

Scalable and Continuous Production of iPSC-derived Macrophages for Therapeutic and Research Applications

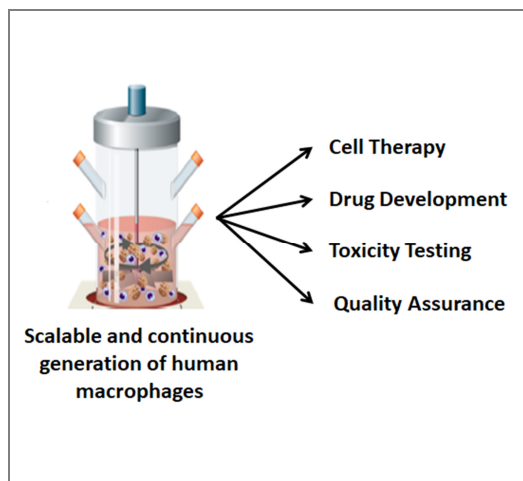
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Challenge

The number of severe infections with multi-drug-resistant bacteria increases worldwide. Especially the treatment of patients suffering from chronic respiratory diseases that are affected by such pathogens is a challenge in clinical practice. Bacteria often are not only refractory to standard antibiotic therapy but even resistant against drugs of last resort. Therefore, alternative approaches targeting bacterial infections are urgently needed.

Technology

The present invention provides a method for scalable and continuous production of iPSC-derived macrophages. The method comprises optimized culturing conditions for generating embryoid bodies and their subsequent differentiation into mature blood cells in suspension



culture. Utilization of iPSCs as a source for pluripotent progenitor cells allows large scale culture and expansion of therapeutic cell products. Moreover, culturing parameters have been successfully adjusted for use of industry-standard stirred bioreactors, which allow continuous production and harvesting of sufficient and GMP compliant amounts for human cell therapy over several months. Antimicrobial activity of bioreactor derived macrophages has been shown in several *in vitro* and mouse model studies making them a highly promising tool for difficult to treat infections and diseases related to macrophage dysfunction. Furthermore, iPSC-derived macrophages can be applied

for industrial research applications in drug development, toxicity testing, and quality assurance.

Commercial Opportunity

In-licensing or collaboration for further development is possible.

Developmental Status

Proof-of-concept for therapeutic efficacy of (hu)iPSC-derived macrophages has been demonstrated in a humanized mouse model. Protocols for continuous production of macrophages in a stirred bioreactor have been established.

Patent Situation

PCT application PCT/EP2018/061574 with priority of 2017 is pending.

Further Reading

Happle et al. (2018) Pulmonary Transplantation of Human iPSC-derived Macrophages Ameliorates Pulmonary Alveolar Proteinosis. *Am J Respir Crit Care Med.* 2018 Apr 13. doi: 10.1164/rccm.201708-1562OC.

Lachmann et al. (2015) Large-scale hematopoietic differentiation of human induced pluripotent stem cells provides granulocytes or macrophages for cell replacement therapies. *Stem Cell Reports* 2015; 4: 282–296.

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