PHEMA and YIGSR Reverse gradients selectively control directional migration of endothelial cells and smooth muscle cells

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Introduction

Competitive migration of endothelial cells (ECs) and vascular smooth muscle cells (SMCs) determines the inclination to either normal or pathological vessel formation[1]. In physiological environment, the migration direction of cells (including ECs and SMCs) is induced by gradient signals [2]. Here we fabricated a surface featured with reverse density gradients of an hydrophilic polymer poly(2-hydroxyethyl methacrylate) (PHEMA) and a ECs binding peptide Thy–Ile–Gly–Ser–Arg (YIGSR) [3], in order to selectively enhanced directional migration of ECs, but not SMCs.

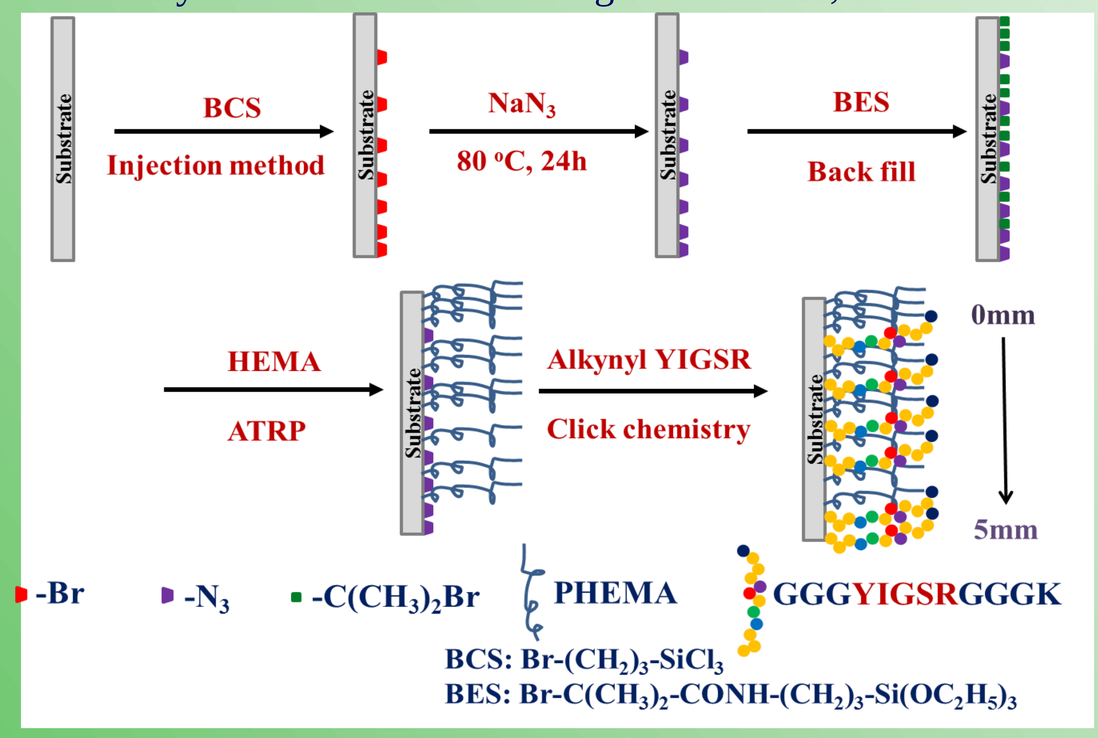

Fig.1 Schematic illustration to show the fabrication of the reverse density gradient of PHEMA and YIGSR, whose density is controlled by the precursory immobilized BCS and BES.

