RSC BIOMATERIALS CHEMISTRY ANNUAL CONFERENCE 2019

Conference Programme

9 JANUARY - 11 JANUARY 2019
STANLEY THEATRE, LIVERPOOL

Dear Delegates,

Welcome to Liverpool! It is with great pleasure that I welcome you to the Annual Conference of the **RSC Biomaterials Chemistry Special Interest Group** here at the University of Liverpool. The RSC Biomaterials Chemistry Special Interest Group was set up in 2005 to provide a focus for groups in universities and industry working on the synthesis and characterisation of biomaterials. The annual meeting brings together researchers from across the UK and internationally, working to advance knowledge and focus on biomaterial chemistry research and development.

The event aims to enhance the understanding of the chemistries underlying the use of biomaterials in applications including antimicrobial surfaces, drug delivery and regenerative medicine. The focus of this year's meeting is Anti-Infective Materials and Device Related Infections, Biomaterials for Therapeutic Delivery, Biomaterials for Tissue Induction and Regenerative Medicine and Bioresponsive Surfaces.

Our plenary speakers are world leaders in their respective fields: **Professor Robert Hancock** (University of British Columbia, Canada), **Professor John Fisher** (University of Leeds), **Professor Graham Leggett** (University of Sheffield) and **Professor Rasmita Raval** (University of Liverpool).

The response from the biomaterials research community has been excellent for this year's meeting with 34 different institutions and companies, including 7 from beyond the UK including The Netherlands, Ireland, Iraq, Pakistan, Brazil, Saudi Arabia and Nigeria. The breadth of work to be presented at this conference reflects the strong multidisciplinary nature of the field.

We hope you enjoy the conference and the city of Liverpool.

Dr. Raechelle D'Sa (Conference Chair)

Organising Committee
Jenny Aveyard, Jude Curran, Kiran Mann
Robert Deller, George Fleming, Man Li, Raj Kaur

Sponsors

We gratefully acknowledge the support of our sponsors

Journal of Materials Chemistry B

The Journal of Materials Chemistry B covers all aspects of the production, properties, and applications of materials related to materials for healthcare and biomedicine, biointerfaces, biomimetic, bio-inspired or natural materials. The journal is published by the Royal Society of Chemistry and includes topics such as antifouling coatings, biocompatible materials, biomimetics, drug delivery, scaffolds, regenerative medicine, stem cells and therapeutic devices.

Polymers is an international open access journal of polymer science. They publish research papers, communications and review articles. Polymers provided an interdisciplinary forum for publishing papers which advance the fields of polymerization methods, theory, simulation, modelling, understanding of new physical phenomena, advances in characterization techniques, and harnessing of self-assembly and biological strategies for producing complex multifunctional structures.

Rheolution was founded in 2009 to bring new ideas and to solve industrial challenges involving materials rheology. Today, Rheolution offers to customers around the world innovative, cost-effective and high added-value testing instruments for industrial quality and process control as well as research & development. We are still pursuing the same simple idea: making mechanical testing of soft materials accessible to everyone and to every industry.

The Stanley Theatre

By car - from the M62 continue onto Edge Lane, follow signs for City Centre and University. The nearest car park is at **Mount Pleasant**, this closes at 8pm, you cannot get your car after that time. The nearest 24 hour car park is **Secure Parking** on Heathfield Street, their website is here. The theatre postcode is **L3 5TR**, **Secure Parking** postcode is **L1 4AT**.

We are a few minutes from **Secure Parking**, turn right on leaving the carpark, left on **Renshaw Street** and right at **The Adelphi Hotel**. Go up Brownlow Hill, pass the **Cathedral** and look for **Starbucks** to your right**,** the entrance is to the right of that, in the **Liverpool Guild of Students.**

By train - we're a ten-minute walk from **Lime Street** station. Leave via the front exit, go left onto Lime Street, turn left at the Adelphi Hotel and go up Brownlow Hill, pass the Cathedral and walk to University Place where you'll find the Conference.

Local Public Transport - Call Traveline on +44 (0)151 236 7676, or log onto their site here. Download the Merseytravel app here, also available on iTunes and Google Play.

RSC Biomaterials Chemistry Annual Conference
University of Liverpool, 2019

Plenary Speakers

Professor Rasmita Raval

Director, Open Innovation Hub for Antimicrobial Surfaces
Director, The Surface Science Research Centre
University of Liverpool, UK. - https://www.liverpool.ac.uk/antimicrobial-surfaces/

Professor Raval is the Director of the Surface Science Research Centre and the Open Innovation Hub for Antimicrobial Surfaces at the University of Liverpool. She is also a Professor in the Department of Chemistry. Her research includes knowledge-based design of functional surfaces, molecular nanoscience and bio-interfaces. Her multidisciplinary research combines protocols for 'bottom-up' assembly of functional nano-architectures and concurrent development and utilisation of powerful scientific techniques to probe the behaviour and performance of these systems at the atomic, molecular and cellular level. This experimental effort is combined with theoretical modelling to yield insights into molecular and biological responses and behaviour at interfaces. She also leads a dedicated innovation team to translate frontier research into technology platforms, with a specific focus on antimicrobial surfaces and materials.

She is also Co-Director of the UK National Biofilm Innovation Centre.

Professor Robert E.W. (Bob) Hancock

Director, Centre for Microbial Diseases and Immunity Research
University of British Columbia - http://cmdr.ubc.ca/bobh/

Professor Hancock is a UBC Killam Professor of Microbiology & Immunology, an Associate Faculty Member of the Wellcome Trust Sanger Institute and a Canada Research Chair in Health and Genomics. His research interests include small cationic peptides as novel antimicrobials and modulators of innate immunity, the development of novel treatments for antibiotic resistant infections, the systems biology of innate immunity, inflammatory diseases and *Pseudomonas aeruginosa*, and antibiotic uptake and resistance. He has published more than 700 papers and reviews, has 64 patents awarded, and is an ISI highly cited author in Microbiology with more than 78,000 citations and an h-index of 145. He has won several awards including the ICAAC Aventis Antimicrobial Research Award, the leading award for research on antimicrobials, and Canada's three top prizes for Health Research, and is an Officer of the Order of Canada.

He was a co-founder of Migenix, Inimex Pharmaceuticals, ABT Innovations, Sepset Biotherapeutics, and the Centre for Drug Research and Development.

Plenary Speakers

Professor John Fisher

Professor of Mechanical Engineering
University of Leeds - https://engineering.leeds.ac.uk/staff/59/professor_john_fisher

Professor Fisher is a leading researcher in Medical and Biological Engineering, as Director of Wellcome Trust/EPSRC Medical Engineering Centre WELMEC, Director of EPSRC Innovation and Knowledge Centre in Regenerative Therapies and Devices, Director of EPSRC Centre for Innovative Manufacturing in Medical Devices, Director of White Rose Doctoral Training Centre in Tissue Engineering and Regenerative Medicine, Co Director of NIHR Leeds Musculoskeletal Biomedical Research Unit. As the former Director of the Institute for Medical and Biological Engineering, he provided leadership to over 200 academic researchers in Medical Engineering at Leeds.

Professor Fisher holds a degree in Physics from Birmingham University and a PhD in Bioengineering from the University of Glasgow. He is a chartered Mechanical Engineer, having been appointed to the Chair of Mechanical Engineering at the University of Leeds in 1993 being awarded a DEng degree in 1996. Professor Fisher received his CBE for services to Biomedical Engineering, is a Fellow of the Royal Academy of Engineering, FREng, and of the Academy of Medical Sciences, FMedSci, a Chartered Engineer, CEng, and Chartered Scientist, CSi.

Professor Graham J. Leggett

Professor of Nanoscale Analytical Science and Head of Department
The University of Sheffield. - http://www.leggett.group.shef.ac.uk/

Graham Leggett is Professor of Analytical Science and Head of the Department of Chemistry at The University of Sheffield. He is the Co-chair of the Leeds/Sheffield Centre for Doctoral Training in Molecular-Scale Engineering, a member of the AVS Program Committee, Departmental Director of Research and Chair of the Department of Chemistry's Laboratory Committee. Professor Leggett obtained a BSc in Chemistry from UMIST in 1987. His PhD from the same institution, obtained in 1990, was followed by consecutive appointments as Research Associate at Universities of Washington and Nottingham. In 1994 he was appointed as lecturer at the University of Nottingham. He became a Lecturer at UMIST in 1998, where he was subsequently promoted to senior lecturer and reader. In 2002 he was appointed as Professor of nanoscale analytical chemistry at the University of Sheffield. He was appointed as the Head of Department in 2018.

RSC Biomaterials Chemistry Annual Conference

Overview

Wednesday, Jan 9th

12:00 - 12:10	**Welcome from Professor Dame Janet Beer, Vice Chancellor.**
12:10 - 14: 30	**Session 1**: Chairs, Timothy Douglas and Jenny Aveyard
12:10 - 13:00	**Plenary** - **Rasmita Raval**: Biofilms: Biology meets Surface Science
14:30 - 15:15	*Lunch and Poster Session*
15:15 - 17:30	**Session 2**: Chairs, Giuseppe Tronci and Emma McCarthy
17:35 - 19:00	*Poster Session and Drinks Reception*

Thursday, Jan 10th

09:00 - 10:50	**Session 3**: Chairs, Raechelle D'Sa and Sophie Louth
09:00 - 09:50	**Plenary** - **Robert Hancock**: High throughput approaches for development of peptides for treatment and prevention of surface biofilm infections
10:50 - 11:15	*Break and Poster session*
11:15 - 12:30	**Session 4**: Chairs, Annalisa Tirelli and Morgan Lowther
12:30 - 13:30	*Lunch and Poster Session*
13:30 - 15:30	**Session 5**: Chairs, Jude Curran and Samuel Moxon
13:30 - 14:20	**Plenary** - **John Fisher**:
15:30 - 15:55	*Break and Poster session*
15:55 - 17:10	**Session 6**: Chairs, Victoria Kearns and Caroline Harrison
19:00 - 00:30	*Welcome drinks and conference dinner at the Royal Liver Building*

Friday, Jan 11th

10:00 - 11:35	**Session 7**: Chairs, Francisco Fernandez-Trillo and Robert Deller
10:00 - 10:50	**Plenary** - **Graham Leggett**: Polymer brush microsystems for the study of membrane processes
11:35 - 12:00	*Break and Poster Session*
12:00 - 12:45	**Session 8**: Chairs, Paul Roach and Pallavi Deshpande
13:00 - 13.30	*Conference closes with lunch in the Stanley Theatre*

RSC Biomaterials Chemistry Annual Conference

Wednesday 9th January

11:00 – 12:00 Registration

12:00 – 12:10 Welcome from the Vice Chancellor, Professor Dame Janet Beer

12:10 – 13:00 Plenary Speaker, Rasmita Raval

University of Liverpool

13:00 – 13:15 Tuning long-acting HIV drug release from a nanogel-based in situ forming implant

Department of Chemistry, University of Liverpool

Adam R. Town, Jessica Taylor, Karl Dawson, Edyta Niezabitowska, Nancy M. Elbaz, Andrew Corker, Esther Garcia-Tuñón and Tom O. McDonald.

13:15 – 13:30 Utilisation of an oxidation sensitive trigger with combined temperature response for drug delivery applications

Department of Chemistry, University of Sheffield

Emma Owens and Sebastian Spain

13:30 – 13:45 Rheo-Dissolution: A new technique for the simultaneous measurement of rheology and drug release from hydrogels

Department of Pharmacy, University of Huddersfield

Faria Senjoti, Muhammad U. Ghori, Barbara R. Conway and Alan M. Smith

13:45 – 14:00 Delivery Systems for a therapeutic demineralising agent

School of Chemical Engineering, University of Birmingham

Thomas Robinson, Sophie Cox and Liam Grover

14:00 - 14:15 Real time non-invasive optical tracking of label-free nanoparticles and proteins

School of Engineering, University of Liverpool

Francesco Giorgi, Judith M. Curran and Eann A. Patterson

14:15 – 14:30 Development of Ti-Ag alloys and investigation of antimicrobial response

School of Chemical Engineering, University of Birmingham

Morgan Lowther, Liam Grover and Sophie Cox

14:30 – 15:15 Late Lunch and Poster Session

15:15 – 15:30 The synthesis of a nano silver-graphene oxide system and efficacy against endodontic biofilms using a novel tooth model

Department of Tissue Engineering and Biophotonics, King's College London

Konstantinos Ioannidis, Sadia Niazi, Petros Mylonas, Francesco Mannocci, Sanjukta Deb

15:30 – 15:45 Nitric Oxide Releasing Titanium Surfaces for Antimicrobial Applications

School of Engineering, University of Liverpool

Man Li, Jenny Aveyard, George Fleming, Jude Curran, Fiona McBride, Rasmita Raval and Raechelle A. D'Sa

15:45 – 16:00 Synthesis and evaluation of novel selenium nanoparticles for development of antibacterial healthcare textiles

School of Pharmacy and Biomolecular Sciences, University of Brighton

Qiaoyi Wang, Lara Barnes, Carol Howell, Matthew Illsley, Patrick Dyer, Irina Savina.

16:00 – 16:15 Development of a radiopaque liquid embolic for use in therapeutic embolization

Department of Chemistry, University of Sheffield, UK.; Biocompatibles UK Ltd

Jasmine Lord, Sebastian Spain and Andrew Lewis

16:15 – 16:30 Development and characterization of nano-hydroxyapatite by freeze drying method

Metallurgical & Material Engineering Department, University of Engineering & Technology Pakistan.

Maheera Abdul Ghani, Ehsan Ul Haq and Sidrah Majeed

16:30 – 16:45 Engineering organic piezoelectricity using computational chemistry

Department of Physics, Bernal Institute, University of Limerick, Ireland

Sarah Guerin, Joseph O' Donnell, Tofail Syed and Damien Thompson

RSC Biomaterials Chemistry Annual Conference

Wednesday 9th January – Rapid Fire

16:45 – 16:50 Probing the composition of extracellular vesicles in bone formation
Chemical Engineering, University of Birmingham
Adam J. A. McGuinness, Sophie C. Cox, Owen G. Davies and Liam M. Grover

16:50 – 16:55 Antimicrobial peptide hydrogels as bandage contact lenses
Department of Eye and Vision Science, University of Liverpool
Pallavi Deshpande, Stephnie Kennedy, Andrew Gallagher, Mal Horsburgh, Heather Allison, Stephen Kaye, Don Wellings and Rachel Williams

16:55 – 17:00 Harnessing the antibacterial properties of chitosan to tackle dental biofilms
School of Pharmacy and Biomedical Science, University of Portsmouth
Dien Puji Rahayu, Katerina Lalatsa and Marta Roldo

17:00 – 17:05 Differentiation of mesenchymal stem cells in an injectable hydrogel under the conditions of the degenerate intervertebral disc.
Materials Engineering Research Institute, Sheffield Hallam University.
Joseph W. Snuggs, Abbey A Thorpe, Cameron Hutson, Simon W Partridge, Chris Sammon, Christine L Le Maitre.

17:05- 17:10 Polymeric artificial cellular environments for vibrio cholera aggregation
School of Chemistry, University of Birmingham, McGovern Medical School, University of Texas Health, Houston, USA
Oliver Creese, Francisco Fernandez-Trillo and Anne-Marie Krachler

17:10 – 17:15 Stimuli-responsive nanogels with controlled size and architecture
Department of Chemistry, University of Sheffield
Marissa Morales-Moctezuma, Sebastian Spain

17:15 – 17:20 UPLC-DAD-ESI-QTOF-MS Characterization of anthocyanin pigments extracted from the leaves of *Justicia secunda* Vahl (Acantaceae) growing abundantly in the lowland rainforests in the Niger Delta region of Nigeria.
Department of Chemistry, Federal University Otuoke, Yenagoa, Nigeria,
Department of Biology, Federal University Otuoke, Yenagoa, Nigeria.
Akens Hamilton-Amachree, Eneni Inara Mercy Roberts

17:30 Poster Session and Drinks Reception at The Stanley Theatre

RSC Biomaterials Chemistry Annual Conference

Thursday 10th January

9:00 – 9:50 **Plenary Speaker, Robert Hancock**
University of British Columbia

9:50 – 10:05 **Light controlled release of antimicrobial peptides for the treatment of pathogenic bacteria**
School of Physics and Astronomy, University of Leeds
Samuel Moorcroft, Zhan Yuin Ong, David Jayne and Stephen Evans.

10:05 – 10:20 **Role of nano topography and bioactive coated 2D/ 3D titanium lattices on mesenchymal stem cells and *Pseudomonas aeruginosa* behaviour**
Centre for the Cellular Microenvironment, University of Glasgow
Laila Damiati, Virginia Llopis-Hernández, Bo Su, Richard Oreffo, Peifeng Li, Penelope M. Tsimbouri, Manuel Salmeron-Sanchez and Matthew J. Dalby.

10:20 – 10:35 **Dual action antimicrobial surfaces**
School of Engineering, University of Liverpool
George Fleming, Jenny Aveyard, Joanne L Fothergill, Fiona McBride, Rasmita Raval and Raechelle A D'Sa

10:35 – 10:50 **Photodynamically active electrospun scaffolds for antibiotic-free infection Control**
Institute of Medical and Biological Engineering, University of Leeds
Amy Contreras, Michael J. Raxworthy, Simon Wood, Jessica D. Schiffman, Giuseppe Tronci

10:50 – 11:15 **Break and Poster session**

11:15 – 11:30 **Ultra-short self-assembling amphiphilic peptides: a versatile platform for soft biomaterials fabrication**

School of Pharmacy & Biomedical Sciences, University of Central Lancashire

Mohamed A. Elsawy, Jacek Wychowaniec, Alberto Saiani, Ronak Patel, James Leach

11:30 – 11:45 **Insights into the structure of self-assembly histidine peptide with Glucose Oxidase Enzyme**

School of Chemical Engineering and Analytical Science, University of Manchester,

Xiaoxia Huang, Alberto Saiani and Aline F. Miller

11:45 – 12:00 **Surface-mediated self assembly of supramolecular structures Teaching an old dog new tricks**

School of Pharmacy, University of Nottingham

Mischa Zelzer

12:00 – 12:15 **Controlling the enzymatic degradability of self-assembled peptide nanostructures via supramolecular cohesion**

School of Engineering and Materials Science & Institute of Bioengineering, Queen Mary University of London.

Yejiao Shi, Daniela S. Ferreira, Jayati Banerjee, Xinqing Pang and Helena S. Azevedo

12:15 – 12:30 **Peptide-graphene oxide hydrogel nanocomposites for intervertebral disc tissue engineering applications**

School of Materials, University of Manchester

Cosimo Ligorio, Mi Zhou, Aravind Vijayaraghavan, Judith Hoyland, Alberto Saiani

12:30 – 13:30 **Lunch**

RSC Biomaterials Chemistry Annual Conference

Thursday 10th January

13:30 – 14:20 **Plenary Speaker, John Fisher**
University of Leeds

14:20 – 14:35 **Synergistic integrin-growth factor microenvironment to bioengineer the bone marrow niche *in vitro*.**
Centre for the Cellular Microenvironment, University of Glasgow. MRC Centre for Regenerative Medicine, University of Edinburgh
Hannah Donnelly, Ewan Ross, Christopher West, Bruno Peault, Manuel Salmeron-Sanchez & Matthew J Dalby

14:35 – 14:50 **Hydroxamic acid-conjugated collagen systems for matrix metalloproteinase modulation in chronic wounds**
Textile Technology Research Group, University of Leeds
Giuseppe Tronci, Stephen J. Russell, David Wood and He Liang

14:50 – 15:05 **Manipulation of collagen type I using topographical and chemical cues for corneal wound repair**
School of Chemistry, University of Birmingham
Emma McCarthy, Megan E Cooke, Pola Goldberg Oppenheimer and Liam M Grover

15:05 – 15:15 **Osteoblast behaviour on whey protein isolate hydrogels as scaffolds for bone regeneration**
Materials Science Institute, Lancaster University
Susanne Stählke, Karolina Mazur, Aleksandra Krężel, Jagoda Żydek, Elżbieta Pamuła, Krzysztof Pietryga, Julia K. Keppler, Carmen C. Piras, Sam C. Tsang, J. Barbara Nebe, Timothy E.L. Douglas.

