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Effective control of cell behavior on conducting polymers

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EFFECTIVE CONTROL OF CELL BEHAVIOR ON CONDUCTING POLYMERS

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To my husband, Hongwei Wang and my parents Ziqing Liu and Huifen Wu for their endless love.

CERTIFICATION

I, Xiao Liu, declare that this thesis, submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Department of Chemistry at the University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for any qualifications at any other academic institution.

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PUBLICATIONS

Yong Liu, **Xiao Liu**, Jun Chen, Kerry J. Gilmore and Gordon G. Wallace 3D bio-nanofibrous PPy/SIBS mats as platforms for cell culturing. ***Chemical Communication*** 2008; 28(32):3729-3731.

Xiao Liu, Kerry J. Gilmore, Simon E. Moulton and Gordon G. Wallace Electrical stimulation promotes nerve cell differentiation on polypyrrole/poly (2-methoxy-5 aniline sulfonic acid) composites. ***Journal of Neural engineering*** (Accepted)

Xiao Liu, Jun Chen, Kerry J. Gilmore, Michael J. Higgins, Yong Liu, and Gordon G. Wallace Guidance of Neurite Outgrowth on Aligned Electrospun Polypyrrole/ Poly(styrene-β-isobutylene-β-styrene) (SIBS) Fiber Platforms. ***Journal of Biomedical Material Research A*** (Accepted)

CONFERENCE PRESENTATIONS

Xiao Liu, Kerry J Gilmore, Simon E Moulton and Gordon G Wallace Electrical Stimulation Promotes PC12 Cell Differentiation On Polypyrrole Films (oral presentation), Australasian Society for Biomaterials and Tissue Engineering (ASBTE) 19th Annual Conference Sydney, Australia, Jan. 2009

ABSTRACT

This study explored the potential biomedical applications of polypyrrole (PPy). Electrical and topographic cues have been delivered to cells via composites of these conducting polymers, resulting in the successful control of cell behaviour.

It was found that a clinically-relevant electrical stimulation protocol (250 Hz biphasic pulsed-current) delivered directly via PPy/poly(2-methoxy-5-aniline sulfonic acid) (PMAS) films can significantly promote PC12 nerve cell differentiation in the presence of nerve growth factor (NGF), and can initiate reversible neurite sprouting from PC12 cell in the absence of NGF. The ability to promote neural outgrowth on PPy/PMAS has important implications for improving the neural/electrode interface, and this may be used to effect in nerve regeneration.

The same biphasic 250 Hz electrical stimulations were applied to a monolayer of endothelial cells on PPy/heparin films, and significantly enhanced endothelial cell migration was observed as a result. Combined with the ease of fabrication on metallic stents and the antithrombotic function of heparin, these materials may be utilized for modification of stents to improve the re-endothelialization process after implantation.

Finally, aligned PPy/poly(styrene-β-isobutylene-β-styrene) (SIBS) nanofibrous scaffolds were fabricated by vapor phase depositing PPy onto electrospun SIBS fibrous mats. It was shown that this novel material provided a conductive and biocompatible platform for PC12 cell adhesion and differentiation. Neurite

outgrowth was significantly influenced by the aligned fibers. High resolution AFM provided a closer inspection of the neurite outgrowths and revealed interesting physical interactions between the neurites and the aligned fibers. Aligned electroactive PPy/SIBS fibers have potential applications for improving the electrode-cellular interface of neural electrodes by encouraging guided neurite outgrowth toward the electrode through the use of electrical stimulation.

The knowledge gained during the course of this study could form the basis for improving the cellular interface of neural electrodes and stents using conducting polymers.

ABBREVIATIONS

RGD	Arginine-Glycine-Asparagine
AFM	atomic force microscopy
BDNF	brain-derived neurotrophic factor
i	current
CV	cyclic voltammetry
DEHS	di(2-ethylhexyl) sulfosuccinate
DBSA	dodecylbenzene sulfonic acid
DBS	dodecylbenzene-sulfonate
DRG	dorsal root ganglia
DMEM	Dulbecco's modified Eagle's medium
EIS	electrochemical impedance spectroscopy
ECM	extracellular matrix
FBS	fetal bovine serum
HUVEC	human umbilical vein endothelial cell
HA	hyaluronic acid
LDH	lactate dehydrogenase
NGF	nerve growth factor
NT3	neurotrophin-3
pTS	*para*-toluene sulphonic acid
PNA	peptide nucleic acid
PMAS	poly (2-methoxy-5 aniline sulfonic acid)
PEDOT	poly (3,4-ethylenedioxy-thiophene)
PCL	poly (epsilon-caprolactone)
PLCL	poly(L-lactid-*co*-ε-caprolactone)
PLGA	poly(lactide-*co*-glycolide acid)
PEO	poly(ethylene oxide)
PLA	poly(L-lactic acid)
PMMA	poly(methyl methacrylate)

PVP	poly (vinylpyrrolidone)
PANi	polyaniline
PET	polyethylene terephthalate
PLCL	poly(l-lactid-*co*-ε-caprolactone)
PPy	polypyrrole
PSS	polystyrenesulfonate
PTn	polythiophene
SEM	scanning electron microscopy
SD	standard deviation
SEM	standard error of the mean
SIBS	poly(styrene-β-isobutylene-β-styrene)
THF	tetrahydrofuran
t	time
TC plastic	tissue culture plastic
UV-vis	ultraviolet visible
VPP	vapor phase polymerization

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