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Mesenchymal stem cell expansion with small molecules

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The development of commercially available stem cell sources has let the researchers to modulate the immune system and provide valuable assets for regenerative medicine and cell-based tissue repairing systems. Mesenchymal stem cells are great candidate for transplantation based therapies with their immunomodulatory abilities, differentiation potentials because of their easy accessibility. They are present in the adult body, they can self-renew themselves and exhibit multipotency. They can differentiate to bone, fat, chondrocyte and other various cell types under specific conditions including neuronal cells. They can be obtained from different tissue types including; bone marrow, adipose tissue, umbilical cord, dental tissue, etc. Isolation of MSC is easy but there are major challenges on mobilization, expansion and understanding the differentiation mechanism. If these challenges overcame, MSCs show great potential for experimental and clinical applications. Stem cell based therapeutic approaches have also shown to be affective in neurodegenerative diseases' treatment. In our study we focused on expansion of mouse bone marrow MSCs, with small molecule treatment, with that we hope to achieve increased mobilization results as well. We selected four effective molecules firstly by WST-1 assay, cell viability assay was supported by pyronin y/hoechst staining. To see the effects on cell mechanism; cell cycle analysis, apoptosis analysis were conducted. The results did not suggest any misconduct on our MSC culture. Next, we performed RT-PCR and checked if there were any negative changes on HDR-related, CDKI, S-Phase and MSC immunomodulatory gene expressions. Also with CFU assay, we showed that after small molecule treatment, differentiation ability of our MSC was not lost. Our first and most effective molecule is a GSK-3 inhibitor that stabilizes free cytosolic β-catenin and inhibits differentiation. Second one is a p38-MAPK inhibitor. In conclusion, we found a safe and reliable way of in vitro expansion of mouse BM-MSCs. Our next step is in vivo trials by small molecule treated stem cell transplanation to SCID mice. With all this, our goal is to carry this knowledge to therapeutic field.