15:15 – 15:30 **The visco-elasticity of 2D protein networks – Implication for stem cell expansion**
Institute of Bioengineering and, School of Engineering and Materials Science, Queen Mary University of London
Dexu Kong, Lihui Peng, Khai Nguyen, Pavel Novak and Julien E. Gautrot.

15:30 – 15:55 **Break and Poster session**

15:55 – 16:10 Controlling immune cell activation with bionanomaterials
Dept. Materials, Imperial College London.
Iain E. Dunlop

16:10 – 16:25 Strontium and fluoride c o-doped calcium phosphate nanoparticles for treatment of dental enamel lesions
Institute of Pharmaceutical Science, King's College London
Jana Javorovic, Zi Hong Mok, Nigel Pitts, Rupert Austin, Gordon Proctor and Maya Thanou.

16:25 – 16:40 Nano optical oxygen sensor (nose) for cell physiological condition monitoring
School of Engineering, University of Liverpool
Manohar Prasad Koduri, Yu Wei Shao, John Hunt , James Henstock , Fan Gang Tseng and Jude Curran

16:40 – 16:55 Development of blended alginate/collagen hydrogels for 3D neural cell culture applications
Neuroscience and Experimental Psychology, University of Manchester
Samuel R. Moxon, Nicola J. Corbett, Kate Fisher, Geoffrey Potjewyd, Marco Domingos, Nigel M. Hooper

16:55 – 17:10 Versatile hydrogel composites with osteogenic ions for bone substitutes
Faculty of Dentistry, Oral & Craniofacial Sciences, King's College London
Lilis Iskandar, Jonathan Acheson, Lucy Di-Silvio, Sanjukta Deb

17:10 – 17:40 RSC Biomaterials Chemistry Special Interest Group AGM

RSC Biomaterials Chemistry Annual Conference

Thursday 10th January

Conference Dinner
Thursday 10th January

THE VENUE AT THE ROYAL LIVER BUILDING

Pier Head, Liverpool, L3 1HU.
Entrance via main doors on Canada Blvd
DRINKS RECEPTION AT 7.30PM SHARP

Delta Taxi - 0151 922 7373
Alpha Taxi - 0151 722 8888

RSC Biomaterials Chemistry Annual Conference

Friday 11th January

10:00 – 10:50 **Plenary Speaker, Graham Leggett**
University of Sheffield

10:50 – 11:05 **3D printed flexible composite scaffolds with high ceramic content for bone regeneration**
School of Pharmacy, University of Nottingham
Aruna Prasopthum, Kevin Shakesheff, Jing Yang

11:05 – 11:20 **Suspended layer additive manufacture and the fabrication of complex 3D tissue scaffolds**
Department of Pharmacy, University of Huddersfield
Jessica Senior, Megan E. Cooke, Liam M. Grover and Alan M. Smith

11:20 – 11:35 **Effect of laponite on the thermoresponsive nature of poly NIPAM based nanocomposites**
Materials Engineering Research Institute & Biomolecular Sciences Research Centre, Sheffield Hallam University.
Simon William Partridge, Joseph Snuggs, Christine Le Maitre and Chris Sammon

11:35 – 12:00 **Break and Poster session**

12:00 – 12:15 **Electrospinning for regenerative medicine; challenges and solutions to bring products to the market.**
IME Medical Electrospinning, Waalre, The Netherlands
Marc Simonet and Judith Heikoop

12:15 – 12:30 **Bioactive hybrid materials for soft and hard tissue engineering**
Department of Materials, Loughborough University
Adja Touré, Elisa Mele and Jamieson Christie

12:30 – 12:45 **In Situ Screening Of functional polymers for biomedical applications**
School of Chemistry and Institute of Microbiology and Infection, University of Birmingham.
Francisco Fernandez-Trillo

The conference will finish with a lunch served in the Stanley Theatre at 1pm. We would like to thank you for your participation and engagement throughout the event and look forward to working with you all in the future.

If you have some time there are dozens of attractions within walking distance that might be worth popping into see. These are our favourites.

If you have any questions or need any advice please feel free to ask a member of the organising team.

Thanks again for coming.

RSC Biomaterials Chemistry Annual Conference

Poster Presentations

P01 **Triply-responsive hydrogels constructed from microgel building blocks containing a photo-cleavable**

School of Materials, University of Manchester

Dongdong Lu, Brian Saunders

P02 **Synthetic bone graft with potential application in oral and maxillofacial bone defects**

Faculty of Dentistry, King's College London

Alexandre Marques, Agamemnon Grigoriadis and Sanjukta Deb

P03 **Supramolecular Design of Cytoskeletal Protein-based Hydrogels, Characterization and Potential Applications in Regenerative Medicine**

School of Engineering and Materials Science, Queen Mary University of London

Babatunde O. Okesola, Burak Derkus, Sonya R. Manic, Dave Adams and Alvaro Mata

P04 **Characterisation of oxidized alginate-gelatin hydrogels for in vitro models**

Division of Pharmacy and Optometry, University of Manchester

Chen Zhao, Enrique Lallana, Ayşe Latif, Kaye Williams and Annalisa Tirella

P05 **A biocompatibility study of a versatile ultra-short self-assembling peptide hydrogel for dental and soft tissue regeneration.**

Centre for Biomedicine, Manchester Metropolitan University

Claire-Marie Nuttegg, Ronak Patel, Mohamed Elsawy, Araida Hidalgo-Bastida

P06 **Rheological and recovery properties of self- assembly peptide hydrogels**

Chemical Engineering and Analytical Science, University of Manchester

Cong Ding, Alberto Saiani, Aline F. Miller

P07 **Peptide-graphene oxide hydrogel nanocomposites for intervertebral disc tissue engineering applications**

School of Materials, University of Manchester

Cosimo Ligorio, Mi Zhou, Aravind Vijayaraghavan, Judith Hoyland, Alberto Saiani

P08 **Control of neuronal alignment and circuit formation in 3D hydrogel cultures**
Department of Chemistry, Loughborough University
Daniel Merryweather, Joran Roe and Paul Roach

P09 **Neuronal Alignment using Polymeric Micro-Hollow Fibres for Spinal Cord Injury Regeneration**
Department of Life and Health Sciences, Aston University
David Jenkins, Scott Allan, Marianne J Ellis, Patricia P Esteban

P10 **Schiff base new ligand derived from camphor with folic acid synthesizing and characterizing it with some metal ions.**
Department of Chemistry, Faculty of Science and Health, Koya University, Iraq
Iman I. Alsalihi

P11 **Fast Synthesis of ZnMgO Nanowires by the Microwave-Assisted Hydrothermal Method**
Department of Physics, Faculty of Science, King Abdulaziz University, Saudi Arabia
Faten E. Al-Hazmi

P12 **Core–shell–shell cytocompatible polymer dot-based particles**
School of Materials, University of Manchester
Hannah R. Shanks

P13 **Synthesis and optimisation of lipid-hybrid nanoparticles loaded with a mixture of two antiretroviral drugs for the treatment of HIV**
Department of Chemistry, University of Liverpool
Heba Elkateb, Steven P. Rannard and Tom McDonald

P14 **ACELULLAR GELATINE-ALGINATE SCAFFOLDS FOR DENTINE-PULP REGENERATION**
Department of Bioengineering, Imperial College
Ignacio Medina-Fernández, Adam D. Celiz

P15 **Developing a novel ocular adhesive for corneal perforations**
Chemical Engineering, University of Birmingham
Inês Barroso, Anita Ghag and Sophie Cox

P16 **Control of Mesenchymal Stem Cell and Articular Chondrocyte Morphology using Large-Area Chemical Nanoarrays by Polymer Pen Lithography**
School of Engineering, University of Liverpool
I-Ning Lee, John A Hunt, Lu Shin Wong, Nick Rhodes, Judith M Curran

P17 **Magnetic hydrogels: Tissue engineering constructs with switchable stiffness**
Materials Department, Loughborough University
Jordan Roe, Paul Roach and Helen Wilcock

P18 **Poly(acryloyl-hydrazide) as a versatile scaffold to induce bacterial aggregation**
School of Chemistry/School of Chemical Engineering, University of Birmingham
Jose Luis Brioso, Francisco Fernandez-Trillo and Tim W Overton

P19 **Investigation of the anticancer activity of electron-deficient organometallic complexes**
School of Chemistry and Biosciences, University of Bradford
Maria Azmanova, Joan J. Soldevila-Barreda, Anaïs Pitto-Barry, Steven M. Picksley, and Nicolas P. E. Barry

P20 **A novel pH/strain sensing blue-emitted nanogel probe and hydrogel application**
School of Materials, University of Liverpool
Mingning Zhu, Brian R Saunders

P21 **A novel calcium chelating agent for the treatment of corneal mineralisation**
School of Chemical Engineering, University of Birmingham
Naomi Bennett, G. Begum, L.J Hill and L.M. Grover

RSC Biomaterials Chemistry Annual Conference

Poster Presentations

P22 **Mechanical Properties of Gelatin-GO hydrogels for biomedical applications**
Chemical Engineering, University of Birmingham
Natalie Parsons, Alberto Saiani and Aravind Vijayaraghavan

P23 **Polymer scaffolds for 3D biocatalysis**
School of Chemistry, University of Birmingham
Pavan Adoni, Francisco Fernandez-Trillo and Timothy Overton

P24 **Next-generation 2.5D tissue culture surfaces to study cancer cell aggregation**
School of Science and Technology, Nottingham Trent University
Rajeharish Rajendran, Graham J Hickman, Carole C Perry and David J Boocock

P25 **A dentine adhesive with remineralising potential**
School of Chemistry/School of Chemical Engineering, University of Birmingham
Rana Alkattan, Subir Banerji and Sanjukta Deb

P26 **Polyions complex and mesoporous silica nanoparticles for the fluorogenic detection of endotoxin and the delivery of Polymxin B**
School of chemistry, University of Birmingham
Sameh El Sayed, Francisco Fernandez-Trillo, Ismael Otri, Elena Azna, Félix Sancenón, Ramón Martínez-Máñez.2,3

P27 **Plasmonic and colloidal stability behaviours of Au-acrylic core–shell nanoparticles with thin pH-responsive shells**
School of Materials, University of Manchester
Shanglin Wu, Mingning Zhu, Qing Lian, Dongdong Lu, Ben Spencer, Daman J.Adlam, Judith A. Hoyland, Kirsten Volk, Matthias Karg and Brian R. Saunders

P28 **Design and Test of self-assembling peptide systems for target cancer drug delivery**
Chemical Engineering and Analytical Science, University of Manchester
Siyuan Dong, Alberto Saiani, Aline Miller

P29 **Towards the development of a mechanically and biologically relevant oral mucosa model to evaluate tissue integration approaches for dental implants**

Chemical Engineering, University of Birmingham

Sophie E Mountcastle, Victoria E Seville, Richard M Shelton, Rachel L Sammons, Sophie C Cox, Sara Jabbari, and Sarah A Kuehne

P30 **A Comparison of Lattice Designs to Optimise Mechanical Properties in a Novel Lattice Hip Spacer Implant**

School of Chemical Engineering, University of Birmingham

Sophie Louth, Kenneth Nai, Neil Eisenstein, Sophie Cox

P31 **GD-peptide functionalised Highly branched Poly(N-isopropylacrylamide)-Synthesis and Cell-Lifting application**

School of Science and Technology, Nottingham Trent University

S.R. Carter, S.Rimmer, L. Swanson, J. Haycock, S. MacNeil, S. Rutkaite, S. Hopkins, B. Hunt

P32 **NOVEL ANTIMICROBIAL EMULSIONS: FORMULATION OF A TRIGGERED RELEASE REACTIVE OXYGEN DELIVERY SYSTEM**

School of Chemistry/School of Chemical Engineering, University of Birmingham

Thomas Hall, Liam Grover and Sophie Cox

P33 **Rapid Screening of Polymeric Transfection Agents for the Treatment of Glaucoma**

School of Chemistry, University of Birmingham

Thomas Leigh, Ghazala Begum, Zubair Ahmed, Ann Logan, Richard Blanch,and F. Fernandez-Trillo.1

Tuning long-acting HIV drug release from a nanogel-based in situ forming implant

Adam R. Town,[1] Jessica Taylor, [1] Karl Dawson,[2] Edyta Niezabitowska,[1] Nancy M. Elbaz,[1] Andrew Corker,[2] Esther Garcia-Tuñón [2] and Tom O. McDonald * [1]

1: Department of Chemistry, University of Liverpool, Crown Street, Liverpool, L69 7ZD, UK. 2: School of Engineering, Brownlow Hill, University of Liverpool, Liverpool, L69 3GH, UK. *tomm@liverpool.ac.uk

Oral ☒ Poster ☐

INTRODUCTION

HIV is a global public health threat and requires life-long, daily oral dosing to effectively treat. This pill burden often results in poor adherence to the medications. An injectable in situ forming implant (ISFI) with tuneable drug release kinetics would allow patients to replace some of their daily pills with a single infrequent injection. We have recently shown promising proof of concept data for a novel ISFI based on a colloidal assembly of two types of nanoparticles that avoids many of these issues. In this system, poly(N-isopropyl acrylamide) (polyNIPAm) nanogels responded to the stimuli present upon injection into the body to form a solid implant.[1] The reservoir of drug was provided by solid drug nanoparticles (SDNs)[2–4] which are nanoparticles composed entirely of solid drug, stabilised by amphiphilic molecules. This ISFI system exploited a synergistic dual-stimuli responsive behaviour of the nanogels which require the simultaneous stimuli of body temperature and physiological ionic strength to cause aggregation of the nanogel particles causing the formation of a solid implant. In our new work, we show how drug release behaviour can be tuned by changing the size of the nanogels.

MATERIALS & METHODS

Four polyNIPAm nanogels were synthesised by precipitation polymerisation with mean diameters of 65, 160, 310 and 450 nm. SDNs of the HIV drug lopinavir were prepared with a mean diameter of 330 nm.[3] The drug release behaviour and stability of these nanocomposite implants were then assessed in vitro over 360 hours.

RESULTS & DISCUSSION

The exposure of a mixed dispersion of the nanogels and SDNs resulted in the formation of a solid nanocomposite implant. The samples displayed a single phase of drug release and application of Ritger-Peppas equation indicated Fickian diffusion. Nanocomposites with the lowest loading of SDNs (33%) showed a linear relationship between nanogel diameter and the dissolution constant. We hypothesise that the larger nanogels result in more porous nanocomposites which leads to faster drug release.

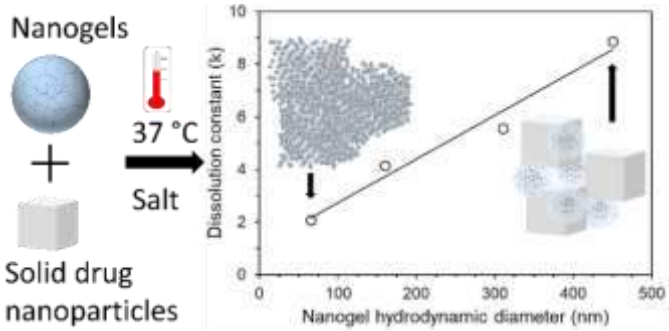

Figure 1: Nanocomposites of nanogels and SDNs are formed upon exposure to physiological temperature and ionic strength. The drug release showed a linear relationship between nanogel diameter and the dissolution constant.

CONCLUSION

These results show an attractive method for tuning the release of lopinavir from in situ loading implants with high loadings of solid drug nanoparticles (up to 66%) that provide extended drug release behaviour.

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Utilisation of an oxidation sensitive trigger with combined temperature response for drug delivery applications

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Oral ☒ Poster ☒

INTRODUCTION

Targeted drug delivery utilises stimuli produced by diseases to deliver encapsulated drugs to the site in the body where they are needed, thus improving treatment and minimising side effects from large doses. Autoimmune diseases produce reactive oxygen species (ROS), such as hydrogen peroxide, in elevated levels compared to normal immune response, meaning these can be used as a target molecule. This has been utilised as an oxidative trigger on a variety of polymeric systems to develop an oxidative responsive drug delivery system.

MATERIALS & METHODS

RAFT polymerisation was used to synthesise a range of nanogels of p(hydroxyethyl acrylamide)-*b*-p(*N*-isopropyl acrylamide) (pHEA-*b*-pNIPAM) crosslinked with methylene bisacrylamide (BIS) in a cononsolvent of ethanol and water. An oxidation responsive monomer based on a boronic acid pinacol ester (BAPE) was also incorporated into these nanogels as a statistical copolymer with NIPAM. These were analysed by DLS at various temperatures and TEM to determine their size and morphology.

RESULTS & DISCUSSION

Nanogels of pHEA-*b*-pNIPAM with and without the incorporation of BAPE have been successfully synthesised with a variety of different chain lengths, different crosslinking ratios and amount of BAPE in the hydrophobic block. These show shrinkage on heating above the LCST and the nanogels with BAPE show a change in size on oxidation.

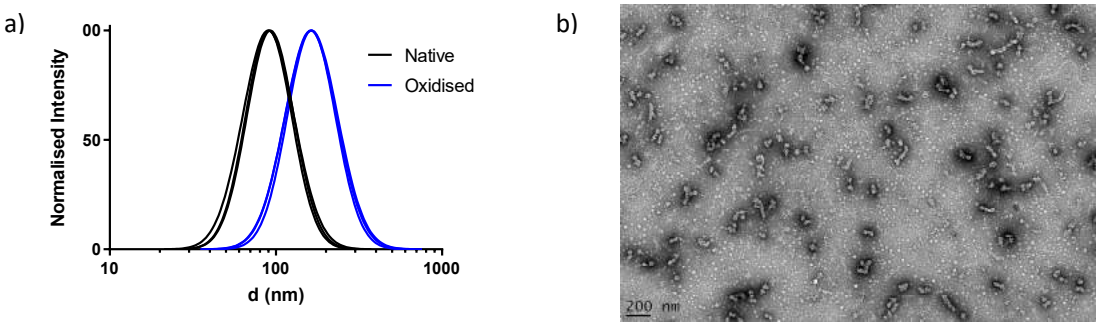

Figure 1: pHEA$_{35}$-b-p(NIPAM-st-BAPE)$_{250}$ nanogel with a crosslinker to mCTA ratio of 5:1 a) DLS of the polymer at 0.1 wt% before and after oxidation of 37 °C, b) TEM prepared at room temperature of the nanogel at 0.05 wt%

CONCLUSION

The above nanogels show promising attributes for oxidation responsive drug delivery systems. They are less than 100 nm, respond to low concentrations of H_2O_2, they shrink on heating above the LCST and their LCST can be tuned by varying the concentration of BAPE incorporated. The LCST before oxidation is less than 37 °C but on oxidation increases above this which should enable successful drug loading and release.

ACKNOWLEDGEMENTS

The University of Sheffield and EPSRC (Grant no. EP/P027989/1) are thanked for funding of the PhD and thank you to Dr Spain and the rest of the group for their continued help and support.