Gradient characterization

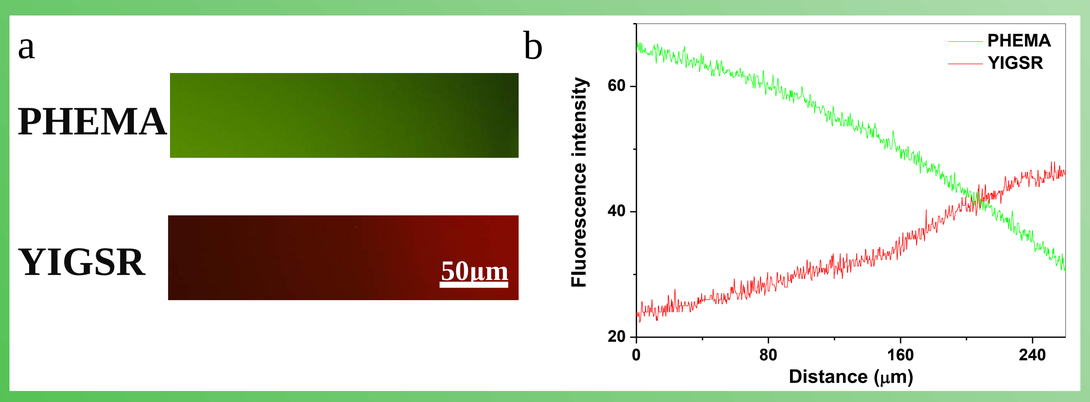

Fig.2 (a) Fluorescent images showing the density gradient of PHEMA (upper) and YIGSR (lower) on glass surfaces, respectively. HEMA was copolymerized with Fluorescein O-methacrylate (green) and YIGSR was stained with Rhodamine B isothiocyanate (red), respectively; (b) fluorescent intensity as a function of position corresponds to the lines shown in (a).

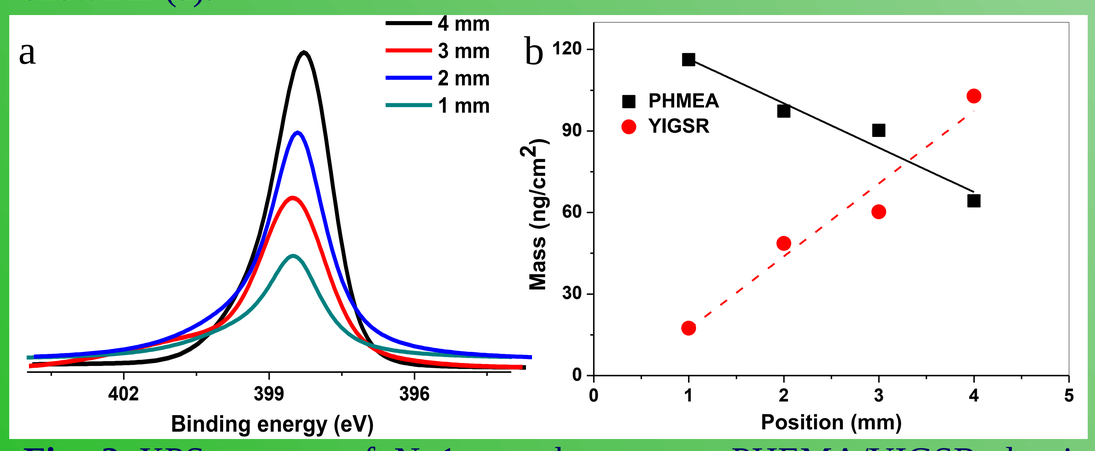

Fig. 3 XPS spectra of N 1s on the reverse PHEMA/YIGSR density gradient surfaces with variable positions. (b) the mass of PHEMA and YIGSR on the reverse gradient as a function of gradient position, respectively.

