

Simulated Microgravity Approach for Enhanced Stem Cell Potency

Simple and convenient method for enhancing medically-relevant stem cell properties (expansion and potency).



Schematic illustrating the method of using simulated microgravity to improve stem cell differentiation potency.

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Technology

The Teo Lab has developed a simulated microgravity (s-µg) approach to enhance medicallyrelevant stem cell characteristics, such as expansion and differentiation capacity, for use in stem cell-based therapies. In this approach, stem cell cultures in proprietary polydimethylsiloxane (PDMS) microvessels are subjected to specific s-µg conditions using a random positioning machine (RPM). The RPM settings and s-µg culture conditions have been experimentally optimized for augmented pluripotency. As described in an unpublished study, human adiposederived stem cells (hADSCs) subjected to s-µg exhibited a 59% increase in the number of adherent cells in culture compared to the control group (Earth's gravity). To induce differentiation, s-µg treated hADSCs were incubated with adipogenic and osteogenic factors for two weeks, triggering their development into adipocytes and osteocytes, respectively. For adipocyte differentiation, s-ug treated hADSCs produced a significantly greater number of adipogenic-committed cells (2.1-fold increase relative to the control). For osteogenic differentiation, s-µg treated hADSCs demonstrated enhanced calcium production (two-fold increase relative to the control), and exhibited superior bone formation activity, as evidenced by increased alkaline phosphatase (ALP) activity. The differentiated state of the s-µg treated stem cells was further validated by high-throughput sequencing and PCR analysis of pluripotency gene expression markers, such as Oct4, Sox3, and Nanog. Analysis at the genetic level determined simulated microgravity preserves hADSC stemness, an important element in regenerative medicine. Notably, the hADSCs maintained their improved differentiation potency after one month of cryopreservation, enabling future use or transportation. In summary, the

Teo Lab has identified a simulated microgravity method to significantly enhance stem cell characteristics, paving the way for more effective stem cell-based therapies for disease treatment, tissue engineering, and regenerative medicine.

Background

Stem cells possess the remarkable ability to differentiate into over 200 different cell types, making them highly valuable for tissue engineering and the treatment of various diseases, including cardiovascular disease, neurological disorders, and degenerative conditions. A critical step in the production of a successful stem cell-based therapy is the robust expansion and differentiation of these cells. Yet, millions of differentiated cells are required for therapeutic applications, and efficient methods to produce such quantities are lacking. Previous studies have shown that three-dimensional culture in simulated microgravity (s-µg) can direct stem cells toward differentiation and facilitate the formation of functional tissues through cell self-aggregation. In the context of regenerative medicine particularly, there is a significant unmet need for a simple and convenient method to effectively enhance the differentiation potency of adult stem cells for tissue regeneration.

Development Status

Ongoing work includes RNA-seq analyses of the s-µg treated hADSCs and gene ontology analysis of differentially expressed genes.

Applications

s-µg treated stem cells could be used in a variety of regenerative and therapeutic applications, including:

- Regenerative medicine, such as organoid implants and tissue regeneration
- · Cosmetic and plastic surgery
- Degenerative diseases
- Cardiovascular diseases
- Neurological diseases

Advantages

- Speed: s-µg treated stem cells exhibit an enhanced differentiation and proliferation profile
- **Increased potency:** Boosted pluripotent state allows for cell differentiation versatility and unlimited self-renewal
- **Shelf life:** s-µg treated stem cells can be cryopreserved for future use/transportation while maintaining enhanced a differentiated state
- **Applicable to multiple stem cell types:** hADSCs, bone marrow-derived stem cells, iPSCs, and tissue-specific stem cells
- Improved stem cell integrity: PDMS microvessels used in culturing protect against RPMinduced stress

Intellectual Property

NYU holds a U.S. provisional patent application covering the method of using simulated microgravity to improve stem cell differentiation potency.