Rheo-Dissolution: A new technique for the simultaneous measurement of rheology and drug release from hydrogels

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Oral ☒ Poster ☐

INTRODUCTION

In situ gel forming materials are useful approach to control the release of drugs and increase retention time at the application site. Critical to the success of such systems is the rheological behavior before, during and after *in situ* gelation as this will impact upon methods of application, retention time and importantly drug release rates. Currently measurements of gelation and drug release in such systems are performed separately. Furthermore, it is difficult to change the chemical environment during rheological measurements which is required when the sol-gel transitions are triggered by pH or crosslinking ions. Here, we have developed a rheo-dissolution cell that can be attached to the lower plate of a commercially available rheometer that allows changing of the chemical environment during rheological measurement and also has the ability to measure dug release simultaneously. This was demonstrated using a drug loaded *in situ* gelling hydrogel.

MATERIALS & METHODS

The rheo-dissolution cell was constructed from acrylonitrile butadiene styrene using a Makerbot Replicator™ 2 3D printer. The cell consisted of a circular reservoir (55 ml) with inlet and outlet port that can be filled with physiological fluids. A stainless steel mesh was placed on top of the reservoir and acted as the lower plate of the rheometer allowing loaded samples to come into contact with the fluids in the reservoir. An *in situ* gelling ophthalmic formulation was prepared using 0.4% gellan gum and timolol maleate (6.8 mg/ml). Simulated lachrymal fluid (SLF) was then loaded into the reservoir and peristaltic pump was used to create a flow-through system [Figure 1(A)]. Sample was placed on the mesh and measurements of storage modulus (G') and loss modulus (G") were recorded as a function of time when exposed to SLF. Samples of the SLF were collected at regular time interval and analysed for release of timolol using HPLC.

RESULTS & DISCUSSION

On exposure to SLF the formulation began to gel rapidly indicated by an increase in G' and forming strong gel (G'>>G") [Figure 1(B)]. Drug release into the SLF was simultaneously observed with 46% timolol released at 3 hours and showed clear differences in rate of release as the gel was structuring.

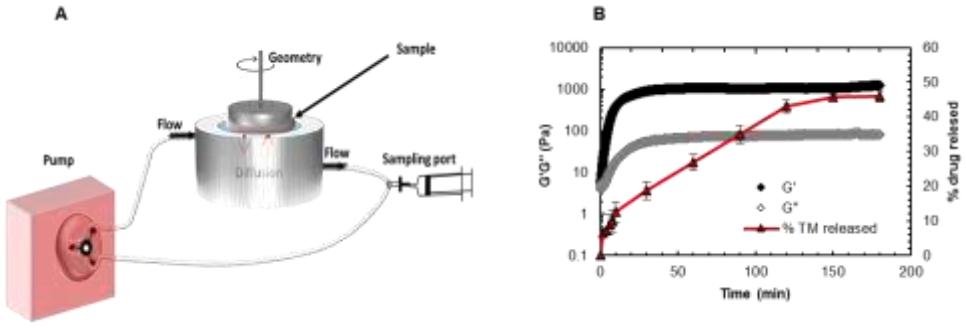

Figure 1: (A) Schematic diagram of the experimental set up of rheo-dissolution cell (B) Rheo-dissolution experiments of *in situ* gel forming ophthalmic formulation

CONCLUSION

This novel method can be used as a model to simultaneously measure rapidly changing rheological behavior and drug release from polymeric drug delivery systems when the formulations are exposed to various physiological fluids (such as gastric fluid, saliva, lung fluid, lacrimal fluid, nasal fluid) with a facility of changing environment such as pH, ionic strength or additional additives ([crosslinkers/chelators) in process.

Delivery Systems for a Therapeutic Demineralising Agent

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Oral ☒ Poster ☐

INTRODUCTION

Pathological calcifications vary in scope and location, from small mineral nodes in the eye, aggregated stones in the kidney and gall bladder, to the formation of lamellar bone in soft tissues. This latter case, heterotopic ossification (HO), can form as a result of musculoskeletal trauma, burns, central nervous system injury, or rare genetic conditions. HO has become unusually common in the military in recent years, due to increased survivorship and the nature of injuries caused, particularly the upsurge of blast injuries. HO can cause chronic pain, skin ulceration, and limited joint movement for patients, and can prevent the fitting of prosthetic limbs. Many of these calcifications do not have suitable preventions or treatments. In the case of HO, NSAIDs and radiotherapy are currently used as preventions, however their efficacy is inconsistent and they have side effects, such as non-union, delayed wound healing, and gastrointestinal bleeding, that make them unsuitable in combat injured casualties. Once formed, the only way to treat HO is via a technically demanding surgical excision of the bone from the soft tissue, giving increased risk of hemorrhage and infection.

MATERIALS & METHODS

In this study we use hexametaphosphate (HMP) as our demineralising agent, and use spectrophotometric measurement to demonstrate that is prevents and reverses the precipitation of several relevant calcium salts. We then incorporate HMP into several delivery vehicles, and use techniques such as rheology, zeta potential and FTIR to characterise the targeted therapeutic. We have used microCT both *ex vivo* and *in vivo*, in an Achilles tenotomy rodent model of HO, to characterise the potency of the delivery vehicles.

RESULTS & DISCUSSION

We have shown that HMP is capable of preventing and dissolving several relevant calcium salts. We have incorporated it into an injectable delivery vehicle, and shown that the material is shear thinning, and will release the active over time. We have also demonstrated that the formulation is potent at demineralising bone *ex vivo*. However, the effect *in vivo* is more complicated, as increasing injection frequency increases the amount of HO formed. This is most likely a result of repeatedly aggravating the region, increasing the inflammation which causes HO.

CONCLUSION

HMP is a powerful calcium chelator, which seems to be non-toxic *in vivo*, which is capable of dissolving a range of pathological calcium salts. We have created and characterised an injectable delivery vehicle which performs well *in vitro* and *ex vivo*, however, more investigation is required to understand the condition *in vivo*, in order to properly deliver the drug to give the required therapeutic effect. Investigation into implantable delivery vehicles may also be helpful, to eliminate the need to repeated interventions.

ACKNOWLEDGEMENTS

We would like to acknowledge the EPSRC and the RCDM for their funding for this work.

Real time non-invasive optical tracking of label-free nanoparticles and proteins

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Oral ☒ Poster ☐

INTRODUCTION: Thanks to their unique chemical properties and flexibility in design, nanoparticles can be used as successful drug delivery systems or as effective tools for the advancement of regenerative medicine[1]. At present there are few non-invasive real time techniques that can be used to track the dynamics and the direct interaction of non-labelled nanoparticles with cells/bacteria in vitro. Within this study we will validate the use of caustics and optical microscopy as a potential methodology to track proteins, protein based nanoparticles and metallic nanoparticles dynamics and interactions in vitro in real time.

MATERIALS & METHODS: The experiments were conducted using a conventional inverted optical microscope (Axio Observer.Z1 m, Carl Zeiss). Some simple adjustments were made to the classical microscope set up to allow the formation of a caustic by nanoparticles and proteins in the solution following the technique proposed by Patterson and Whelan[2]. Bovine serum albumin (BSA, purity > 96%) was commercially supplied by Sigma Aldrich (Saint Louis, USA). 50 nm BSA nanoparticles were synthesised following a modified desolvation process[3]. Spherical gold nanoparticles were purchased from BBI Solutions (Crumlin, UK), with a nominal diameter of 50 nm.

RESULTS & DISCUSSION: Figure 1 shows the characteristic caustic generated by gold nanoparticles, BSA nanoparticles and BSA proteins in solution. It can be seen that the caustic is of the order of magnitude of microns, allowing the direct observation and tracking of the non-labelled proteins and nanoparticles even if they are below the visibility limit. Caustic generated by spherical nanoparticles consist of a central bright spot surrounded by concentric and much fainter diffraction rings. The caustic generated by BSA protein is similar to the caustic generated by sperical nanoparticles but the diffraction rings are less evident. However, the central bright spot allows its tracking. This capability offers the prospect of tracking the real time interaction of nanoparticles and proteins with biological components as shown in figure 1 (d).

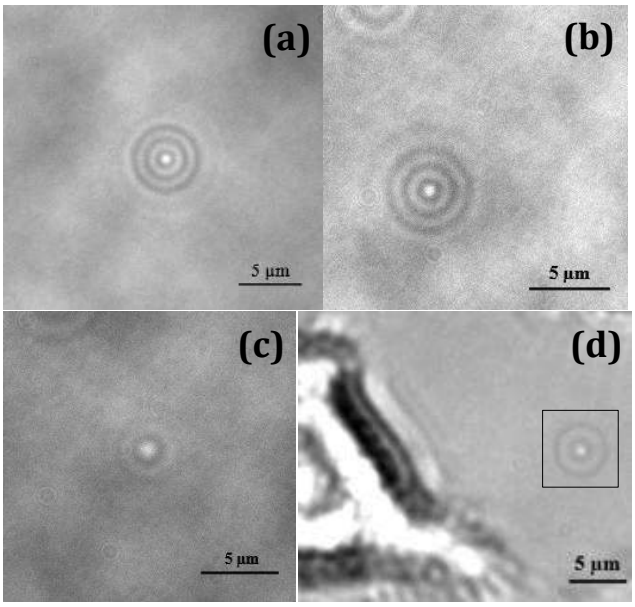

Figure 1: Photograph of the caustic in deionised water generated by: (a) 50 nm gold nanoparticle; (b) 50 nm BSA nanoparticle; (c) BSA protein. (d) 50 nm gold nanoparticle approaching the extracellular membrane of a fibroblast. Cell is out of focus to allow the correct formation of the particle caustic.

CONCLUSION: The results obtained demonstrate that proteins and nanoparticles generates caustics signature at several orders of magnitude larger than their real size, allowing the direct and real time observation of their dynamics and interactions with any other component of the surrounding media without the need of fluorescent tag, which can have a non-negligible impact on their dynamics and on protein structure and function[4].

ACKNOWLEDGEMENTS: FG was supported from the EPSRC Doctoral Training Account of the School of Engineering at the University of Liverpool.

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Development of Ti-Ag alloys and investigation of antimicrobial response

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Oral ☒ Poster ☐

INTRODUCTION

Infections initiated at implant surfaces are responsible for around 22 % of orthopaedic[1], and up to 30 % of craniomaxillofacial revisions[2]. Coatings integrating silver as a prophylaxis have shown clinical efficacy, but direct integration of silver into alloys has seen variable results with no clear relationship between concentration of silver, and efficacy [3, 4].

In order to improve implant design, Additive Manufacturing techniques are frequently applied. Alongside allowing greater customisation of implants, processes such as Selective Laser Melting (SLM) enable rapid alloy development due to the use of powder feedstocks. Due to highly localised heating, SLM generates extremely high cooling rates of around 107 $K.s^{-1}$, producing non-equilibrium microstructures. Such materials may help elucidate how bacterial response relates to phase distribution.

MATERIALS & METHODS

Materials were manufactured from blended 15-45 µm Ti-6Al-4V and Ag powders, with feedstock size distribution, morphology, and chemistry assessed by laser particle diffraction, scanning electron microscopy (SEM) and Inductively Coupled Plasma emission spectroscopy respectively. To optimise manufacture, a 2-dimensional parameter space of laser scanning speed and power was explored. Sample microstructure was characterised by Scanning Electron Microscopy (SEM) and micro X-ray computed tomography (XCT), whilst He pycnometry and micro X-ray fluorescence (XRF) were used to measure bulk density and chemistry.

Optimised manufacturing parameters were used to produce samples for antimicrobial assessment. A derivative of the Japanese industrial standard technique (JIS Z 2801) for surface bacteriology was used with *S. Aureus* (NCTC 6571).

RESULTS & DISCUSSION

Maximising sample density and silver content, whilst reducing minimising porosity, optimum manufacturing parameters were identified as a power of 225 W and scanning speed of 1500 mm/s. Microstructural investigation with SEM confirms segregation is observed within the alloy with regions of pure silver within a Ti-6Al-4V matrix. However, pore volume of below 10^{-4} % indicates effective consolidation of the material.

Bacteriological comparisons to conventional Ti-6Al-4V alloy showed no significant difference in replication. This correlates with previous findings that indicated a Ti_2Ag intermetallic mediates efficacy [3].

CONCLUSION

Antimicrobial behaviour of silver in alloys is dependent not only on concentration, but may also be reliant upon specific phase formation. Whilst this may be directly linked to elution of Ag+ ions, further assessments are needed to counter studies showing surface efficacy with negligible elution under physiological conditions.

ACKNOWLEDGEMENTS

We acknowledge the EPSRC for funding (EP/P02341X/1) and author ML thanks the School of Chemical Engineering at the University of Birmingham for financial support.

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The synthesis of a nano silver-graphene oxide system and efficacy against endodontic biofilms using a novel tooth model

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Oral ☒ Poster ☐

INTRODUCTION

Sodium hypochlorite (NaOCl) remains the gold standard for irrigation of infected root canals in dentistry. However, its deleterious caustic effects and generation of toxic volatile compounds with disinfection by-products makes it imperative that alternative methods are developed for root canal disinfection[1]. The purpose of this study was to examine the antimicrobial efficacy of silver nanoparticles (AgNPs) synthesized on an aqueous graphene oxide (GO) matrix (Ag-GO), with different irrigant delivery methods to enhance the disinfection regimen, using a novel *ex vivo* infected tooth model.

MATERIALS & METHODS

AgNPs were prepared by reducing $AgNO_3$ with 0.01M $NaBH_4$ in presence of GO. Elemental analysis was performed with scanning electron microscopy/energy dispersive X-ray spectroscopy (SEM/EDS) and scanning transmission electron microscopy (STEM) was used for size and morphology analysis of GO and AgNPs. Nutrient stressed, multi-species biofilms were grown in prepared root canals of single-rooted teeth. The tested irrigants were sterile saline, 1% and 2.5% sodium hypochlorite (NaOCl), 2% chlorhexidine gluconate (CHX), 17% EDTA and an aqueous suspension of 0.25% Ag-GO. The antimicrobial efficacy of root canal irrigants was performed with paper point sampling and measurement of quantitative microbial counts. The biofilm disruption capacity in dentine tubules was analysed with confocal laser scanning microscopy (CLSM). Two-way analysis of variance (ANOVA) with post hoc Tukey tests was used for data analysis. The level of statistical significance was set at $P<0.05$. The acquisition of total biovolume (um^3/um^2) and the percentages of biofilm viability was performed with the software BioImage_L.

RESULTS & DISCUSSION

SEM/EDS analysis confirmed impregnation of Ag within the GO matrix. TEM images showed edge-shaped GO sheets and spherical AgNPs of diameter 20-50nm, forming a network on the surface of GO sheets. The microbial killing efficacy of 2.5% NaOCl was superior compared to the experimental groups. The use of ultrasonic activation enhanced the efficacy of Ag-GO compared to 1% NaOCl, 2% CHX, 17% EDTA and sterile saline ($P<0.05$). The maximum biofilm disruption, in dentine tubules, was achieved by 2.5% NaOCl. Ag-GO caused a significant reduction of total biovolumes compared to the rest experimental groups ($P<0.05\%$).

CONCLUSION

The biofilm killing and disruption capacity of Ag-GO was successfully documented in a novel *ex vivo* infected tooth model. Ultrasonic activation selectively improved the antimicrobial efficacy of Ag-GO.

ACKNOWLEDGEMENTS

The authors deny any conflict of interest

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Nitric Oxide Releasing Titanium Surfaces for Antimicrobial Applications

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Submitted for either/ both
POSTER ☐
ORAL ☒

Introduction

Titanium is commonly used in the fabrication of orthopaedic implants owing to its biocompatibility and mechanical properties. Bacterial adhesion and biofilm formation on the surfaces can lead to infections and failure of the implant.[1] Compared to traditional bactericidal agents such as antibiotics, antiseptics and silver, which can lead to drug resistance or high cytotoxicity, nitric oxide (NO) is an attractive antimicrobial as it highly effective without leading to antimicrobial resistance.[2, 3] However as NO is a reactive gas, with a relatively short half-life, delivery of this antimicrobial is challenging. In this study we have synthesized NO releasing coatings on Ti surfaces with varying antimicrobial payloads. The NO donor used are *N*-diazeniumdiolate which are formed using an immobilised aminosilane precursor. We have developed a mechanistic understanding of diazeniumdiolate formation and NO release rate based on the aminosilane precursor.

Materials and Methods

Polished titanium (Ti) samples were immersed in trimethoxysilylpropyldiethylenetriamine (DET3), 6-aminohexyl-3-aminopropyl trimethoxysilane (AHAP3), 11-aminoundecyltriethoxysilane (AUTES), n-decyltrimethoxysilane (DTMS) (10 vol%. in ethanol) with stirring for 4 h, respectively. Samples were washed with ethanol for 3 times before curing in the oven at 80 ° C for a further 4 h. Then samples were placed in a NO reactor to synthesis diazeniumdiolates. Diazeniumdiolates modified samples were analysed using AFM, contact angle and XPS. NO release was monitored using a chemiluminescent NO detector. Antimicrobial property was tested with *Staphylococcus aureus* (*S. aureus*). Cytotoxicity of NO release samples was studied using MTT and the effect of NO on cell behaviours was observed using laser scanning confocal microscopy (LSCM).

Results and Discussion

Results have demonstrated that the formation of diazeniumdiolates on DET3, AHAP3, AUTES and DTMS coated Ti surfaces. The binding energies of N 1s peak at ~401 eV for N^+ and ~402 eV for N-O were observed from XPS analysis, representing the $–(O^-)N^+=N(O^-)$ group. The kinetics of release of the NO were different for each diazeiumdiolated surface and were dependent on pH. The NO release of samples in pH=4 buffer showed the highest maximum instantaneous NO-releasing concentration of diazeniumdiolates on AUTES, which is 5.6 $\mu M \cdot s^{-1}$, followed by AHAP3, DET3 and DTMS. Both AUTES and AHAP3 showed a burst release of NO at pH 4. NO release from diazeniumdiolates showed a positive effect on inhibition of biofilm formation on substrates. Low concentration of NO benefits the proliferation of osteoblast, resulting in an increase number of cells on Ti-AHAP3-NO and Ti-AUTES-NO after a 7-day cell culture.

Conclusions

Diazeniumdiolates were successfully tethered four selected silanes to produce NO releasing surfaces with varying release profiles. These surfaces have the potential to be antimicrobial surfaces for orthopaedic applications.

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Synthesis and evaluation of novel selenium nanoparticles for development of antibacterial healthcare textiles

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INTRODUCTION

It is estimated that 300,000 patients a year in England acquire a healthcare-associated infection as a result of care within the NHS and the related cost is approximately £1 billion a year[1]. In a hospital environment, textiles can provide ideal substrates for microorganisms to grow and become a vehicle for the transmission of pathogens[2]. In this study, selenium nanoparticles were investigated as novel antibacterial agents for the development of antibacterial textiles to control the growth and spread of pathogens in hospitals.

MATERIALS & METHODS

Firstly, a cation-generating agent, 3-chloro-2-hydroxypropyl trimethyl ammonium chloride (CHPTAC), was used to graft quaternary groups onto cotton surfaces. The cationic quaternary groups were able to attract anionic selenite groups and provide sites of reaction for the reduction of selenite into elemental selenium nanoparticles. The grafting of cationic groups and formation of selenium nanoparticles on cotton surfaces were confirmed by FTIR, SEM and EDX. The antibacterial activities of the selenium nanoparticle-coated cationic cotton textiles (Se-cotton) were then evaluated against Gram-positive and Gram-negative bacterial strains using a method based on the Absorption Method of ISO 20743:2013 standard. The fabrics were inoculated with 1 - 3 x 10^5 CFU/mL of bacteria in dilute Nutrient Broth. The number of viable bacteria recovered from the samples at 0 h and after 24 h incubation was determined by colony counting.