ECs and SMCs migrate on reverse gradients

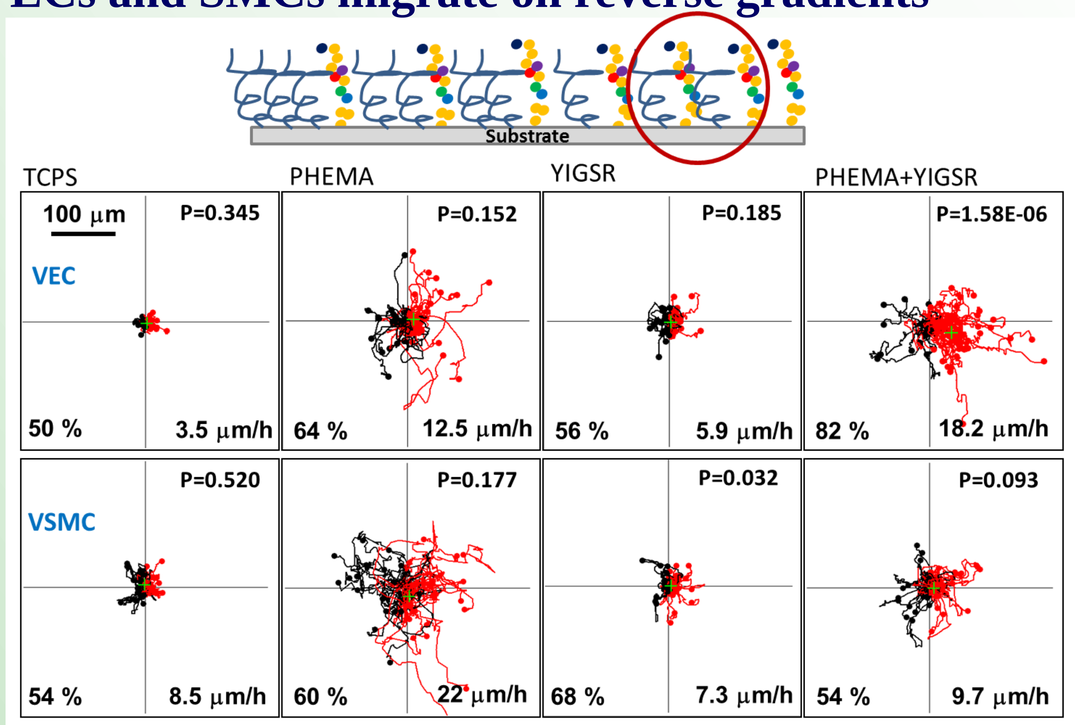

Fig.4 Migration traces of the ECs and the SMCs on different surfaces. The migration traces of the cells migrating to the X direction and –X direction were drawn in red and black lines, respectively. The number at the lower indicates the percentage of cells moving to the +X direction; at the lower right indicates the migration rate of the cells in statistics. The center of mass for the endpoint positions is marked with a green cross.

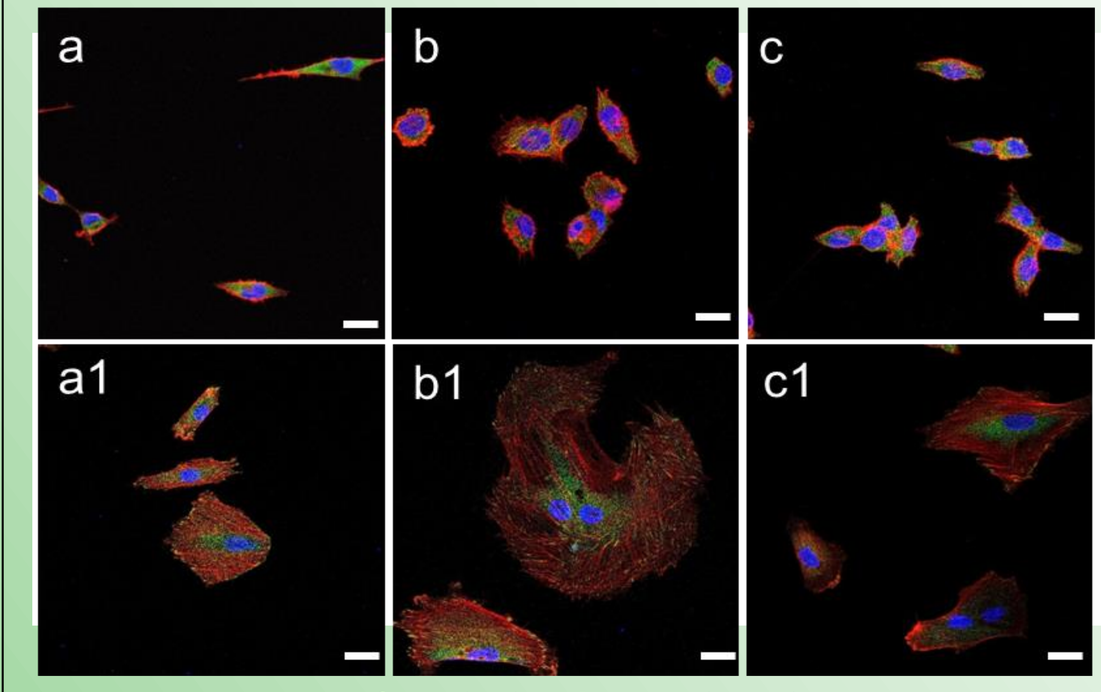

Fig.5 CLSM images of Ecs (a-c) and SMCs (a1-c1) on PHEMA gradient (a and a1), YIGSR gradient (b and b1), and PHEMA/YIGSR reverse density gradient (c and c1). Vinculin (green), F-acitn (red) and nucleus (blue) were stained to show cellular morphology and cytoskeleeton.

Conclution

The reverse gradients of hydrophilic polymer PHEMA and a ECs binding peptide YIGSR were fabricated on glass surfaces by microinjection method. Surface initiated ATRP and dipole cycloaddition were adopted to create a controllable composition of the two components at the relevant position of the gradient. Significantly different migration behaviors of ECs and SMCs were observed: migration rate of ECs was dramatically increased on the surfaces with reverse gradients while the mobility of SMCS was not improved.

Reference

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3. Massia P, Hubbell JA. J Biol Chem 1993;268(11):8053-8059.

Acknowledgement

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