

THE UNIVERSITY OF MELBOURNE

Graeme Clark Institute









38 APS 2024

Self-assembled peptide hydrogels to avoid tissue overgrowth in progenitor cell grafts

Engineering Materials for Future Healthcare



The Problem

The Cell Transplantation Journey





Self-assembling Peptides

• Laminin

- Epitope for laminin (IKVAV: Isoleucine-Lysine-Valine-Alanine-Valine)
- Supports cell positioning, neural differentiation & neurite growth
- Enhanced efficiency







A/Prof. Richard Williams, Deakin

4

Advanced Materials 30 (50), 1805209, 2018 Advanced Functional Materials 30 (9), 1900390, 2020











Prof. Clare Parish, Florey Neuroscience Institute Dr Lachlan Thompson, Florey Neuroscience Institute

Cell reports 20 (8), 1964-1977, 2017

Molecular hydrogels enhance cell integration post stroke.



Controlling neuronal differentiation with engineered materials



Cell reports 20 (8), 1964-1977, 2017

Protein engineering to achieve sustained growth factor delivery





Dr Kiara

ANU

Dr Richard Williams, Deakin

Dr Alexandra Rodriguez, Bruggeman, ANU





Prof. Clare Parish, Florey



Dr Lachlan Thompson, Florey

Advanced Functional Materials, 2105301, 2021

Optimizing graft size with myoglobin

- •We can fine-tune the oxygen binding kinetics
- •Alter the structure and function of a protein
- •4 different myoglobin variants already tested
- •Electrostatic interactions between the myoglobin and SAP are also important.



Structure of wildtype or native sperm whale myoglobin showing important elements for oxygen binding





Ms Liz Zoneff, UOM Dr Yi Wang, UOM



Prof. Colin Jackson, ANU



Structure of high affinity sperm whale myoglobin showing change of leucine amino acid to phenylalanine



Structure of low affinity sperm whale myoglobin showing change of histidine amino acid to leucine

Nature Communications 14 (1), 457, 2023











Nature Communications 14 (1), 457, 2023

Suicide gene activation

A

PSC ,

1282

B



Prof. Clare Parish, Florey



Ms Negar Mahmoudi, ANU

Advanced Functional Materials, 2305771, 2023



Advanced Functional Materials, 2305771, 2023



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Second Story



Prof Alan Harvey, UWA



Ms Negar Mahmoudi, ANU

Can we achieve this without cell transplantation?



Advanced Healthcare Materials 10 (1), 2001238, 2021 Advanced Materials, 2108757, 2022

What is the best serotype for reprogramming in the brain?







A/Prof Leszek Lisowski, USyd



Ms Shiva Soltani Dehnavi, ANU



Advanced Science, 2303707, 2023

NeuroD1 Transcription Factor



ACS Nano, Accepted 14/1/2024

Primary astrocytes infected with DJ gfaABC1D-NeuroD1-mCherry 10 DPI



Betatubulin mCherry GFAP DAPI

Primary astrocytes infected with DJ gfaABC1D-NeuroD1-mCherry 28 DPI



Betatubulin

mCherry

GFAP



A) Representative data of FACS for the percentage of Betatubulin+, mCherry+, and Betatubulin+/mCherry+ B) Quantified data for conversion efficiency based on FACS method. ANOVA statistical testing to compare statistical differences between groups where *p < 0.05; **p < 0.01.

Electrophysiology





The ND1-mediated astrocytes reprogramming was monitored in vitro and functionally characterized.