RESULTS & DISCUSSION

Selenium nanoparticles were successfully synthesised *in situ* on CHPTAC treated cotton surfaces. Antibacterial assessments indicated that cationic cotton had slight antibacterial activities primarily by the electrostatic interaction between quaternary groups and bacterial cells, while Se-cotton prepared with all 3 different concentrations of selenium precursor (0.2 mM, 0.5 mM and 1 mM) had strong antibacterial activity towards both *Staphylococcus aureus* and *Klebsiella pneumoniae* (Figure 1), indicating the excellent antibacterial efficacy of selenium nanoparticles with the presence of the cationic surface charge.

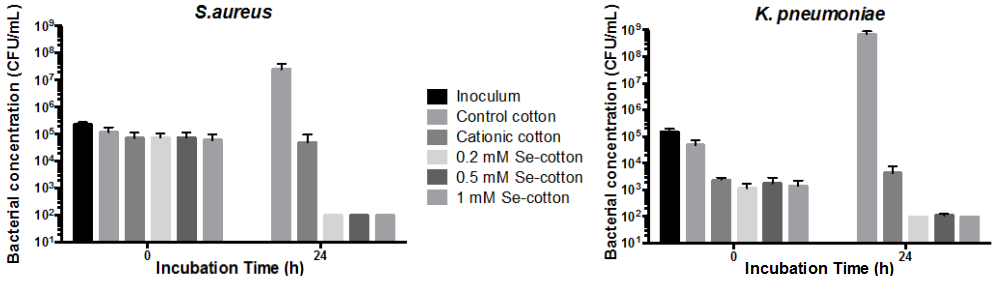

Figure 1 Antibacterial assessment of Se-cotton against *S. aureus* and *K. pneumoniae.* Mean ± SD, n = 3

CONCLUSION

Selenium nanoparticles were successfully prepared *in situ* on the surface of cationic cotton textiles. The cationic Se-cotton demonstrated excellent antibacterial performance towards both *S. aureus* and *K. pneumoniae* and has great potential to serve as an anti-infective material in hospital settings.

ACKNOWLEDGEMENTS

The author would like to thank University of Brighton for funding the PhD studentship.

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Development of a radiopaque liquid embolic for use in therapeutic embolization

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Oral ☒ Poster ☒

INTRODUCTION

Therapeutic embolization involves the deliberate blockage of blood vessels in the treatment of conditions such as arteriovenous malformations, aneurysms, hemorrhaging and hypervascularised tumours.[1] The use of liquid embolics provides an ideal route to embolization in that the liquid precursor can be delivered by the minimally invasive placement of a microcatheter. The resulting solid embolic forms a cast of the vasculature at the delivery site blocking the blood flow past this point. For this purpose, an inherently radiopaque liquid embolic has been developed allowing the delivery of liquid embolic into the vasculature to be monitored by X-ray methods both during and post-procedure.

MATERIALS & METHODS

A radiopaque liquid embolic has been prepared by modification of poly(vinyl alcohol) hydroxyl groups with a triiodinated aromatic ring and formulated into DMSO solutions. Evaluation of the solutions has been performed using a vascular flow model mimicking the conditions of an embolization procedure followed by characterisation of the embolic material by microCT imaging to gauge X-ray visibility.

RESULTS & DISCUSSION

Sample performance has been evaluated using a vascular flow model demonstrating high rates of occlusion and suitable delivery behaviour as an injectable embolic (Figure 1A). The rate of injection alongside the flow conditions within the ‘vasculature’ were found to impact the structure of the solidified material (Figure 1B-C). An optimal radiodensity for X-ray imaging within the body was demonstrated using microCT analysis.

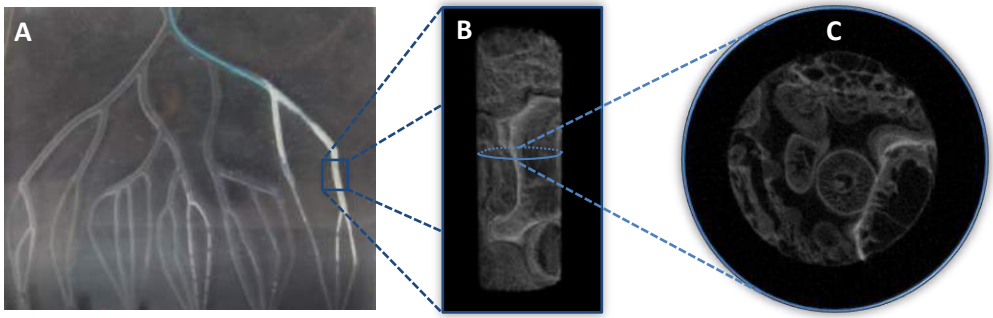

Figure 1 – (**A**) Embolized channel of Vascular Flow Model. (**B**) Reconstructed microCT surface view. (**C**) Reconstructed 2D microCT cross section.

CONCLUSION

Suitable delivery and visibility properties have been demonstrated for the developed radiopaque material. This suggests *in vivo* testing is required for the next stage of evaluating suitability of the radiopaque liquid embolic material for use in therapeutic embolization.

ACKNOWLEDGEMENTS

University of Sheffield, EPSRC and Biocompatibles UK Ltd for funding.

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Title of paper: Development and Characterization of Nano-Hydroxyapatite by Freeze-Drying Method.

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Oral ☒Poster ☐

INTRODUCTION

Problem associated with nano-particles is that these are more reactive and convert to bulk particles more readily. The objective of current study is to prove that freeze drying method can be a good technique to improve the shelf life of NANO-particles [1].

MATERIALS & METHODS

Freeze drying method can be a good technique to improve the shelf life of NANO-particles. In this study nano-hydroxyapatite powder was successfully prepared through sol gel assisted with freeze drying method. This method resulted in a Nano-hydroxyapatite with increased shelf life and controlled particle size. Calcium Nitrate tetra hydrate and phosphoric acid with few drops of ammonia are the precursors for synthesis of hydroxyapatite. Through FTIR the molecular composition of the prepared NANO-HAP powder was studied. The crystalline phase, determined by XRD. Microstructure, chemical composition, morphology, opted by SEM/EDS indicate that due to high vacuum [1].

RESULTS & DISCUSSION

Among many practicable routes to synthesis NANO-HAP, the sol gel method with combination of freeze drying technique provides us a better particle size and impurity control. Freeze-drying has been considered as a good technique to improve the long-term stability of colloidal nanoparticles. XRD shows that the particle or crystallite size is of 4-6nm. Microstructure.

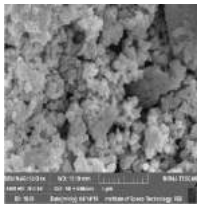

Figure 1: SEM images of nano-HAP

CONCLUSION

It has been concluded that freeze-drying can be used for nanoparticle production with greater stability and low particle size. Hence, coating titanium with nano-HAP makes the coating properties better.

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Engineering Organic Piezoelectricity using Computational Chemistry

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INTRODUCTION

The building blocks of life in the universe are the 20 amino acid molecules. Amino acids generally crystallise in non-centrosymmetric space groups, endowing them with piezoelectric properties; piezoelectricity being a linear relationship between induced electrical charge and applied stress. Here we quantitatively predict the physical properties of organic crystals using Density Functional Theory (DFT) calculations. By predicting the elastic, piezoelectric and dielectric constants of organic materials we can rationally design experiments to maximize piezoelectric voltage generation.

MATERIALS & METHODS

Elastic, dielectric and piezoelectric properties are predicted using density functional perturbation theory (DFPT). Amino acid crystals are grown from aqueous and alcohol-based solutions. They are characterised using XRD and Raman spectroscopy. Piezoelectric constants are verified by measuring the resonance frequency of the crystals.

RESULTS & DISCUSSION

Our calculations predict that the majority of amino acid crystals have predicted piezoelectric constants higher than commonly used piezoelectrics such as aluminium nitrate (6 pC/N), zinc oxide (9 pC/N), and quartz (2 pC/N).

Glycine is the smallest amino acid, and crystallises in three different shapes (polymorphs). One of these polymorphs, β-glycine, has an extremely high piezoelectric constant of 178 pC/N. This value was predicted by our DFT calculations and verified experimentally.

We can grow these amino acids on non-conductive, metallic or flexible polymer substrates, with energy harvesting, and medical device applications. By simply compressing glycine crystals between electrodes we can generate electricity of up to 450 mV (Figure 1). Organic crystals have low dielectric constants (2-3); this allows them to generate higher voltages per units force and area than inorganic materials.

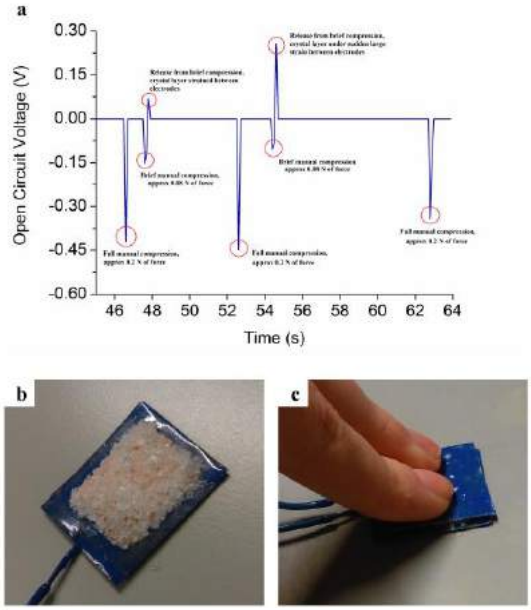

FIGURE 1: Generating voltage from amino acid crystals

CONCLUSION

Until now, very few biological materials had demonstrated technologically significant piezoelectric behaviour, which would be of interest for energy harvesting applications

DFT predictions allow us to screen the large amount of organic crystals available, and focus experiments on the most exciting candidates. Computer simulations can also help us to amplify or engineer piezoelectric responses in crystals.

The high piezoelectricity predicted in glycine polymorphs, among others, paves the way for organic crystal motion sensing and energy harvesting. Organic crystals have optimal properties for non-toxic wearable and implantable devices.

ACKNOWLEDGEMENTS

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Light controlled release of antimicrobial peptides for the treatment of pathogenic bacteria

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Oral ☒ Poster ☒

INTRODUCTION

Recently, the development of stimuli-responsive drug delivery vehicles has emerged as a promising strategy to improve the efficiency of antimicrobial agent administration and reduce the likelihood of inducing bacterial antibiotic-resistance. Plasmonically active nanoparticles offer a facile means of triggering such delivery through the application of an external laser stimulus, providing spatial and temporal control of delivery and minimizing the dosage required for treatment.[1] Novel therapeutics have also been developed as antibiotic alternatives that can reduce drug-resistance development. For instance, certain antimicrobial peptides can exhibit bactericidal effects through the ability to physically lyse and disrupt the bacteria membrane and cell wall inducing cytoplasmic leakage. Here, we present a novel application of liposomes for the delivery of antimicrobial peptides in response to photothermal heating using gold nanorods. This system combines novel therapeutics with efficient delivery to provide a means of infection treatment with greatly reduced risks of resistance development.

MATERIALS & METHODS

The liposomes (DSPC/cholesterol/DSPE-PEG2000) were fabricated using the thin lipid film rehydration method technique and designed to ensure long-term stability, whilst providing high encapsulation efficiencies of the antimicrobial peptide IK8. Vesicle leakage was assessed through the encapsulation of the self-quenching dye calcein and the fluorescent response monitored in the presence of *Staphylococcus aureus*, human dermal fibroblasts and keratinocytes. The antibacterial efficacy of the delivery system was ascertained after the incubating the vesicles with a bacteria suspension for an hour before NIR laser irradiation, absorption spectroscopy and colony counting techniques were used to determine the *S. aureus* viability.

RESULTS & DISCUSSION

The liposomes provide encapsulation of IK8 at 24 times the minimum inhibitory concentration (MIC) of IK8 upon *S. aureus*, and remain stable over the course of several weeks. Investigations into the liposome composition ascertained that DSPC liposomes containing cholesterol (22 mol%), or higher exhibit leakage only in the presence of bacteria. At such high cholesterol content the liposomes have a diminished thermal release profile, however incubation of the vesicles with *S. aureus* for an hour before heating increases the peptide release. As such, laser irradiation one hour after the addition of IK8-loaded vesicles and nanorods to a *S. aureus* suspension initiated bactericidal effects at the IK8 MIC (31 ug/mL), see Figure 1, whereas the same system without irradiation showed no antimicrobial effects. This indicates that the bacteria induced IK8 leakage alone is not adequate to induce bactericidal activity and therefore requires photothermal heating to enhance the vesicle's release profile.

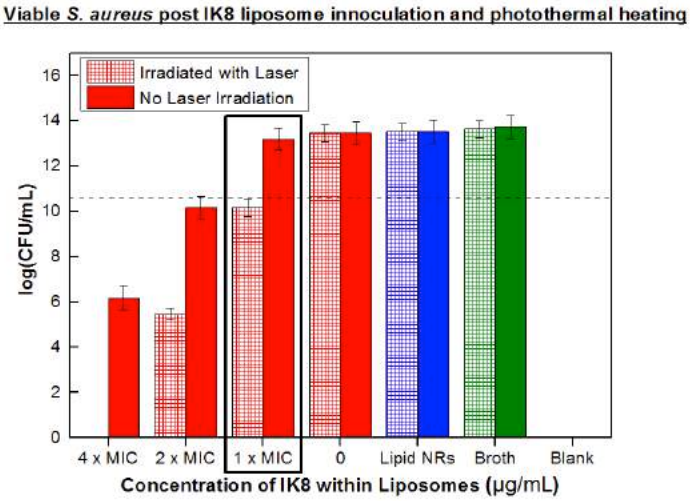

Figure 1: The synergistic photothermal and bacteria induced IK8 release exhibits bactericidal effects at the MIC upon *S. aureus,* as observed through a >10^3 reduction in the number of viable CFUs. A 10^3 reduction in bacteria viability is displayed as the dashed line.

CONCLUSION

We have demonstrated the liposomal encapsulation of antimicrobial peptides at bactericidal concentrations and shown that the resulting vesicles remain stable over the course of several weeks. Utilising gold nanorods for photothermal heating, liposomes containing the MIC of peptide exhibited sufficient release to induce bactericidal effects against *S. aureus*. As such, this study offers an efficient means of stimuli-responsive delivery of antimicrobials that will be taken forward for the development of therapeutic wound dressings, to combat the ever-growing issue of antibiotic resistance.

ACKNOWLEDGEMENTS

We acknowledge the University of Leeds and EPSRC for the funding of the PhD studentship.

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Role of nanotopography and bioactive coated 2D/ 3D titanium lattices on mesenchymal stem cells and *Pseudomonas aeruginosa* behaviour

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Oral ☒ Poster ☒

INTRODUCTION

Titanium is a well-regarded material for the orthopaedic and dental implants. However, an optimal implant should be bioactive towards bone formation and also be bactericidal. Nevertheless, these characteristics are hard to balance without detriment to each other. The physiochemical characteristics such as surface wettability, oxide thickness, surface roughness and nanostructure have a strong influence on the osseointegration and biofilm formation [1].

MATERIALS & METHODS

Alkaline hydrothermal treatment was applied to produce an antimicrobial high-aspect ratio nanotopgrphy on the Ti scaffolds (height of nanowires was Rt~ 400 and~ 550 nm for 1h and 2h TiO_2 respectively). Here, we developed a simple polymer system to help deliver osteogenesis on the antimicrobial features. Polyethylacrylate (PEA) can be applied, via plasma polymerization, as a very thin coating to 2D/3D structures and it causes spontaneous unravelling of fibronectin (FN) upon contact. In the open conformation, FN can be decorated with ultra-low doses of growth factors, such as BMP2 [2]. MSC bone mineralisation was examined using Raman spectroscopy, calcein blue, alizarin red, and giemsa staining. *P. aeruginosa* were cultured on the substrates and the number of viable microbial cells was determined by quantitation of the ATP present. Selective laser melting (SLM) technique used to fabricate a micro-lattice structure (dimeter 300- 600- 900 µm) that could present the topography in 3D.

RESULTS & DISCUSSION

Ti surfaces with PEA/FN/BMP2 coating showed an improvement on cell growth, adhesion and bone mineralisation compering with uncoated substrates. Moreover, Ti nanowires surfaces showed a decrease of *P. aeruginosa* adherence based on the ATP present. The 3D Ti lattice with 900 µm has a better MSCs adhesion and growth, while the 3D/2h TiO_2 showed a potential bactericidal effect on *P. aeruginosa.*

CONCLUSION

An ideal bone implant should enhance the osteogenesis and reduce bacterial adhesion. However, further investigation is required to show the impact of the current coating on the 3D Ti lattices.

ACKNOWLEDGEMENTS

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Dual-action Antimicrobial Surfaces

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INTRODUCTION

As medicine and technology develops so does life expectancy and the prevalence of age-related diseases. Due to this, implantable medical devices, such as: pacemakers, catheters and orthopaedic prostheses have become paramount in modern healthcare and are necessary for prolonging and improving the life of critically ill patients. The increased use of such devices is not without significant problems; one being their susceptibility to bacterial adhesion and subsequent biofilm formation. In this work dual-action micropatterned PDMS surfaces that release nitric oxide (NO) have been fabricated with the aim of controlling bacterial response with both physical and chemical surface modifications, for the potential use in medical implant applications.

MATERIALS & METHODS

PDMS replicas were moulded over micropatterned silicon wafers to give PDMS with defined microtopographical features (rectangles, rectangles, inverted rectangles). Aminosilanisation of these surfaces was then carried out using N-(3-trimethoxysilylpropyl)diethylenetriamine (DET3). The amine groups in DET3 facilitated the formation of the NO donor groups, *N*-diazeniumdiolates, when in the presence of high pressures of NO.

RESULTS & DISCUSSION

XPS confirmed the presence of the *N*-diazeniumdiolate groups and AFM analysis showed the well-defined microtopographical features on the PDMS surface. NO release was monitored by chemiluminescence detection and surfaces released up to 981 µmol over 20 hrs at pH 7.4. Planktonic and adhered cell colony forming unit (CFU) assays were carried out against a lab strain of *Pseudomonas aeruginosa* (PA14), to assess the bactericidal and anti-adhesion abilities of the surfaces, respectively. In the presence of non-structured NO-releasing PDMS a bactericidal effect resulted in the complete eradication of bacteria by 4 hrs, due to large NO payloads. Structured NO-releasing PDMS was bactericidal due to NO (62 % reduction) and anti-adhesive due to microtopography (52 % reduction). The results are in agreement with findings reported by Lu *et al*,[1] that microtopography controls bacterial response, through alterations in the cell-surface contact area; when the diameter of surface features are smaller than the diameter of the bacterial cell, cell-surface contact area is minimised and a reduction in adhesion is observed.

CONCLUSION

Novel dual-action surfaces have been engineered to control bacterial response through multiple mechanisms. Micropatterned PDMS surfaces that release bactericidal concentrations of NO over 20 hrs were successfully fabricated. At 24 hrs, dual-action PDMS surfaces were bactericidal due to NO release and anti-adhesive due to their distinct microtopography.

