Using small molecules for improved static 3D culture of human induced pluripotent stem cells.

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Induced pluripotent stem cells (iPSC), which can be derived from mature differentiated cells, provide an excellent source of cells to study human diseases mechanisms and screen for lead molecules for drug discovery[1]. A fundamental element needed to exploit the potential of stem cells throughout these applications is the ability to produce a large number of cells of a consistent quality and in a cost-effective manner[2].

3D cultures systems are expected to meet the high demand for cells needed for such applications. However, this approach faces problems with cell aggregation[3]. Cells in the centre of large aggregates are generally underexposed to nutrients, resulting in variable growth rates, apoptosis and uncontrolled differentiation. This heterogeneity leads to challenges in standardization with respect to culture and assay protocols, and data for analysis[4].

Unlike any other approach focusing on the maintenance and expansion of iPSC, our innovative research project applies synthetic organic chemistry as an enabling tool to produce cells of a consistent quality on a cost-effective clinically-relevant scale. A screening of compounds has enabled the identification of teleocidin natural products that led to derivatives that were thoroughly optimized and used as medium additives allowing a better expansion of iPSC via an easy, standardized and xeno-free suspension method. Treated iPSC formed significantly smaller aggregates and dissociated more easily. Additionally, this control of aggregate size was done in a scaffold-free manner while overcoming issues of diffusion and lack of homogeneity.

In summary, our innovative technology hypothesizes the fact that smaller and therefore more viable aggregates can be cultured in the presence of small molecules by disrupting cell-cell adhesion when targeting key adhesive molecules. Moreover, this culturing technic could bridge the gap between in vitro and in vivo studies with the potential to have huge impact on drug screening and possibly decreasing the use of animal models.

References

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