main concern and lentiviral vectors are suitable for a high yield stable gene delivery to these stem cells.

Keywords: Mesecnchyal Stromal Cells, Gene Transfere Techniques.

Oral Presentation

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