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Photodynamically Active Electrospun Scaffolds for Antibiotic-Free Infection Control

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INTRODUCTION

Antimicrobial biomaterials are critical to aid in the regeneration of oral soft tissue and to prevent or treat localised bacterial infections[1]. At the same time, the growing trend in antibiotic resistance raises issues regarding the long-term antimicrobial functionality and safety of current commercial dressing products. Therefore, there is a pressing clinical need for new antibiotic-free biomaterials enabling on-demand activation of antimicrobial functionality following an infection that are environment-friendly, flexible and commercially-viable[2]. This study explores the feasibility of integrating a bioresorbable electrospun polymer scaffold with localised antimicrobial photodynamic therapy (aPDT) capability. To enable aPDT, we aimed to encapsulate a photosensitiser (PS) in polyester fibres in the PS inert state, so that the antibacterial function would be activated on-demand via a visible light source[3].

MATERIALS & METHODS

Fibrous scaffolds were successfully electrospun from either poly(ε-caprolactone (PCL) or poly(rac-lactide-co-glycolide) (PLGA) solutions containing either methylene blue (MB) or erythrosin B (ER). Electrospun scaffolds were characterised with regards to their PS loading efficiency (UV-Vis spectroscopy), microarchitecture (SEM, porometry and BET analysis), tensile properties, hydrolytic behaviour (contact angle, dye release capability, degradability) and aPDT effect.

RESULTS & DISCUSSION

The electrospun scaffolds achieved ~100% loading efficiency of PS and exhibited significantly increased tensile modulus and reduced average fibre diameter and pore size with respect to PS-free controls. *In vitro*, complete PS release was observed within 100 hours with PCL scaffolds, whilst PLGA scaffolds displayed significant macroscopic shrinkage and fibre merging following incubation in phosphate buffered saline (PBS) solution. Exposure of PS-encapsulated PCL fibres to visible light successfully led to at least 1 log reduction in *E. coli* viability after 60 minutes of light exposure whereas PS-free electrospun controls did not inactive microbes.

CONCLUSION

This study successfully demonstrates the significant potential of PS-encapsulated electrospun fibres as photodynamically active biomaterial for antibiotic-free infection control.

ACKNOWLEDGEMENTS

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Ultra-short self-assembling amphiphilic peptides: a versatile platform for soft biomaterials fabrication

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INTRODUCTION

Molecular self-assembly has been exploited in Nature to develop the complex higher macromolecular structures of both the genome and proteome. Inspired by nature, we have recently developed ultra-short amphiphilic peptides that self-assemble into bioinspired β-sheet nanofibers.[1] The amphiphilic nanofibers system is a versatile platform that we exploited for the fabrication of various bio-inspired soft materials, such as hydrogels in aqueous medium, emulgels in biphasic media and nanofibrillised microspheres (Fig. 1). The developed materials have a great potential for various pharmaceutical and biomedical applications due to their inherited biocompatibility, biodegradability and physicochemical tunability. In this presentation, we will report on the design of amphiphilic peptide nanofibers, and using those fibers for the formulation of hydrogels, emulgels and nanofibrillised microspheres (loaded with 5-fluorouracil (5-FU) and camptothecin (CPT)). The effectiveness of amphiphilic nanofibers at stabilizing oil-in-water (O/W) emulsions in comparison to traditional surfactants will be presented.

MATERIALS & METHODS

FTIR was used for the molecular characterisation of self-assembly. Oscillatory rheology was used for the characterisation of the viscoelasticity of the fabricated materials. AFM, SEM, TEM and SAXS were used for the characterisation of nanofibrillar systems topology, morphology and structure.

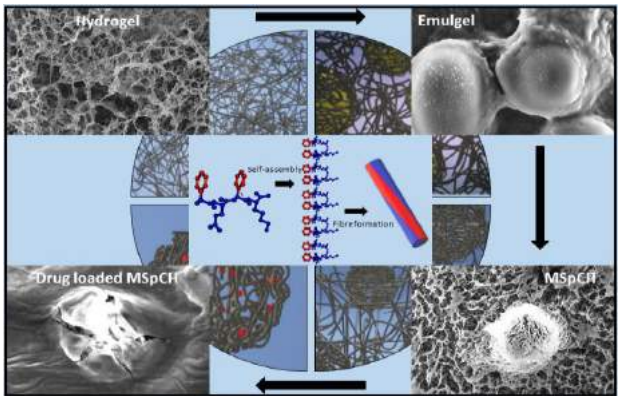

Figure 1: An illustration of the self-assembly of the amphiphilic ultra-short peptide and the versatile systems fabricated from the nanofibers

RESULTS & DISCUSSION

FTIR showed that ultra-short peptides self-assemble to form anti-parallel β-sheet structure in response to pH change of the aqueous solution. The β-sheet structure formed nanofibers as shown from AFM micrographs, which exhibit diameter size of ~9nm from SAXS Guinier analysis. The formed nanofibers entangled into networks as observed from SEM and TEM micrographs, forming hydrogels in aqueous medium with critical gelation concentration of 3-4% W/V. In biphasic media, the amphiphilic nanofibers formed stable O/W emulsions (Melissa oil phase: anti-infective Melissa oil) compared to commercial emulsifiers such as poloxomer, cetrimide, SDS and Tween 80 at same molar concentrations under various environmental conditions. AFM, TEM and SEM micrographs showed the formation of nanofibrillised microspheres at the O/W interface confirming that the emulsion stabilisation was mediated by the amphiphilic nanofibers (Fig. 1). Oscillatory rheology data showed the viscoelasticity and injectability of the formulated emulgels. The nanofibrillised microspheres were formulated from emulgels by vacuum evaporation and were loaded with 5-FU and CPT. Both drugs showed sustained release profiles compared to hydrogels, following Korsmeyer-Peppas release model.

CONCLUSION

Ultra-short amphiphilic peptides were designed to self-assemble into bioinspired β-sheet nanofibers that formed the bases for the fabrication of various soft materials with great potential for biomedical (and pharmaceutical applications.

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Insights into the structure of self-assembly histidine peptide with Glucose Oxidase Enzyme

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Oral ☒ Poster ☐

INTRODUCTION

The Self-assembling peptide-based hydrogels have gained great interest in biomedical applications, such as cell culture[1], drug delivery systems[2], and biosensors[3] as this type of materials are fully defined and biocompatible. The formation of self-assembling peptide hydrogels consist of two processes: firstly, the peptide self-assembly to form a fibrillary structure; then the fibres entangle and associate with each other to form a network[4]. In this study, two type of self-assembly histidine peptide were investigated in the relationship between net-charge, fibre formation, and mechanical properties. Since they are sensitive to pH and with abundance positive charge, they have potential application on biosensors. Thus the properties of peptide mixing with Glucose Oxidase Enzyme (GOD) were also explored in this study.

MATERIALS & METHODS

The peptides which sequences are FKFHFRFH (FKHR8) and FKFHFKFHK (FKH9) used in this study were purchased as TFA salts from BIOMATIK Corporation (Delaware, USA) and used without further purification. The purity of the peptides was verified by HPLC and Modi-Tof. The TFA content in peptides was calculated from element test and HPLC results. The dynamic oscillatory shear rheometer was used to analyze the mechanical property. The LCMS was used to explore the degradation of the peptide by GOD and the peptide/GOD complex forming.

RESULTS & DISCUSSION

By the increase of pH in peptide solution, the net-charge on peptide surface will sharply drop. When changing pH from 2 to 7, the histidine peptides will form hydrogels from solution, and the storage modulus will increase significantly. However, if the pH continues to increase and more positive charge congregate on the surface of peptide fibres, the peptide will precipitate from water. When mixing GOD with a high concentration of peptide, they easily congregate to form a complex over 0.2μm. Moreover, in a high concentration of peptide, GOD hardly degrades the peptide molecular into small fragments.

CONCLUSION

The charge on self-assembly histidine peptide will influence significantly on their morphology and mechanical properties. The GOD enzymes can be entrapped in histidine peptide fibres and form a large size complex. Thus these two types of histidine peptides have potential use in drug delivery systems and biosensors.

ACKNOWLEDGEMENTS

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Surface-mediated self assembly of supramolecular structures - Teaching an old dog new tricks

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Oral ☑ Poster ☐

INTRODUCTION

The elegance of biological systems that exploit self-assembly of molecules into larger, functional structures continues to capture our imagination to develop new materials and technologies in biomaterial science, drug delivery and electronics to name but a few. This is notwithstanding the inherent challenges posed to control or direct the self-assembly process due the multitude of parameters (pH, temperature, solvent etc.) influencing the formation of supramolecular materials. Despite its importance, the effect of the surrounding material, i.e. the vessel or environment that the supramolecular material is formed in, is largely neglected. An injectable, supramolecular drug delivery system, for example, may behave considerably differently when formed in a reaction vessel or in biological tissue due to interference of the environment on the self-assembling process. The importance of surfaces in the self-assembly process is increasingly recognised[1, 2] but systematic studies that explore and exploit these phenomena are lacking.

MATERIALS & METHODS

We have used well-defined surfaces to explore how the environment affects the self-assembly of a nucleoside based gelator, identify key surface parameters that enable improved control over interfacial self-assembly.[3, 4] We use this understanding to create peptide based hydrogels that display chemically homogeneous but mechanically heterogeneous properties which can be spatially controlled.

RESULTS & DISCUSSION

Surface properties are shown to influence the properties of hydrogels both on a nanoscale (self-assembly structure) and macro-scale (hydrogel stiffness) level. The parameters governing the changes imparted by surfaces to the supramolecular material are shown to be related to descriptors of the hydrophobicity of surface immobilised molecules. These properties were subsequently exploited to generate patterned surfaces and gels with chemically homogeneous and mechanically heterogeneous properties.

CONCLUSION

Surface properties, in particular the hydrophobicity of surface immobilised molecules, influence the nanostructure of supramolecular materials. This translated into a macroscopic change in hydrogel stiffness and can be exploited to spatially control the stiffness of the hydrogel without altering its chemistry.

ACKNOWLEDGEMENTS

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Controlling the enzymatic degradability of self-assembled peptide nanostructures via supramolecular cohesion

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Oral ☒ Poster ☐

INTRODUCTION

Peptide amphiphiles (PAs), a class of self-assembling molecules developed by the Stupp laboratory, have received considerable interest over the past decades to fabricate biomaterials for application in regenerative medicine and cancer therapies [1]. Compared to other biomaterial building blocks, PAs have advantageous properties, such as biocompatibility, biodegradability, as well as design versatility over both the structure and function of their assemblies [2]. Previous studies have unveiled the role of molecular cohesion in PAs on the mechanical and biological properties of their self-assembled nanostructures [3-6]. However, to the best of our knowledge, the effect on their enzymatic degradability has not been investigated. Here, we present a detailed study to gain insights into the enzymatic degradability of self-assembled PA nanostructures with distinct internal order.

MATERIALS & METHODS

A series of PAs were designed to adopt different types of secondary structure. They were synthesized based on the standard Fmoc solid phase peptide synthesis method and purified using reverse-phase HPLC. The critical aggregation concentration of PAs was determined using the fluorescence dye nile red and their secondary structure was analysed by circular dichroism spectroscopy. The presence of β-sheet structures was detected by the thioflavin-T assay. TEM imaging was performed to reveal the morphology of the self-assembled PA nanostructures. The enzymatic degradability of PA assemblies was assessed using enzymes commonly targeted in the design of enzyme-responsive biomaterials, matrix metalloproteinase-1 (MMP-1) and cathepsin-B, and followed by reverse-phase HPLC.

RESULTS & DISCUSSION

Enzymatic degradation efficiency was reduced upon the addition of a palmitoyl tail to the enzyme cleavable peptide sequence, as well upon the PAs self-assembly. Moreover, tuneable enzymatic degradability of the PA nanostructures could be achieved by tweaking the internal order of the assemblies, adjusted through their secondary structure.

CONCLUSION

Our results shown that the enzymatic degradation of self-assembled PA nanostructures could be tuned through molecular design. These findings have implications in the design of enzymatic responsive self-assembled peptide biomaterials for tissue engineering scaffolds and drug delivery applications.

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Peptide-graphene oxide hydrogel nanocomposites for intervertebral disc tissue engineering applications

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Oral ☒ Poster ☒

INTRODUCTION

Intervertebral disc degeneration (IVDD) has been classified as a major contributor of global disability[1]. Current treatments are highly invasive and poorly efficient in the long-term. Cell-based therapies allow a minimally-invasive delivery of cell-seeded biomaterials at the injury site to promote regeneration. Among injectable biomaterials, self-assembling peptide hydrogels (SAPHs) represent potential candidates as 3D cell carriers, due to their tissue biomimicry and ability to support cell viability and differentiation[2,3]. Moreover, the advent of graphene-based materials has made the fabrication of graphene-hydrogel nanocomposites appealing, allowing graphene features to be exploited to direct cell fate[4]. In this study, we incorporated graphene oxide (GO) within a SAPH to develop novel peptide-GO nanocomposites as potential cell carriers for IVD repair.

MATERIALS & METHODS

Peptide-GO hydrogels were prepared by incorporating 0.5 mg/ml GO (mean size <5µm) into a FEFKFEFK (F8) peptide solution (10, 15 and 20 mg/ml). Hydrogel microstructures were assessed *via* atomic force and transmission electron microscopy (AFM, TEM), while rheological behaviour was studied *via* oscillatory rheometry. Nucleus pulposus cells (NPCs) were then encapsulated within the hydrogels for 3D cell culture and cell viability and metabolic activity were assessed over time.

RESULTS & DISCUSSION

GO flakes were homogenously dispersed in F8 hydrogels, revealing different levels of interactions with the peptide-based network. Incorporation of GO within F8 enhanced the mechanical properties of peptide hydrogels, achieving average storage moduli (G'~12.8 kPa) comparable with human NP tissue (G'~10 kPa). Moreover, hybrid hydrogels showed shear-thinning properties and injectability, making them suitable for minimally invasive applications. GO-containing F8 hydrogels resulted biocompatible for NPCs, preserving their characteristic rounded morphology, high cell viability and metabolic activity over time.

CONCLUSION

Results showed that GO can be added to SAPHs to create injectable and mechanically-reinforced scaffolds which are biocompatible for 3D culture of NP cells and appealing as cell carriers for IVD repair therapies.

ACKNOWLEDGEMENTS

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Synergistic integrin-growth factor microenvironments to bioengineer the bone marrow niche *in vitro*

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Oral ☒ Poster ☐

INTRODUCTION

Stem cells lose their regenerative capacity when they are removed from their regulatory microenvironment, termed the stem cell niche. Pericytes are key bone marrow niche cells, they have immune modulatory and inflammatory functions, and act to support hematopoietic stem cells (HSCs). In order to maintain both pericytes and HSCs in culture, aspects of the niche microenvironment should be recapitulated *in vitro*, we aim to create a system supporting a niche-like pericyte phenotype. Noting that soft gels can support nestin[1] expression, a key niche marker, we have shown stiffness related support of nestin and other markers important in the niche. Here, poly(ethyl acrylate) (PEA) was used to assemble fibronectin (FN) into physiological-like networks, thus allowing growth factor tethering and presentation in synergy with integrin binding sites[2]. Then, a soft gel or hypoxia was used, to investigate the metabolic mechanisms required to support niche phenotypes in this bone marrow-like microenvironment. We used poly(methyl acrylate) (PMA) as a control where FN is not assembled into networks[2].

MATERIALS & METHODS

PEA was polymerised then spin coated on 12 mm glass coverslips[2]. FN from human plasma was adsorbed (20 µg/mL) followed by BMP-2 (50 ng/mL). Pericytes were isolated from human adipose tissue. Then a collagen gel (2 mg/mL stiffness to match bone marrow) or 1% hypoxia was added at 72h. Metabolites extracted 7 & 14 days after seeding, relative abundance measured using liquid chromatography-mass spectrometry (LC-MS). RNA-Seq whole transcriptome profiling after 7 days. (N= 3; 4). Immunofluorescence was used to asses lactate dehydrogenase (LDH) levels (n=3, $p < 0.05$), levels of phenotypic markers and transcription factor hypoxia-inducible factor 1 (HIF1α) levels and activity (Hypoxyprobe™).

RESULTS & DISCUSSION

Immunocytochemistry revealed a sustained increase in activated HIF1α with soft gels up to 7 days, whereas similar levels of HIF1α activation were observed in the absence of gel and in 1% hypoxia, where activation levelled out after ~12h. Correspondingly, levels of glycolytic enzyme LDH showed a trend towards increased levels with gel addition, suggesting a switch to an anaerobic metabolic profile. Metabolomic analysis revealed strong agreement in down-regulation of metabolites involved in oxidative phosphorylation with the soft gel and hypoxic system. Genome-wide transcriptomic analysis identified key genes similarly expressed, such as glycolytic enzymes, and identified genes differentially expressed, such as increased expression of nestin and HIF1α after 7 days with soft gels but not hypoxia. However, downstream analysis of HIF1α-driven VEGF production did not increase with gel addition, suggesting differing mechanisms of action.

CONCLUSION

Using this material-based system, we have found that soft gel addition drives a 'hypoxic-like' mechanistic response, that could be a key facet in maintaining and supporting niche-like phenotypes *in vitro.* This can have large implication for production of pericytes *in vitro* that can be used to support, for example, tissue engineered construct implantation via enhanced anti-inflammatory & immune modulatory properties.

ACKNOWLEDGEMENTS

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Hydroxamic acid-conjugated collagen systems for matrix metalloproteinase modulation in chronic wounds

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Oral ☒ Poster ☐

INTRODUCTION

Medical devices with matrix metalloproteinase (MMP)-modulating functionality are highly desirable to restore tissue homeostasis in non-self-healing chronic wounds. The introduction of MMP-modulating functionality in such devices is typically achieved *via* loading of either rapidly diffusing chelating factors, *e.g.* EDTA, or MMP-cleavable substrates, raising issues in terms of non-controllable release profiles and enzymatic degradability. Here, we investigated the synthesis of a hydroxamic acid (HA)–methacrylated collagen conjugate as the building block of a soluble factor-free hydrogel network with inherent MMP-modulating capability [1].

MATERIALS & METHODS

Type I collagen was reacted with methacrylic anhydride to generate photoactive methacrylamide groups. The resulting collagen product was activated with a water-soluble carbodiimide prior to the reaction with hydroxylamine, resulting in grafted MMP-chelating HA functions. A 2,4,6-trinitrobenzenesulfonic acid (TNBS) assay was employed to measure the degree of collagen methacrylation; whilst the molar content of grafted HA groups was indirectly quantified via derivatisation of carboxyl in to amino groups. HA-conjugated methacrylated collagen product was activated with UV light (365 nm, 8 $mW \cdot cm^{-2}$) to create a covalently-crosslinked network. The MMP-modulating capability of UV-cured hydrogels was measured via hydrogel incubation in MMPs, e.g. MMP-9, followed by supernatant fluorometric assay and gravimetric analysis. Hydrogels swelling ratio, gel content (*G*), compressability and G292 cellular tolerability were also characterised

RESULTS & DISCUSSION

Nearly-quantitative methacrylation of collagen was achieved, so that unwanted intramolecular crosslinking reactions during the conjugation reaction with hydroxylamine could be avoided. Derivatisation of collagen carboxyl functions into amino groups could be realised via reaction with ethylenediamine (as proven by both TNBS and ninhydrin assays, so that 12–16 mol.% HA was measured. UV-cured networks with HA pendant groups were successfully formed (G> 85 wt.%). Up to ~30 RFU% MMP activity reduction was measured following 4-day hydrogel incubation in vitro, despite an averaged hydrogel mass loss of up to 20 wt%. Dichroic and electrophoretic patterns of native type I collagen were still observed following conjugation with HA, whilst no toxic response was observed with G292 cells. Interestingly, a lower compression modulus and gel content were measured in HA-bearing compared to HA-free hydrogels, likely related to HA radical scavenging activity.

