Control and Manipulate Cell Behaviors on Functionalized and Nanostructured Conducting Polymer Biomaterials

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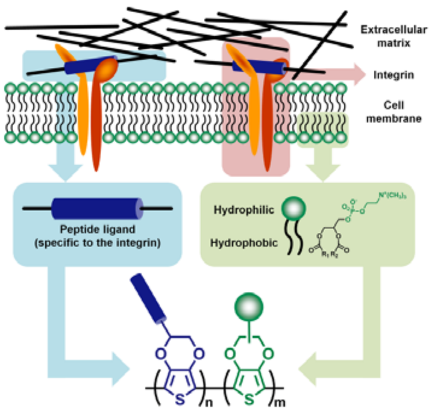
Statement of Purpose: Cell-materials interface holds the key for advancement of many bioengineering applications. Conducting polymers represent a key class of materials which could potentially provide matching properties of mechanical strength, nanostructures, and ligand/receptor interactions, that potentially biomimic extra-cellular matrix. Herein, we would like to present our research efforts toward rationally design novel conducting polymers materials from molecular building blocks which control and manipulate cell behaviors on top of conducting polymer materials. The general Scheme is presented below.



Methods: The ethylenedioxythiophene monomers with hydroxyl (EDOT-OH) and carboxylic acid groups (EDOT-COOH) were synthesized as described in our previous works,[1,2] and used as starting materials for preparation of protein-resistant phosphorylcholine-functionalized EDOT (EDOT-PC) and conjugatable maleimide-functionalized EDOT building blocks. With emulsified by Aerosol OT (AOT) in organic solvent, hydrophobic and hydrophilic EDOT monomers were electrochemically copolymerized on ITO and Au electrodes. The topography, composition, hydrophilicity/hydrophobicity and protein-resistance of conductive copolymer thin films were characterized by AFM, XPS, contact angle and QCM measurements, respectively. The conjugation of copolymer substrates with the IKVAV ligand and the ligand-induced specific binding were further investigated by QCM and cell adhesion and culture experiments. The complex micro-pattern consisting of protein-resistant and conjugatable copolymer was fabricated bylithographical procedures

Results: To mimic biomembrane, the phosphorylcholine-functionalized EDOT (EDOT-PC) and maleimide-functionalized EDOT (MI-EDOT) were prepared as protein-resistant and conjugatable building blocks for the targeted conductive biointerface. EDOT-PC was synthesized by reaction of EDOT-OH with 2-chloro-2-oxo-1,3,2-dioxaphospholane and followed trimethylamine-induced ring-opening. EDT-MI was synthesized by condense reaction of EDOT-COOH with 2-maleimidoethylamine. With emulsified by AOT in organic solvent, the hydrophilic EDOT-PC and hydrophobic EDOT-MI could be electro-deposited simultaneously on ITO and Au electrodes to form multi-functional and fully conjugated copolymers. The composition and hydrophilicity/hydrophobicity of copolymers could be well tuned by adjusting feeding ratio of monomers. The non-specific interaction of copolymer substrates with proteins and cells could be dramatically weakened by increasing EDOT-PC composition, and be very small even when the PC-EDOT composition is as low as 50%. The neuron-targeted IKVAV peptides were further introduced to the copolymer substrates via conjugation of maleimide groups with thiol-terminated ligands. In this way, the cell adhesion on conductive substrates was controlled to be specific to neuron. It was found that the specific cell-substrate interaction was quantitatively correlated with ligand density, and could be optimized to sustain long-term of cell culture.

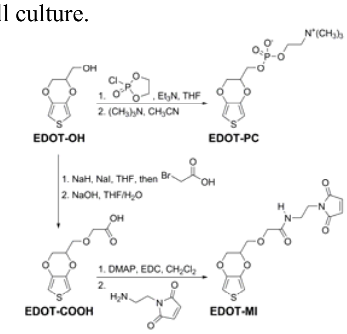


Figure 1. Synthetic schemes of EDOT derevatives.

The micro-pattern with alternated protein-resistant and conjugatable EDOT copolymers was simply fabricated by step by step electrodeposition and photolithography-defined plasma etching. After conjugation, the IKVAV micropattern was available to load spacial confinement on cell adhesion on EDOT substrates. In this way, neuron cells could be patterned and cultured on copolymer substrates even at a cellular level.

Conclusions: The biomimicking conductive biointerface was built on electropolymerization and synthesis of EDOT-PC and EDOT-MI. With EDOT-PC composition higher than 50%, the EDOT copolymer could be antifouling to both proteins and cells, and become specific binding toward neuron cells after conjugated with IKVAV ligands. The conductive biointerface could sustain long-term cell culture, and the cell-substrate interaction could be well tuned by adjusting comonomer composition to give optimized cell adhesion, proliferation. Micro-pattern fabrication on the EDOT copolymers was further developed, and their potential of applications in biodevices toward electrically stimulating and/or sensing cells was demonstrated.

References:

1. Luo S.-C. et al. Langmuir 2008;24:8071-8077.
2. Ali E. M. et al. Macromolecules 2007; 40:6025-6027.