MULTIFUNCTIONAL SURFACE MODIFICATIONS TO CAPTURE AND EXPAND FLOWING ENDOTHELIAL COLONY-FORMING CELLS

Corinne A Hoesli, Department of Chemical Engineering & Department of Biomedical Engineering; McGill
corinne.hoesli@mcgill.ca
Mohamed A Elkhodiry, Department of Chemical Engineering, McGill University
Omar S Bashth, Department of Chemical Engineering, McGill University
Julia Manalil, Department of Chemical Engineering, McGill University
Jean-François Tanguay, Montreal Heart Institute, Université de Montréal
Gaétan Laroche, Department of Materials Engineering U. Laval & Centre de recherche du CHU de Québec

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Endothelial colony-forming cells (ECFCs) are rare progenitor cells present in human blood and arterial wall of significant interest for regenerative medicine. The high proliferative potential of ECFC subsets makes them outstanding candidates for the endothelialization of vascular substitutes such as stents or vascular grafts, but also for *in vitro* expansion as a cell therapy product. Conventionally, primary ECFC colonies are isolated *in vitro* using undefined culture conditions, including animal-derived collagen-coated polystyrene plates and medium containing fetal bovine serum. For cell therapy applications, xeno-free defined conditions are desirable.

We demonstrated that ECFCs can be isolated on polystyrene surfaces functionalized with RGD peptides, with no significant differences in surface marker expression or *in vitro* vascular network formation capacity compared with ECFCs isolated on collagen-coated surfaces [1]. The ECFC expansion potential from single cells surpassed the collagen condition. Building on these promising findings, we now report that surfaces modified with combinations of ECFC capture antibodies and RGD peptides can mediate both cell adhesion from flow and subsequent expansion [2]. Surfaces functionalized with anti-vascular endothelial growth factor receptor-2 (α-VEGFR2) significantly increased circulating (1 dyn/cm^2 wall shear stress) ECFC capture compared to RGD and unmodified controls. The presence of RGD together with α-VEGFR2 promoted cell spreading and led to significantly higher surface coverage compared to α-VEGFR2 alone. Additive effects of antibodies and peptides were observed both on planar substrates and on more complex geometries such as stents (Figure 1).

Future work will combine stem cell derived ECFCs, combinatorial surface modifications and screening design of experiments to identify functionalized surfaces which maximize cell capture selectivity, proliferation and differentiation. This technology could be implemented in many commercial applications such as pro-healing vascular biomaterials, but also functionalized bags, plates or microcarriers for cell isolation and culture.

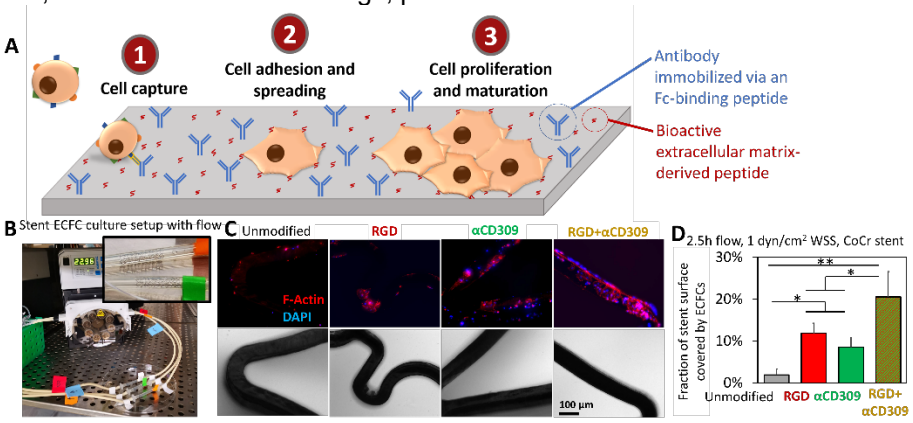

Figure 1. Endothelial colony-forming cell capture and expansion on bi-functional surfaces. (A) Schematic representation of bifunctional surfaces. In a flow loop setup (B), additive effects of capture peptides and antibodies observed on stents (C-D).

1. Elkhodiry et al., Isolating and expanding endothelial progenitor cells from peripheral blood on peptide-functionalized polystyrene surfaces. Biotechnol Bioeng, 2019. 116(10): p. 2598-2609.
2. Hoesli et al., Dual function surface for cell capture and spreading, USPTO 63051608 (2020), International application number CA2021050968.