CONCLUSION

This collagen conjugation strategy may provide a novel strategy to support wound healing in chronic wounds, minimizing potential side effects associated with the systemic administration of MMP chelating agents.

ACKNOWLEDGEMENTS

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Manipulation of Collagen Type I using Topographical and Chemical Cues for Corneal Wound Repair

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Oral ☒ Poster ☐

INTRODUCTION

Ocular trauma and ulceration are responsible for up to 2 million cases of blindness every year, with half a million of these resulting from corneal trauma[1]. Currently, the only treatment for corneal blindness is keratoplasty. This relies heavily on highly skilled surgeons, good surgical facilities and reliable eye-bank services, something not readily available within the developing world[1,2]. The predominant role of the extracellular matrix (ECM) in the eye is to focus light towards the retina, therefore, it needs to be both transparent and curved. These qualities are achieved by the highly organised, hierarchical structure of the ECM, characteristics which are often disrupted during wound healing and results in corneal blindness[3]. In this work, we have investigated the role of topographical and chemical cues to guide the organisation of the collagen matrix. The intention is to incorporate these cues into a dressing material to facilitate the deposition of an aligned matrix, restoring the native structure and function of the cornea.

MATERIALS & METHODS

Silicon surfaces with patterned nanostructures were created to influence collagen formation. Scanning electron microscopy was used to determine the level of alignment of collagen type I which was deposited onto the surface at a range of concentrations. Chemical alteration of the surface allowed for further optimisation of the patterned surfaces for collagen organisation.

RESULTS & DISCUSSION

Each surface provided a different level of alignment in the perpendicular direction, referred to as 80-110º from the ridge edge. Surfaces with a ridge to gap (RTG) ratio of 1.4 (depth of 500 nm) and an RTG ratio of 1.5 (depth of 1000 nm) provided the highest percentage of collagen fibrils aligned within the perpendicular direction. Collagen of different concentrations was deposited onto the two optimal surfaces to determine concentration effects. The surface with an RTG ratio of 1.4 was inconsistent between concentrations, determining that the nano-parameters were not optimal. The surface with an RTG ratio of 1.5, however, had a more consistent level of alignment between collagen concentrations. To determine the effect of surface chemistry, collagen organisation on PDMS, plasma treated PDMS, gold sputtercoated PDMS and APTES treated PDMS were investigated. It was found that gold sputtercoated PDMS provided a higher level of collagen organisation than other surfaces.

CONCLUSION

Collagen is subject to organizational influences from nano-topographical cues alongside changes to surface chemistry. By utilizing this external influence, we can create a highly aligned collagen matrix to aid corneal wound repair and reduce corneal blindness.

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Osteoblast behaviour on whey protein isolate hydrogels as scaffolds for bone regeneration

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Oral ☒ Poster ☐

INTRODUCTION

In this study, hydrogels were formed from whey protein isolate (WPI), a by-product from the production of cheese and Greek yoghurt. These products are being consumed in increasing quantitites, and hence there is a drive to find new applications for the by-products. WPI consists mainly of β-lactoglobulin (bLG) and WPI in solution has enhanced cell proliferation and osteogenic differentiation [1] in previous work. Hence, it was hypothesized that WPI hydrogels would support adhesion, growth and differentiation of osteoblast cells. A further advantage of using WPI is its relatively low cost.

MATERIALS & METHODS

WPI (Bipro) was obtained from Davisco Inc. WPI hydrogels of different concentrations (20, 30, 40, 50%, all w/v) were produced by heating WPI solution to 80ºC and subsequently sterilized by autoclaving. Hydrogel formation was characterized by rheometry and FTIR analysis. Subsequently, the adhesion, spreading, proliferation and osteogenic differentiation of human MG-63 osteoblasts [2] were compared.

RESULTS & DISCUSSION

The temperature at which gelation occurred decreased with increasing WPI concentration. Increasing WPI concentration from 20% to 50% increased compressive modulus from 0.2 to 4 MPa. All WPI hydrogels supported the adhesion and growth of MG-63 osteoblasts. Actin skeleton organization was superior on 40% and 50% hydrogels. Cell spreading and proliferation were highest on 40% hydrogels. Differentiation was highest on 50% hydrogels.

CONCLUSION

WPI hydrogels show potential as biomaterials for bone tissue engineering. Further work will focus on in vivo studies.

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The Visco-Elasticity of 2D Protein Networks – Implication for Stem Cell Expansion

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Oral ☒ Poster ☐

INTRODUCTION

The mechanical behaviour of the extracellular matrix has an important impact on cell phenotype. Despite the importance of mechanotransduction in regulating a wide range of phenotypes, we recently reported the surprising observation that cells (keratinocytes and mesenchymal stem cells) can adhere, spread and proliferate at the surface of liquids[1-3]. This observation is particularly surprising as the reinforcement of cell adhesion is thought to require a solid elastic or viscoelastic substrate that can resist cell-mediated contractile forces. Our work has evidenced the formation of protein nanosheets, self-assembled at the liquid-liquid interface, displaying strong mechanical properties that can provide a sufficient mechanical scaffold to promote cell adhesion and expansion. We showed that this is sufficient to regulate stem cell phenotype. However, the parameters controlling the self-assembly and the mechanical properties of protein nanosheets remain poorly understood. In this work we investigate the assembly of polymers and proteins at liquid-liquid interfaces, and the impact of pro-surfactants with a wide range of chemistries. We identify structural features that control the visco-elastic properties of the resulting nanosheets and regulate associated cell phenotype.

MATERIALS & METHODS

Assembly at liquid-liquid interfaces is studied using interfacial rheology. Protein nanosheets are characterised by scanning electron microscopy, atomic force microscopy and X-ray photoelectron spectroscopy. Cell adhesion and phenotype was characterised by fluorescence microscopy and qPCR.

RESULTS & DISCUSSION

In this work, we show the importance of parameters such as pH and concentration on protein self-assembly and the impact it has on interfacial mechanics. Importantly, we demonstrate the impact that pro-surfactant-protein interactions play on regulating the assembly and the interfacial mechanical properties of the corresponding interfaces. In addition, we show how these parameters regulate interfacial viscoelasticity over a wide range, and ultimately regulate cell adhesion and proliferation. Finally, we demonstrate the proof-of-concept of using such liquid substrates, in the form of emulsions, for stem cell culture in 3D bioreactors, and their simple recovery by centrifugation.

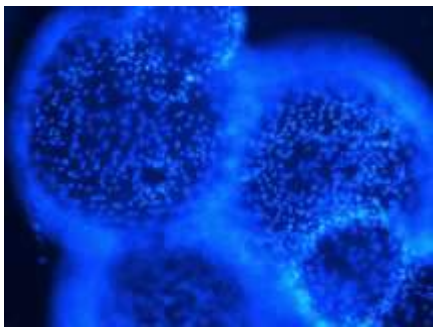

Figure 1: Mesenchymal stem cells culture on an emulsion.

CONCLUSION

Overall, our results suggest that nanoscale mechanical properties of biomaterials may dominate over bulk physical properties. This concept has important implications for the design of biomaterials in the field of regenerative medicine and allow the rational design of liquid substrates for tissue engineering.

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Controlling immune cell activation with bionanomaterials

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Oral ☒ Poster ☐

INTRODUCTION

The next generation of cancer therapies will be dominated by immunotherapies that control the body's own immune response, directing it against the disease. This has focused attention on the key biological processes by which immune cells such as T cell and Natural Killer (NK) are activated: a key step in many proposed immunotherapies. Advanced studies in microscopy have shown that the key signalling structures in T cell and NK cell activation are not individual cell surface receptors, but rather supramolecular receptor clusters on the c. 10 - 200 nm lengthscale. This poses questions as to how nanostructural effects contribute to cell signalling, and whether they can be manipulated to control leukocyte activation. In particular it raises the prospect of developing immunomodulatory bionanomaterials controlled stimulation of immune cells in a clinical context.

RESULTS & DISCUSSION

In a key study, my lab has shown that T cell and NK cell activation can be controlled by varying the spacing between receptor-binding points on a biomaterial surface[1]. This was achieved by creating precisely-spaced nanoscale arrays of antigen molecules, templated by arrays of gold nanoparticles. Surprisingly, activation was supressed when the spacing is greater than c. 70 nm for T cells or c. 100 nm for NK cells, despite the fact that these arrays were still presenting a large number of antigen molecules to the cell. This is a key result, indicating that nanoscale structure can override simple biochemical effects in controlling cell signalling.

Taking the insight of nanostructural control in a more therapy-oriented direction, recently, we used nanoscale graphene oxide (NGO) flakes as templates to create soluble molecular nanoclusters that mimic natural supramolecular assemblies which activate NK cells[2]. We applied this approach to create for the first time a soluble reagent that nano-clusters activating receptors on NK cells (CD16) and demonstrated that molecular (mAb) nanoclusters activated NK cells more potently than unclustered mAb. This demonstrates the potential for future immunomodulatory nanomedicines to outperform simple biologics.

CONCLUSION

We have shown that bionanomaterials can be used as viable tools to direct immune cell activation.

ACKNOWLEDGEMENTS

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Strontium and Fluoride Co-doped Calcium Phosphate Nanoparticles for Treatment of Dental Enamel Lesions

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Oral ☒ Poster ☐

INTRODUCTION

Dental lesions may develop as a result of dental enamel dissolution. Bacterial infiltration through the lesions leads to formation of caries within the underlying enamel structure of the tooth[1]. Lesions that affect only surface enamel could potentially be reversed with the aid of remineralising agents, such as calcium phosphate nanoparticles (CPNP)[2], fluoride or strontium ions [3]. The aim of this work is to prepare nano-sized strontium and fluoride co-doped CPNPs (Sr/F-CPNPs) for the purpose of enhanced remineralisation of these lesions and test their efficacy on artificially demineralised [4] enamel-mimicking hydroxyapatite discs.

MATERIALS & METHODS

Sr/F-CPNPs were prepared using co-precipitation method. Nanoparticles were imaged using scanning electron and atomic force microscopy (SEM and AFM). Crystallinity, elemental composition and substitution levels of strontium were assessed using Fourier-transform infrared (FTIR), Raman spectroscopy and inductive plasma coupling-mass spectrometry (ICP-MS). Levels of fluoride were determined using fluoride-selective electrode. Nanoparticles were subsequently suspended in solution with aid of 0.1M tri-ammonium citrate and applied to hydroxyapatite discs, which were pre-demineralised using citric acid (0.3% w/v) to test for remineralisation effects. Hydroxyapatite samples were assessed for changes in surface micro-hardness with Knoop hardness test as well as visually using SEM.

RESULTS & DISCUSSION

Prepared Sr/F-CPNPs appeared disc-shaped, with mean diameter of 50 ± 14 nm and height of 15-20 nm. The calcium and strontium to phosphorous ratio of nanoparticles was lower than in crystalline enamel hydroxyapatite, however FTIR spectra showed split phosphate peak at 560-600 cm^{-1} characteristic of crystalline hydroxyapatite, suggesting partial crystallinity. Assessment of Sr/F-CPNP strontium and fluoride levels showed nearly complete Sr substitution at target substitution levels 4-15% and fluoride concentration of 21 ± 0.5 % w/w in the sample. Assessment of Knoop microhardness of hydroxyapatite samples 30 h post-application demonstrated a statistically significant increase of 12.3 ± 3.8 % in hydroxyapatite surface micro-hardness post-treatment.

CONCLUSION

Sr/F-CPNPs were prepared using co-precipitation method and characterized. These nanoparticles were shown to be effective in promoting remineralization of enamel-mimicking hydroxyapatite discs and could potentially be used as treatment for early dental erosion.

ACKNOWLEDGEMENTS

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NANO OPTICAL OXYGEN SENSOR (NOSE) FOR CELL PHYSIOLOGICAL CONDITION MONITORING

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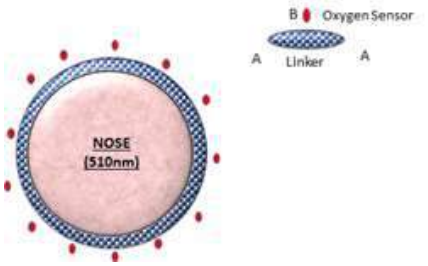
Oral ☒ Poster ☐

INTRODUCTION

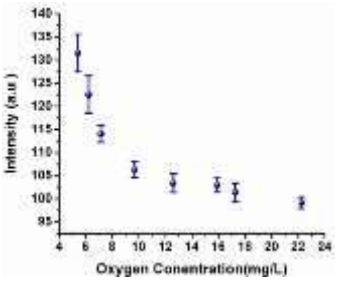
Oxygen levels have been identified as an important parameter in stem cell cultivation and differentiation [1]. Therefore real time monitoring of Oxygen, in defined spatial locations within a tissue/cell construct can provide abundant and valuable information directly relating to the optimal conditions required to control cell function and performance within a 3D construct in vitro.

MATERIALS & METHODS

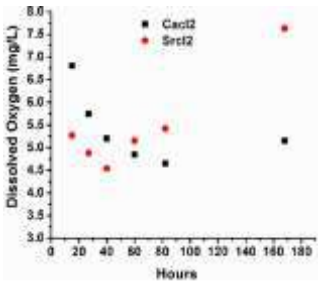
Nano Optical Oxygen Sensor (NOSE) sensors were fabricated using Polystyrene Nano beads (PSB) with surface modified by carboxyl groups (Thermo SCI-ENTIFIC, W050CA). Pluronic F127 (a triblock copolymer), poly (propylene oxide) (a central hydrophobic polymer), and poly (ethylene glycol) (PEG, a hydrophilic ends) were employed (Sigma) and attached onto the surface of PSB by an esterification process. Oxygen-sensitive red fluorescent molecule Ru (dpp) 3Cl2, (C72H48Cl2N6Ru) (Fluka, excitation at 470-490 nm and emission at 613 nm), was attached to the structure of a hydrophobic polymer Pluronic F-127 [2] in ethanol to form functional NOSE sensors; a schematic is as shown in **figure 1**.



[Figure 1: Schematic of NOSE sensor]



[Figure 2: Calibrated Curve]



[Figure 3 Oxygen gradient in Rin-m5F cell]

RESULTS & DISCUSSION

The in-house synthesized NOSE sensor was calibrated inside electro sprayed alginate-filled hydrogels and demonstrated a good broad dynamic range (2.73–22.23) mg/L as well as a resolution of −0.01 mg/L with an accuracy of ±4% as shown in **figure 2**. For continuous monitoring of the oxygen distribution inside RIN-m5F filled alginate hydrogel spheres, NOSE sensors were pre-mixed inside the gel and the spheres were incubated at 1atm pressure and at 37°C for seven days and measured oxygen levels are as shown in **figure 3.**

CONCLUSION

In this study we demonstrated the successful [production and calibration of a novel NOSE sensor for monitoring in vitro oxygen concentration/distribution by measuring the fluorescence intensity in RIN-m5F cells filled alginate hydrogel sphere.

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Development of Blended Alginate/Collagen Hydrogels for 3D Neural Cell Culture Applications

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Oral ☒ Poster ☐

INTRODUCTION

Alginate has previously shown promise as a neural cell scaffold due to structural similarities to hyaluronic acid, a primary component of brain extracellular matrix (bECM). A lack of cell adhesion motifs in the native structure, however, means alginate often has to be modified for neural cell culture applications [1]. This study presents a simple method for functionalising alginate hydrogels with collagen fibrils to create a hydrogel suitable for 3D culture of induced pluripotent stem cell (iPSC) derived neurons. The two materials function synergistically with alginate providing structural analogy to bECM and collagen providing sites for cell-matrix interactions.

MATERIALS & METHODS

iPSCs (University of Oxford, UK) were induced down a neuronal lineage via a previously published protocol [2]. After 35 days of neural induction, cells were dissociated and encapsulated in a blend of 10mg/ml alginate (Sigma, UK) and 2.5 mg/ml collagen (PureCol EZ Gel – Sigma, UK). Gelation kinetics and mechanical tuneability were analysed using oscillatory rheology; transmission electron microscopy (TEM) was applied to study the hydrogel microstructure. Additionally, real time PCR was used to study expression of collagen-binding integrins and mechanotransductive responses of encapsulated neurons. Immunofluorescence microscopy (IFM) was employed to study cell morphology and maturation with ImageJ used to quantify images.

RESULTS & DISCUSSION

Rheological analyses indicated the gelation of collagen and alginate could be selectively triggered. This initiated a two-stage gelation process that yielded a single, self-supporting hydrogel. TEM images demonstrated that controlling the gelation of both materials allowed for penetration of collagen fibrils throughout the alginate network. Encapsulated human iPSC-derived neurons adhered to the hydrogel matrix via collagen fibrils as evidenced by a significant upregulation in collagen-binding integrins α1β1 and α2β1. IFM imaging of encapsulated cells also revealed neurons within the hydrogel formed complex, 3D neural networks as a consequence of interactions with the collagen fibrils. Additionally, encapsulated neurons developed a mature, neuronal phenotype with formation of more branched neural processes and expression of pre-synaptic vesicle proteins in the neurites. The presence of alginate within the hydrogel also allowed for tuning of the matrix stiffness by varying the $CaCl_2$ concentration employed in crosslinking. Modifying the stiffness to better reflect that of native bECM resulted in enhanced neurogenesis, suggesting encapsulated cells gain mechanotransductive feedback from the bulk structure.

CONCLUSION

Alginate/collagen hydrogels show promise as scaffolds for engineering of 3D human neural networks. Mechanical properties can be easily tuned to enhance neurogenesis and the hydrogel matrix promotes neuronal maturation. This platform therefore represents a potential model for studying neuronal development and function in neurogenesis and neurodegeneration.

ACKNOWLEDGEMENTS

Authors acknowledge the Dr. Donald Dean Fund for Dementia Research, the Medical Research Council and the University of Manchester for funding this work.

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Versatile hydrogel composites with osteogenic ions for bone substitutes

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Oral ☒ Poster ☐

INTRODUCTION

Synthetic substitutes based on calcium phosphates have received much attention, furthermore several ions such as zinc, strontium and calcium are now known to be capable of inducing stem cell differentiation and show promise in bone regeneration, however the brittle nature of calcium phosphates and ion-substituted hydroxyapatites limits application.

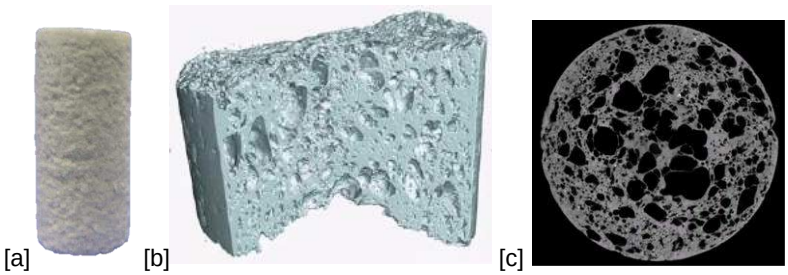
In this study we report hydrogel network composites with our previously reported calcium metaphosphate (CMP) scaffold that showed robust bone formation in a rabbit model [1]. A combinatorial approach to create a hydrogel composite of CMP and poly(vinyl alcohol) (PVA) earlier resulted in superior mechanical properties and good biocompatibility in vitro [2]. The current study reports on the development of network composites by interpenetrating PVA-CMP composite with sodium alginate crosslinked with osteogenic ions: calcium, zinc, and strontium.

