DESIGN AND IN VITRO VALIDATION OF SMART MICROCARRIERS FOR NEXT-GENERATION CELL CULTURE

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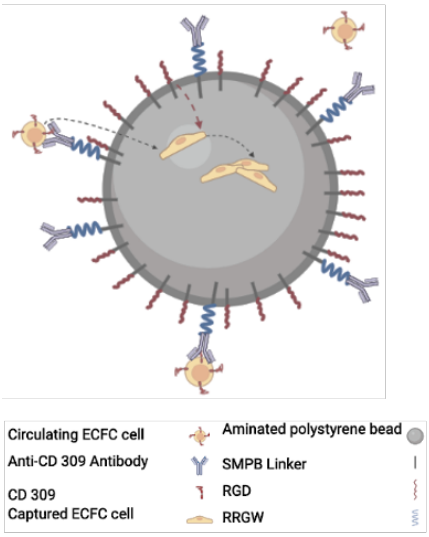
Cellular therapy has been described as the third pillar of contemporary medicine - complementing the arsenal of small molecules and biologics. However, access to advanced cell therapies is often limited by the complexity of the biomanufacturing process and the high associated costs. Our team has developed a technology protected by an international patent application that allows the selection of cells from a mixture [1]. In addition, the selected cells immediately enter in contact with specific biomolecules which trigger, via specific surface markers, selective induction of physiological effects in the captured cells. More generally, this method can be used to combine two steps of conventional cell culture processes. By eliminating manipulations and consumables between steps, we can reduce the complexity of the process while eliminating sources of cell loss and the creation of biohazardous plastic waste. To test our technology with clinically-relevant cells, we assessed the capacity of bifunctional surfaces to capture and expand endothelial colony-forming cells (ECFCs). This cell type can be isolated from a blood sample and proliferate to high numbers. When delivered to ischemic tissues, they participate directly in new blood vessel formation, making them ideal therapeutic targets for the treatment of major vascular conditions such as heart disease.

For the first time, we report adaptation of the bifunctional surface modification method to microbeads which can be used as microcarriers. The bi-functional surface modifications were applied to aminated polystyrene microbeads of 200 µm diameter in a simple and easily scalable one-pot reaction. The surface modification comprised capture antibodies that target the endothelial growth factor receptor on ECFCs with a biomimetic peptide containing the RGD sequence to promote the firm adhesion and proliferation of the cells. Validation protocols consisting in sensitive immunoassays (ELISA) showed the presence of the proper bio-functional groups on the beads. *In vitro* testing of the microcarriers in presence of ECFCs was performed both in static and dynamic conditions. A significant increase in cell attachment and spreading on the bi-functional surfaces compared to the same unmodified polystyrene beads was observed after only 1 hour of incubation. Future work includes promising applications for immune and stem cell therapy by adapting the surface functionalities.



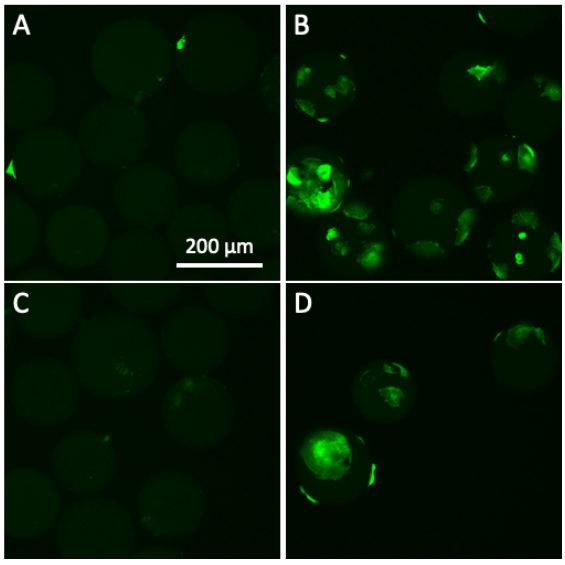


Figure 1 – Left: representation of a modified microcarrier. Right: cell coverage on microcarriers after 1hr seeding in dynamic (A,B) and static (C,D) conditions. A and C are unmodified surfaces, B and D are bi-functional beads. Cytoskeleton is stained with FITC Phalloidin (green)

1- Bashth, Omar S et al. “Surface grafting of Fc-binding peptides as a simple platform to immobilize and identify antibodies that selectively capture circulating endothelial progenitor cells.” Biomaterials science vol. 8,19 (2020): 5465-5475. doi:10.1039/d0bm00650e