PROOF-OF-CONCEPT OF A NOVEL SCALABLE MAGNETIC BEAD-BASED CELL SEPARATION TECHNOLOGY

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Cell-based therapies have gained vibrant interest in the last years with the potential to treat a vast number of diseases currently considered uncurable. Especially, iPSC-based therapies provide the possibility for off-the-shelf cell therapies. Off-the-self therapies provide the advantage of lowering production cost and ultimately the therapy costs, while also delivering the therapy more rapidly compared to autologous therapy approaches. Beside the production of these cell systems being expensive, complex and lack, nowadays, scalability both for their cultivation and the purification, the efficacy, integrity and safety of the therapeutic cell are of great concern and reliable methods for the purification of those cells are important for the commercialization. Ensuring the safety of the treatment is a pivotal factor for therapies derived from iPSCs, as any remining pluripotency can have significant impact in the patient's health. With large production scales needed for said commercialization, isolation methods need to be efficient, simple, universal applicable and should provide functional and safe cells. Magnetic beads are well-established for sorting of cells, e.g. magnetic activated cell sorting. But today´s systems size is still limited in terms of scale-up potential. We have previously published that our new magnetic bead system MAGicbeads is extremely gentle towards cells1 and can easily be scaled up at pilot-scale for mAb purification2. In the present study, this magnetic bead system (MAGicBeads) has been further developed for cell separation for iPSCs and other cell types e.g. hMSCs. We have developed a new method for cell separation based on flexible protein A/G base conjugated magnetic agarose-based beads.

Protein A/G base conjugated magnetic agarose-based beads provided flexible adjustment of the receptor recognising antibodies, potentially targeting different receptors at different stages throughout the process. In a proof-of concept set up with model populations in a mix of hMSC and HER2+ SK BR3 cells (80:20, 30:70,70:30) the system demonstrated exceptional elimination of the HER2+ cells. The novel cell separation system showed an isolation efficiency of up to 91 %3 with consistent isolation performance throughout heterogenous cell populations. Additionally, the beads provided a high biocompatibility as well as the system showed high robustness against mechanical stress and minimal unspecific binding. This delivers an important insight for further large-scale application using high magnetised particles for the purification of cells prior to the application to patients.