MATERIALS & METHODS

PVA-CMP composites [2] were immersed in sodium alginate solution then fully crosslinked with calcium, zinc, and strontium salt solutions. The scaffolds were characterized using infrared spectroscopy, mechanical tests, water uptake, degradation, differential scanning calorimetry (DSC), µCT and *in vitro* evaluation.

RESULTS & DISCUSSION

Alginate and the osteogenic ions were incorporated into the composites creating a new class of network composites with superior mechanical and osteogenic properties in vitro. Composites crosslinked with calcium, zinc and strontium result in different properties due to their different ionic radii and different affinity towards the mannuronic and guluronic units in alginates. Different ions also affect cellular viability, proliferation, and metabolism *in vitro*.



[a] [b] [c]

Figure 1: [a] Clinical and [b & c] microCT images of the composites

CONCLUSIONS

A new design of hydrogel composites from relatively affordable materials with simple and non-toxic methods yielding clinically suitable scaffolds as bone grafts with versatile properties.

ACKNOWLEDGEMENTS

LI acknowledges the financial support of the Indonesian Endowment Fund for Education.

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3D printed flexible composite scaffolds with high ceramic content for bone regeneration

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Oral ☒ Poster ☐

INTRODUCTION

3D printed composite scaffolds consisting of ceramics/glasses and polymers often have the limitation of loading high concentrations of ceramic/glass. As a result, the ceramic/glass that is exposed on the surface of composite materials is limited, which compromises the tissue inductivity of these materials. In addition, composite scaffolds with high content of ceramic/glass are brittle and rigid, which limits the amenability of these materials in the theatre when required[1]. We have 3D printed composite scaffolds with high content of synthetic hydroxyapatite (up to 90% by mass). These composite scaffolds are flexible and amenable by trimming.

MATERIALS & METHODS

Composite scaffolds consisting of PCL and hydroxyapatite were fabricated by extrusion 3D printing. Mechanical properties were tested for the 3D printed scaffolds and single struts. Osteogenic differentiation of mesenchymal stem cells in scaffolds with varying content of hydroxyapatite was quantified.

RESULTS & DISCUSSION

The 3D printed scaffolds were made flexible by adding a biocompatible plasticizer in the composites. Interestingly the composites remained flexible even after the leaching out of the plasticizer. Mechanical properties of composite scaffolds with varying content of hydroxyapatite showed a decrease from 75%wt to 90%wt hydroxyapatite. The osteogenic differentiation of mesenchymal stem cells was enhanced with increasing hydroxyapatite.

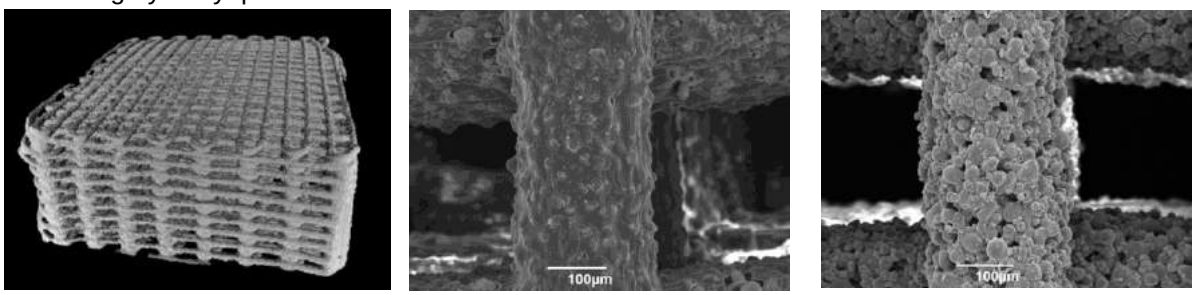

Figure 1: Left) micro CT image of a 3D printed composite scaffold. Middle, Right) SEM images of composite scaffolds with 60%wt and 84%wt hydroxyapatite, respectively.

CONCLUSION

3D printed composite scaffolds with high content of hydroxyapatite were made flexible, which increased their resistance to breakage due to brittleness. Increasing the exposure of hydroxyapatite microparticles on the surface also enhanced the osteogenic differentiation of mesenchymal stem cells.

ACKNOWLEDGEMENTS

The authors thank the Development and Promotion of Science and Talent Project (DPST) for sponsoring Mr. Aruna Prasopthum's studentship.

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Suspended Layer Additive Manufacture and the Fabrication of Complex 3D Tissue Scaffolds

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Oral ☒ Poster ☐

INTRODUCTION

3D bioprinting offers an exciting opportunity to rapidly develop complex tissue engineered structures. Our previous work on suspended layer additive manufacture has shown that the employment of a supporting fluid gel bed during 3D bioprinting allows the use of a wider range of low viscosity bioinks and facilitates the incorporation of multiple materials in order to recreate chemically graduated environments of complex structures[1, 2]. Here we demonstrate the resolution of this technique by creating intricate structures and evaluate the properties of the fluid gel supporting bed that is critical to the success of this approach to 3D bioprinting.

MATERIALS & METHODS

Agarose fluid gels were prepared by shear cooling agarose solutions (0.5% w/v). Structures were printed using a 3D bioprinter (INKREDIBLE®). Briefly, acellular biopolymer materials (gellan gum, ι-carrageenan, alginate, pectin and collagen) or cell-loaded biopolymers (bioink) were printed into an agarose fluid gel bed contained within an extra deep petri dish. Once printed, the constructs were ionotropically crosslinked (or thermally crosslinked for collagen) prior to removal from the supporting bed. Fluid gels were characterised by undergoing rheological testing, particle size analysis and visualisation by optical and scanning electron microscopy.

RESULTS & DISCUSSION

This system allowed the successful fabrication of complex structures such as a perfusable bifurcated carotid artery (fig 1a-b) and has the capacity to print materials with a viscosity as low as water (fig 1c). Rheological analysis showed that the fluid gel behaves as a Bingham plastic, allowing deposition of the polymers within the interstices of neighbouring gel particles (fig 1d) whilst also retaining the scaffolds 3D structure and allowing the diffusion of crosslinker throughout the whole part.

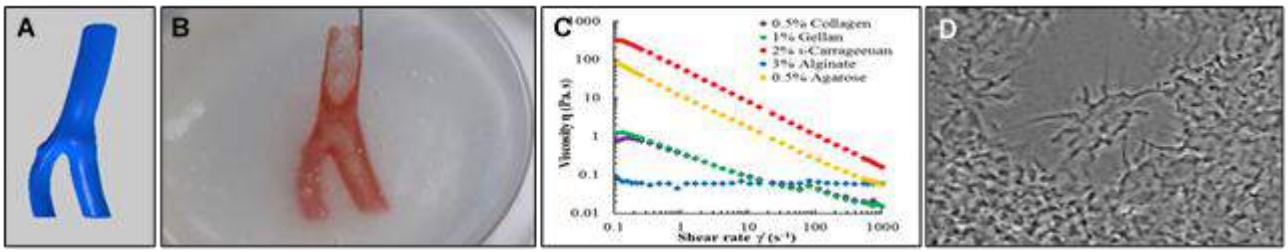

Figure 1: Suspended layer additive manufacture technique analysis. A) G code of a carotid artery, B) gellan carotid artery during printing within an agarose fluid gel, C) shear viscosity of biopolymers used for printing and D) optical micrograph of a single agarose particle within a fluid gel network.

CONCLUSION

Here we conclude that the microstructure and rheological behaviour of the agarose fluid gel bed are critical to the suspension of complex scaffolds that have been printed using a range of low viscosity biopolymers.

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Effect of Laponite on the Thermoresponsive Nature of Poly NIPAM Based Nanocomposites

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Oral ☒ Poster ☐

INTRODUCTION

Thermoresponsive polymers are currently being investigated for a wide range of biomedical applications including drug delivery, as biomaterials and sensors. The lower critical solution temperature (LCST) refers to this thermoresponsive change in material behaviour, which in the case of poly (N-isopropylacrylamide) (pNIPAM) in aqueous solutions results in a conformational coil-to-globule transformation at ~31-33°C. Copolymers can be added to pNIPAM to adjust the overall interaction of the polymer with water and therefore shift the LCST of the material[1]. Laponite® is a synthetic hectorite clay and has been used as a filler and crosslinker in numerous polymeric systems[2]. The polymerisation of NIPAM in the presence of Laponite® results in the formation of polymer clay nanocomposites, which in the case of some copolymers synthesised above the LCST, yields a hydrocolloid suspension suitable for injectable applications.

MATERIALS & METHODS

We have investigated the influence of Laponite® on the LCST of 2, 2-Hydroxyethyl methacrylate (HEMA), 2-Hydroxypropyl methacrylate (HPMA), N,N-dimethylacrylamide (DMAC) and Glycidyl methacrylate (GMAC) copolymers at 10% wt./ wt. relative to NIPAM in water.

RESULTS & DISCUSSION

FTIR characterisation of dried copolymer/ composites confirmed the presence of HEMA, HPMA and GMAC copolymer with an ester associated ν(C=O) stretch peak at 1720 cm^{-1} and Laponite® in the composite groups with a ν(Si-O) peak ~1000 cm^{-1}. Quantification of the ν(C=O) stretch: ν(N-H) bend (1630/ 1536 cm^{-1}) ratio of the DMAC copolymer group showed a reduction compared with control indicating the presence of non ν(NH) containing polymer incorporation, i.e. DMAC. DSC revealed a significant decrease in LCST in the NIPAM control, HEMA and HPMA copolymers in the presence of Laponite®. No significant differences were observed in the DMAC and GMAC copolymer groups in the presence of Laponite®. These measured differences in LCST are a strong indication that the interaction of the polymer with the clay is altered by different functional groups present within the copolymers. Laponite® is generally electronegative; however, given its intrinsically high aspect ratio and ion absorption the edge results in a localised positive charge. The NH group of the NIPAM could be interacting with the edge of the clay restricting the coil-to-globule transformation, and therefore lowering the LCST. This effect also appears exacerbated by the influence of the terminal OH^- groups present from HEMA and HPMA copolymers.

CONCLUSION

There is strong evidence to suggest that laponite interferes with the thermal phase transition of pNIPAM, a process which can be exacerbated by copolymer OH or NH functional groups. This effect could be exploited to include more hydrophilic copolymers, whilst retaining reduced LCST's.

ACKNOWLEDGEMENTS

The authors would like to thank Arthritis Research UK grant number *21497* for supporting this research.

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Electrospinning for regenerative medicine; challenges and solutions to bring products to the market

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Oral ☒ Poster ☐

In the regenerative medicine field, electrospinning has gained widespread interest to produce extracellular matrix (ECM) mimicking scaffolds for tissue engineering. This technique often was and still is the preferred choice due to its capability to produce 3 dimensional fibrous ECM lookalike scaffolds with similar nano- to micrometer length scales using an extensive range of natural and synthetic polymers. The process is highly versatile and tunable, allowing to tailor scaffold properties to fit many demands and various applications. This versatility has led to more than 10'000 scientific publication and nearly 2000 patents on electrospinnning for biomedical engineering, but only handful biomedical products. Controlling all the parameters, which create the base of this method's versatility, has proven to be a challenge holding back the development of medical electrospun products. We will show that thanks to a better understanding and tighter control on process parameters, namely to tackle challenges such as a general lack of reproducibility and a limited heterogeneous cell ingrowth, the number of electrospun products is expected to growth and electrospinning can fulfill its great potential also for the regenerative medicine market.

Bioactive hybrid materials for soft and hard tissue engineering

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Oral ☒ Poster ☐

INTRODUCTION

Bioactive glasses (BGs) can be defined as amorphous materials with good biocompatibility[1]. They have gained a great interest as biomaterials for hard and soft regenerative medicine[2,3]. This work comprises two parts: we first want to investigate the bioactivity properties that fluorinated phosphate-based bioactive glasses (PBGs) will exhibit once implanted in the body for dental repair applications. We are then designing patches containing 45S5 bioactive glasses for tissue engineering.

MATERIALS & METHODS

Bioactivity and structure are closely related[4] so we study the effect of integrating fluorine into the structure of PBGs using classical molecular dynamics (MD) simulations. We developed an empirical force field including polarisation effects. The MD simulations were performed on the following systems (P_2O_5) (50-(x⁄2))− (CaO) (50-(x⁄2)) − (CaF_2) (x) with x = 0,2,5. Cardiac tissue engineering aims to mimic the extra cellular matrix (ECM) using natural or synthetic polymeric materials[5]. To engineer innovative bioresorbable and biocompatible cardiac patches we combine 45S5 BGs with biocompatible polymeric scaffolds to provide suitable surface chemistry. These cardiac patches are engineered using 3D electrospinning techniques and characterised through mechanical tests, scanning electron microscopy, degradation tests and cell studies.

RESULTS & DISCUSSION

In the composition with 2% and 5% of CaF2, there is no bonding between the phosphorus and fluorine atoms. The atomistic visualisation shows the presence of Ca/F clusters (Figure 1). For the cardiac patches we used solutions of biopolymers. The morphological assessment of the demonstrates that the fibres had continuous morphology without any observed beads. Tensile tests and degradation tests show the addition of BGs increases the Young's modulus while keeping the ultimate tensile strength constant and the presence of the BGs helps regulate the pH to a value closer to 7.4.

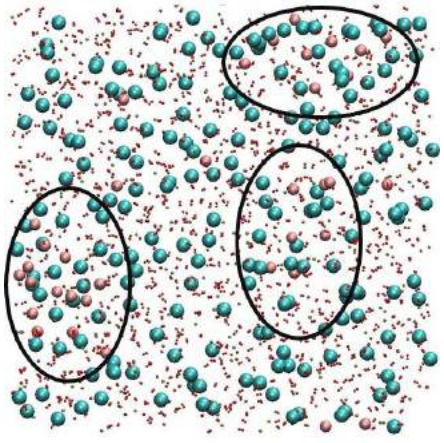

Figure 1: View of a representative composition at 300K with 5% of CaF_2 with shrunk oxygen and phosphorus atoms and clusters highlighted. Phosphorus (green), oxygen (red), calcium (blue) and fluorine (pink).

CONCLUSION

The main effect of fluoride addition is the bonding of the calcium with the fluorine. This bonding leads to a re-polymerization of the network and the formation of F-rich and F-poor regions which, overall, decrease the bioactivity of the glass. The electrospun scaffolds gave good results with no apparent beads. The patches exhibit mechanical properties matching that of the myocardium. Furthermore, the addition of BGs helps regulating the pH which is beneficial for cells biocompatibility and differentiation.

ACKNOWLEDGEMENTS

The authors would like to thank the school of AACME at Loughborough University and the Loughborough HPC facilities.

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In Situ Screening Of Functional Polymers For Biomedical Applications

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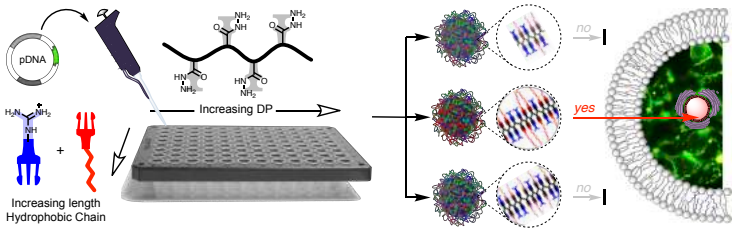
Oral ☒ Poster ☐

Introduction: Polymers are emerging as one of the most promising scaffolds for the multivalent presentation of relevant biological information. In order to identify polymer with relevant biological applications, screening of large polymer libraries is required. However, current screening technologies rely of the synthesis of polymers under "non-biological" conditions and therefore purification/isolation steps have to be implemented, even for inactive candidates, increasing the time required and the cost of the discovery process. Here, we report the application of poly(acryloyl hydrazide)s (PAH) as a versatile platform for the identification of polymers for biological applications. The delivery of nucleic acids is used to demonstrate the versatility of the approach.



Materials and methods: Synthesis of functional polymers: In a typical experiment, 200 µl of a 100 mM solution of PAH in aqueous buffer is mixed with 200 µl of a 100 mM solution of the chosen aldehyde(s) in the required solvent. This mixture was shaken at 60 °C for 24 h. Polymers were used without further purification.

Results & Discussion: The delivery of nucleic acids was used to demonstrate that PAH is an ideal platform for the identification of polymers with biological application. In this case, the challenge lies in getting a negatively charged macromolecule (nucleic acids) across negatively charged membranes. To this end, PAH was reacted with a combination of a guanidine based aldehyde (to complex nucleic acids) and hydrophobic aldehydes. Screening of hydrophobic aldehydes identified that while short and branched hydrophobic aldehydes were suited for the delivery of small interfering RNA, long aliphatic aldehydes were more suited for the delivery of plasmid DNA. Polymer length, concentration and relative ratio of each aldehyde could be readily optimised using this approach.

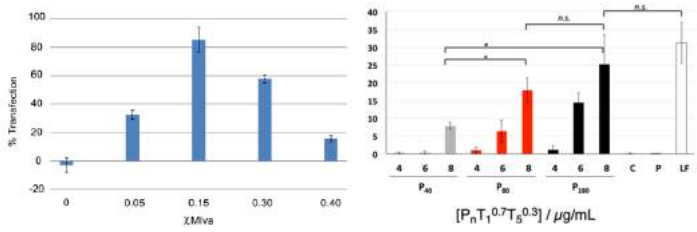


Figure 1. Left: Transfection efficiency of siGFP in HeLa-EGFP cells at different molar ratios of isovaleraldehyde and guanidine-based aldehyde. Right: Transfection efficiencies of pGFP in HeLa cells at different concentrations and different lengths of PAH. Conditions: Guanidine-based aldehyde and oleic aldehyde, 7:3 ratio.

Current efforts to use PAH for the identification of polymers with other biological applications will be also reported.

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Probing the Composition of Extracellular Vesicles in Bone Formation

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Oral ☐ Poster ☒

INTRODUCTION

The presence of key osteogenic proteins[1] and minerals[2] suggest an important role for EVs in new bone formation. There is also evidence that EVs play a role in bone homeostasis[3], osteoblast-osteoclast communication[4] and delivery of miRNA to osteoblasts[5]. Despite this, EVs remain poorly characterized, it is unknown whether stages of differentiation and mineralisation impact upon the content of EVs produced, limiting research into their exploitation as therapeutic agents. This study identifies previously unknown significant differences in the composition of EVs at different stages of the osteoblast maturation process.

MATERIALS & METHODS

Human (HOB) and mouse (MC3T3) osteoblast cells were cultured and osteogenic phenotypes induced by supplementation with β-glycerophosphate and L-ascorbic acid. Murine derived vesicles were isolated by multi step ultracentrifugation[3], whilst human osteoblast derived EVs were obtained using a commercially available kit (Fluorocet, System Biosciences, USA). EV size was measured by nanoparticle tracking analysis (NTA). Protein concentration was assessed via bicinchonic acid assay (BCA) and sample absorbance at 280nm (Nanodrop). Temporal difference in EV composition was assessed by Raman spectroscopy, peak intensities were normalised against the peak intensity associated with membrane lipid (1131 cm^{-1}), to control for differences in EV size and concentration.

