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Review

Specific control of cell–material interactions: Targeting cell receptors using ligand-functionalized polymer substrates

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ABSTRACT

Cells respond to their environment in complex and sometimes poorly understood ways. Protein, peptide and synthetic peptidomimetic ligands may all be used to stimulate cells via receptor signaling, using interactions that are often highly specific. Polymer substrates that present these ligands provide a promising way to control cell development, both for applications in biotechnology and for fundamental studies of cell biology. Here we review a large range of techniques that have been employed to create and characterize ligand-functionalized substrates, with a particular focus on techniques that allow specific and consistent stimulation.

Abbreviations: 2D/3D, two/three dimensional; AA, amino acid; AFM, atomic force microscope/microscopy; ATRP, atom transfer radical polymerization; BCA, bicinchoninic acid; bFGF, basic fibroblast growth factor; BSA, bovine serum albumin; CAM, cell adhesion molecule; CDI, 1,1′ carbonyldiimidazole; CNTF, ciliary neurotrophic factor; CTA, chain transfer agent; CuAAC, copper-mediated azide–alkyne click (reaction); DPN, dip-pen nanolithography; EBL, electron beam lithography; ECM, extracellular matrix; EDC/NHS, *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide with *N*-hydroxysuccinimide activation; EGF, epidermal growth factor; ELISA, enzyme-linked immunosorbent assay; ERK/MAPK, extracellular signal regulated kinase/mitogen-activated protein kinase; FGF, fibroblast growth factor; FRET, Förster resonance energy transfer; GAG, glycosaminoglycan; GF, growth factor; GNP, gold nanoparticle; His-6, hexahistine; HPLC, high performance liquid chromatography; IPN, interpenetrating polymer network; IR, infrared; L-DOPA, L-3,4-dihydroxyphenylalanine; LbL, layer-by-layer (deposition); LIF, leukaemia inhibitory factor; MMP, matrix metalloproteinase; nCP, nanocontact printing; NGF, nerve growth factor; NMP, nitroxide-mediated polymerization; NMR, nuclear magnetic resonance spectroscopy; NTA, nitriloacetic acid; PDMS, polydimethylsiloxane; PEG, poly (ethylene glycol); PI3k, phosphoinositide 3-kinase; QCM, quartz crystal microbalance; RAFT, reversible addition-fragmentation chain transfer; SAM, self-assembled monolayer; SANPAH, *N*-sulfosuccinimidyl-6-(4′-azido-2′-nitrophenyl-amino) hexanoate; SAP, self-assembling peptide; SMCC, succinimidyl-4-(*N*-maleimidomethyl)cyclohexane-1-carboxylate; SPR, surface plasmon resonance; TBTA, tris((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)amine; TGF-β, transforming growth factor beta; ToF-SIMS, time-of-flight secondary ion mass spectrometry; μCP, microcontact printing; UV, ultraviolet; VEGF, vascular endothelial growth factor; XPS, X-ray photoelectron spectroscopy.

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Contents

1. Introduction

Receptors in the cellular membrane are a vital way in which cells can sense and respond to their local environment. Binding between cell receptors and their ligands, which may include proteins, peptides and synthetic molecules, is tightly controlled by physical, electrostatic and hydrophobic/hydrophilic interactions between the two. These interactions make ligand–receptor binding highly specific and therefore a prime candidate for tightly controlled cell stimulation.

Ligand-functionalized culture substrates are a promising method for achieving this stimulation [1]. The advantages of using functionalized polymer substrates, compared to soluble ligands, vary with circumstance. They may include: receptors requiring a surface-bound ligand for activation (e.g., many adhesion signals); increased receptor stimulation time and concordant increased length of signaling period; ability to control ligand release over a period of time; ability to use smaller amounts of (sometimes quite expensive) ligand; and the ability to achieve continual stimulation in vivo without repeated dosing at high concentrations. Functionalized substrates may also be useful for creating simplified models of the in vivo microenvironment for the study of fundamental biological interactions, reproducible drug toxicology/efficacy

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