RESULTS & DISCUSSION

NTA weighted mean sizes indicated that HOB EVs were smallest at day 7 (195 nm) compared to days 14 and 21 (235 and 232 nm respectively). Protein concentration was significantly reduced at day 21 versus days 7 and 14 ($p=0.0286$) when measured using BCA. Nanodrop estimates of protein concentration followed a similar trend but were non-significant. Raman spectroscopy suggested a significant reduction ($p<0.02$) in normalised intensity at day 18 at 1063 cm^{-1} (Figure 1). This wavenumber may correspond to a reduction in several molecules present in bone derived EVs (protein, lipid, nucleic acid[6], or carbonate ions[7]). These data may indicate changes in levels of key osteogenic molecules such as proteins (e.g. alkaline phosphatase), RNAs (miR-214) or minerals (calcium carbonate).

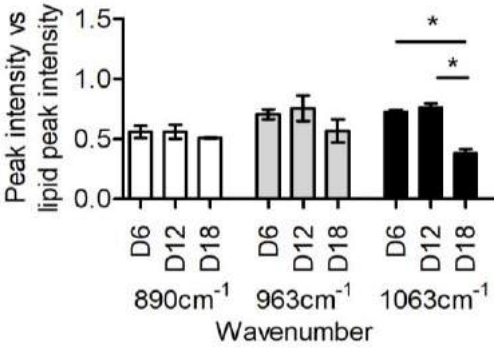

Figure 1: Raman spectroscopy. Normalised intensity at three key wavenumbers corresponding to key EV related molecules 890cm^{-1} = protein bands[8], 963cm^{-1} = PO_4 stretching[7], 1063cm^{-1} = several possible molecules, including protein, lipid, nucleic acid[6], or carbonate ion stretching[7] ($p<0.02$)

CONCLUSION

These data suggest that the composition of mineralising osteoblast EVs change as the cells mature. EVs taken at later time points displayed an increase in size, reduction in protein concentration, and a reduction in one or all of lipid, nucleic acid or carbonate ion concentration. Further work is needed to identify the specific molecules that account for these changes.

ACKNOWLEDGEMENTS

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Antimicrobial peptide hydrogels as bandage contact lenses

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Oral ☐ Poster ☒

INTRODUCTION

Corneal bandage lenses are vital in keeping the eye protected from infections after surgery along with antibiotics. Previous studies in the group[1, 2] have shown that poly- ε -lysine (pεK) hydrogels exhibit adequate mechanical and antimicrobial properties and could potentially be used as antimicrobial corneal bandage lenses. The aim of this study is to improve the properties of the hydrogels further, mainly with respect to the mechanical properties by including additives.

MATERIALS & METHODS

Peptide hydrogels were synthesised from pεK and octanedioic acid using carbodiimide chemistry. The gels synthesised were either at a cross-linking percentage of 60% and polymer density of 0.071g/ml (Su60NHS) using N-hydroxysuccinimide (NHS) as the activator or 70% cross-linking percentage and polymer density of 0.125 g/ml (Su70DMAE) with dimethylaminoethanol (DMAE) as the activator. High molecular weight (≤100kDa) pre-polymerised pεK chains cross-linked with octanedioic acid was added to the gels synthesised using DMAE, at 20% of the initial weight of pεK in the gel. Some of these gels were treated further by addition of pendant pεK, using carbodiimide chemistry, to enhance the antimicrobial properties (Su60NHS+ and Su70DMAE+). The mechanical properties (using a Linkam Stress tester), the transparency using spectrophotometry at 485nm, the water content and oxygen permeability using the gravimetric method and the direct and indirect cytotoxicity of the gels using live/dead staining and the CCK-8 assay respectively were determined. In order to study the antimicrobial properties of the gels, *Staphylococcus aureus* and *Pseudomonas aeruginosa* was seeded onto the gels. After 24 hours, the colony forming units (CFU)/ml was determined. Data analysis was carried out using a one-way ANOVA with Tukey's post-test analysis.

RESULTS & DISCUSSION

The characterisation results have been shown in Table 1.

Table1. Characterisation of the pεK hydrogels

Gel	Tensile strength (MPa)	Elastic modulus (MPa)	Toughness (mJ/mm^3)	Water content (%)	Oxygen permeability	Transparency (%)
Su60NHS	0.06±0.027	0.211±0.046	9.71±7.2	88.1±2.6	55.45±6.2	78.5±11.5
Su60NHS+	0.087±0.025	0.396±0.106	10.5±5.7	85.3±5	50.25±9.9	84.8±5.45
Su70DMAE	0.063±0.037	0.136±0.082	14.5±8.5	80.52±3.14	41.12±5.15	85.68±7.68
Su70DMAE+	0.165±0.038	0.439±0.146	33.9±16.4	78.3±3.46	37.7±5	91.1±4.45

Based on the results, it appeared that by replacing NHS with DMAE and by including an additive to the gels, the tensile strength and toughness improved significantly. The gels showed no cytotoxicity using the direct or indirect method. After 24 hours on the gels, the *S.aureus and P.aeruginosa* showed a ≥ 4 log reduction in CFU/ml in all cases compared to a commercial contact lens control.

CONCLUSION

The properties of the gel fall within the range of commercially available contact lenses. The gels have anti-microbial properties, demonstrating at least a 4 log reduction in the bacteria load after 24 hours. These hydrogels have potential to be used as antimicrobial bandage contact lenses after surgery.

ACKNOWLEDGEMENTS

We thank the Medical Research Council for the Developmental Pathway Funding Scheme Award

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Harnessing the antibacterial properties of chitosan to tackle dental biofilms

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Oral ☐ Poster ☒

INTRODUCTION

Dental biofilms are constituted by a community of microorganism that attach to the teeth surface resulting in the onset of dental diseases that to date are a global health concern. One of the main cariogenic bacterial species forming biofilms is *Streptococcus mutans*[1]. Carbohydrates are metabolized by the biofilm bacteria and produce acids responsible for the demineralization of the hard tissue of the teeth. Chitosan (CS), a natural biodegradable and biocompatible polysaccharide, has been reported to have good antibacterial effects due to its positive charge. Fluoride has been used extensively as an anti-caries agent as it protects dental hard tissue from acid and inhibits bacterial growth of cariogenic species. We aim at combining these two strategies for the development of a novel agent able to reduce biofilm formation and demineralization.

MATERIALS & METHODS

Chitosan (CS) was degraded using hydrochloric acid into low molecular weight chitosan (CS3H) then modified with lysine (CS3H Lys). Fluoride was incorporated into the polymer by dialysis (CS3H Lys NaF). Polymers were characterised by NMR, FTIR, SEM and fluoro selective electrode was used to quantify the flouride. *Streptococcus mutans* biofilms were grown in biofilm medium (BM) containing 0.5 M sucrose in 5% CO_2 at 37°C for 24h. The biofilm formation was quantified by staining with 0.1% crystal violet. The inhibition of acid demineralisation was determined using vanadomolybdate to measure the dissolution of phosphate by acid attack and measured at 450 nm.

RESULTS & DISCUSSION

The antibacterial and anti-biofilm activity of chitosan (CS) and modified chitosan (CS3H, CS3H Lys and CS3H Lys NaF) were determined against dental cariogenic bacteria *S. mutans* using both biofilm and planktonic methods to investigate the reduction of viable cells elicited by the polymers. The biofilm method showed that the modified chitosan (CS3H Lys and CS3H Lys NaF) reduced the *S. mutans* biofilm formation when compared with the original chitosan. The IC_{50} values of chitosan polymers against *S. mutans* biofilms were 121.8, 87.91, 21.24, 63.77 µg/ml, respectively. This study showed that addition the fluoride into polymer could protect demineralisation from acid attack. The percentage reduction of phosphate released were 0.72 ± 3.70, 4.68 ± 4.99, 28.79 ± 2.40, 33.76 ± 3.26, respectively.

CONCLUSION

These results show a good antibiofilm activity against *S. mutans* of CS3H Lys and the potential of CS3H Lys NaF to protect the teeth against demineralisation. A combination of these polymers can be used in the development of novel oral health products to control the formation of dental biofilms and stop the development of further dental diseases.

ACKNOWLEDGEMENTS

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Differentiation of mesenchymal stem cells in an injectable hydrogel under the conditions of the degenerate intervertebral disc.

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Oral ☐ Poster ☒

INTRODUCTION

Low back pain affects 80% of the population at some point in their lives with 40% of cases attributed to intervertebral disc (IVD) degeneration, where cells within the nucleus pulposus (NP) produce catabolic factors which destroy the tissue. We have previously reported the development of NPgel, a synthetic, Laponite® cross-linked pNIPAM-co-DMAc, injectable hydrogel. NPgel has been shown to induce differentiation of human mesenchymal stem cells (hMSCs) towards an NP cell phenotype without the need for additional growth factors *in vitro*[1] and also fully integrates with NP tissue following injection into the disc[2]. However, the translation of this potential treatment strategy into a clinical application is dependent on the survival and differentiation of hMSCs into the correct cell phenotype within the degenerate IVD. Here, we investigated the viability and the differentiation of hMSCs incorporated into NPgel cultured under conditions mimicking the healthy and degenerate microenvironment of the disc.

MATERIALS & METHODS

Human MSCs were cultured in monolayer before encapsulation into NPgel and cultured for up to 4 weeks in 1 of 4 treatment groups (n=3). Each group mimicked conditions from, standard culture (DMEM, pH7.4), healthy disc (DMEM, pH7.1), degenerate disc (low glucose DMEM, pH6) or degenerate disc plus 10ng/mL IL-1β. All culture was performed at 5% oxygen concentration. Cell viability, cell differentiation and catabolic factor production was assessed by histological staining and immunohistochemistry (IHC).

RESULTS & DISCUSSION

Viability of hMSCs was maintained in NPgel after 4 weeks of culture. Differentiation markers increased over the culture period and levels were comparable between healthy and degenerate disc conditions. Expression of catabolic factors remained low across all treatment groups for the culture duration and histological staining also confirmed the deposition of matrix within the NPgel scaffolds. In agreement with our previous findings [1,2] NPgel was able to induce NP cell differentiation of MSCs. Here we have shown that viability and NP cell differentiation of MSCs incorporated within NPgel was mostly unaffected by treatment with conditions such as low glucose, low pH and the presence of cytokines, all regarded as key contributors to disc degeneration. In addition, the NPgel was shown to prevent MSCs from displaying a catabolic phenotype with low expression of degradative enzymes, highlighting the potential of NPgel to differentiate hMSCs and protect them from the degenerate disc microenvironment.

CONCLUSION

The NPgel described here not only has the potential to provide mechanical support and deliver MSCs for regeneration of the IVD but also may simultaneously function to protect delivered hMSCs from the catabolic environment in the degenerate IVD.

ACKNOWLEDGEMENTS

We acknowledge funding from the Medical Research Council.

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Polymeric Artificial Cellular Environments for *Vibrio cholerae* Aggregation

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Oral ☐ Poster ☒

INTRODUCTION

Functional polymers as drug-like molecules are able to interface with biological systems in ways that are not possible with single molecules[1]. Compared to their small molecule counterparts, polymeric materials can display increased avidity towards a biological target, lower toxicity to host cells and a larger scope for tuning properties such as charge, hydrophobicity and specific binding groups. These materials have already shown promise in a wide range of biological applications including biological sensors, sequestering of pathogenic bacteria and gene delivery systems. *V. cholerae's* ability to colonise and cause disease to a host depends on the bacterium's successful attachment to host cells. Here we report the synthesis of poly(acryloyl hydrazide)[2] and how, by modifying the pendant groups along the polymer chain with aldehydes and/or sugars as well as the polymer size we can tune the polymers ability to sequester *V. cholerae* via exploitation of the bacterium's own adhesion mechanisms, for example hydrophobic and electrostatic interactions and lectin binding.

MATERIALS & METHODS

poly(acryloyl hydrazide) was prepared via RAFT polymerisation at varying degrees of polymerisation. Conversion was calculated using NMR and size and dispersity was calculated by GPC.Post polymerisation modification of the scaffold by aldehydes was carried out in 100 mM acetic acid and the resulting conjugates used without the need for further purification. Quantification of the aldehyde loading onto the polymer was performed by NMR. For toxicity and clustering studies, GFP expressing *Vibrio cholerae* were monitored using fluorescence, OD_{600} and time lapse microscopy in brightfield and GFP channel.

RESULTS & DISCUSSION

Poly(acryloyl hydrazide) was modified with 0.25, 0.50, 0.75 and 1.0 equivalents of Imidazole carboxaldehyde to generate a small library of polymers with different degrees of functionalisation. Increasing the density of imidazole on the polymer backbone decreases the toxicity of the polymer towards *V. cholerae* and increases the presence of bacterial clustering (figure 1).

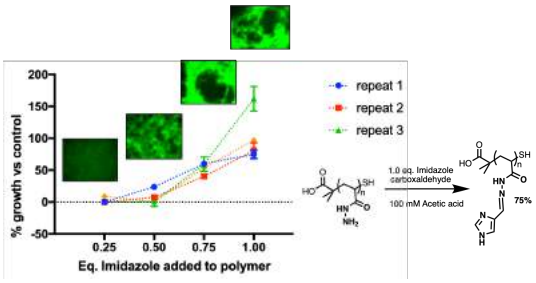

Figure 1: Effect of imidazole modification on *V. cholerae* growth (GFP expression), and GFP images showing heterogeneous growth/clustering.

CONCLUSION

We have shown from initial studies that modulating the chemistry on the polymer can have dramatic effects on the growth and behavior of *V. cholerae*. We are now looking to explore different functionalities and combinations to identify how best to sequester these bacteria, and the effect this has on quorum sensing and virulence. These polymers are thus a promising tool to understand and control pathogenic bacteria.

ACKNOWLEDGEMENTS

Midlands integrative biosciences training program (MIBTP) for funding.

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Stimuli-responsive nanogels with controlled size and architecture

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Oral ☐ Poster ☒

INTRODUCTION

Stimuli-responsive nanogels have shown great potential as platforms for drug delivery and tissue regeneration.[1] These smart nanogels usually undergo reversible volume transitions within their crosslinked structure due to small changes in their environment such as pH, and temperature.[2] Due to the precision required for biomedical standards, high control over the properties of the nanogels is necessary in their preparation.[3] Here, a controlled route for the synthesis of pH- and thermoresponsive core-shell nanogels using reversible-addition fragmentation chain-transfer (RAFT) polymerisation is presented. Along with the evidence to show different strategies to tune the final size of the nanogels and the degree of response from their preparation.

MATERIALS & METHODS

A two-pot method was followed for the synthesis of the nanogels: 1) Synthesis of the polyacrylic acid (pAA) pH-responsive macro chain transfer agent (mCTA) with different degrees of polymerisation (DP). These homopolymers were characterised by ^{1}H NMR and FT-IR spectroscopies. 2) Chain extension of pAA by *N*-isopropylacrylamide (NIPAM) and *N,N'*-methylenebisacrylamide (MBAM) as temperature-responsive and crosslinking monomers respectively. These nanogels were characterised by FT-IR spectroscopy, TEM and DLS.

RESULTS & DISCUSSION

The ease of tuneability of the size of the nanogels was demonstrated by three routes: 1) Addition of ethanol in the reaction media (water:ethanol as cononsolvents), 2) Chain extension of pAA-mCTA at different NIPAM molar ratios, and 3) the use of pH-responsive pAA of different chain lengths. Overall, it was shown that by adding ethanol in the reaction media, nanogels with a smaller final size were obtained. The limit at which stable and monodisperse nanogels could be synthesised in a cononsolvents mix was found to be 0.89:0.11 (water:ethanol) as shown by DLS data. At a fixed 0.11 ethanol molar ratio, the size of the thermoresponsive core was easily controlled by varying the molar ratio of [NIPAM]:[mCTA] from 100:1 to 300:1 to form colloidal stable nanogel dispersions. The temperature profiles showed that the bigger the thermoresponsive core, the greater the change in the hydrodynamic size (20 nm against 100 nm transitions between the smallest to the biggest targeted core). Tuneability of the outer-shell size was easily controlled by using pAA-mCTA with different DP. The use of a larger pAA-mCTA still allowed effective self-assembly and crosslinking at different NIPAM molar concentrations during the synthesis at pH 7. The pH response of the synthesised nanogels was proved by decreasing the pH below 7. The size of the negatively charged outer-shell decreased as the pH decreased due to the protonation of the carboxylate groups. In addition, salt-induced aggregation of the nanogels was tested at different NaCl or $CaCl_2$ concentrations at 37 °C, however only calcium-gel aggregates were formed at a minimum concentration of 15 mM $CaCl_2$.

CONCLUSION

A controlled and versatile route to produce a series of pH-and thermoresponsive nanogels *via* two-pot RAFT dispersion polymerisation was shown. The size of the nanogels (core and shell) can be easily tuned as desired from their preparation at a wide range of compositions with a controlled architecture.

ACKNOWLEDGEMENTS

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UPLC-DAD-ESI-QTOF-MS Characterization of Anthocyanin Pigments Extracted from the Leaves of *Justicia secunda* Vahl (Acantaceae) Growing Abundantly in the Lowland Rainforests in the Niger Delta Region of Nigeria.

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This study reports for the first time the characterization of anthocyanin pigments isolated from the aqueous fraction of the methanolic extract of the leaves of the uncultivated plant, *Justicia secunda* Vahl (Acantaceae). It grows abundantly in the lowland rain forests and courtyard gardens of the Niger Delta region of Nigeria and other African Countries [1,2] Its traditionally home made red aqueous leaf extract is reportedly rich in anthocyanins and is widely used in folk medicine [2,3,4,] Purification of the resultant anthocyanin-rich aqueous extract was achieved by means of an Amberlite XAD-7 column and Sephadex LH-20 gel filtration. The isolation and characterization of individual anthocyanins was achieved by means of Ultra-Performance Liquid Chromatography (Waters ACQUITY UPLC system) coupled to an electrospray ionization-time-of-flight mass spectrometer (Q-Tof micro, Waters). The detection of anthocyanins was achieved by utilizing an on-line photodiode array chromatogram (DAD) analysis, while MS spectra were recorded that led to the identification of the anthocyanins based on characteristic fragmentation patterns. Five major anthocyanins whose molecular structures have been confirmed by LC-MS in this study justifies the therapeutic potential of this plant.

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Triply-responsive hydrogels constructed from microgel building blocks containing a photo-cleavable crosslinker

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Oral ☐ Poster ☒

INTRODUCTION

Degeneration of the intervertebral disc (DIVD) and osteoarthritis (OA) result in chronic pain. They are major UK healthcare problems such as society ages and increased NHS costs. The pH responsive doubly crosslinked nano-hydeogels (DX NGs) have therapeutic (load support) and diagnostic (stress-strain data) capabilities [1]. This work developed a novel multi-sensitive (pH, temperature and light) MGs and DX MGs and investigated the relationship between this new MGs and DX MGs.

MATERIALS & METHODS

Multi-responsive MGs were synthesised via copolymerized MEO_2MA, MAA and photo-cleavable crosslinker nPh (or nomal crosslinker (EGD) as controlled MGs). The MGs were vinyl-functionalised using glycidyl methacrylate. Concentrated MG dispersions constructed DX MG via free-radical inter-MG crosslinking.

RESULTS & DISCUSSION

The MGs swelled or collapsed in response to temperature and pH changes (Fig. 1A-B). The MGs also degraded when UV irradiated (Fig. 1C)). Comparison of the responsive properties of the DX MGs and MGs showed that the temperature and pH responses of the former were mostly governed by the latter (Fig. 1D-E). However, the compression modulus (E) and swelling (Q) of the DX MG gels were strongly affected by x (Fig. 1D -F) even though it did not change MG particle swelling. UV irradiation of the DX MGs enhanced gel mechanical photostability in contrast to the behaviour of the MGs (Fig. 1F and C).

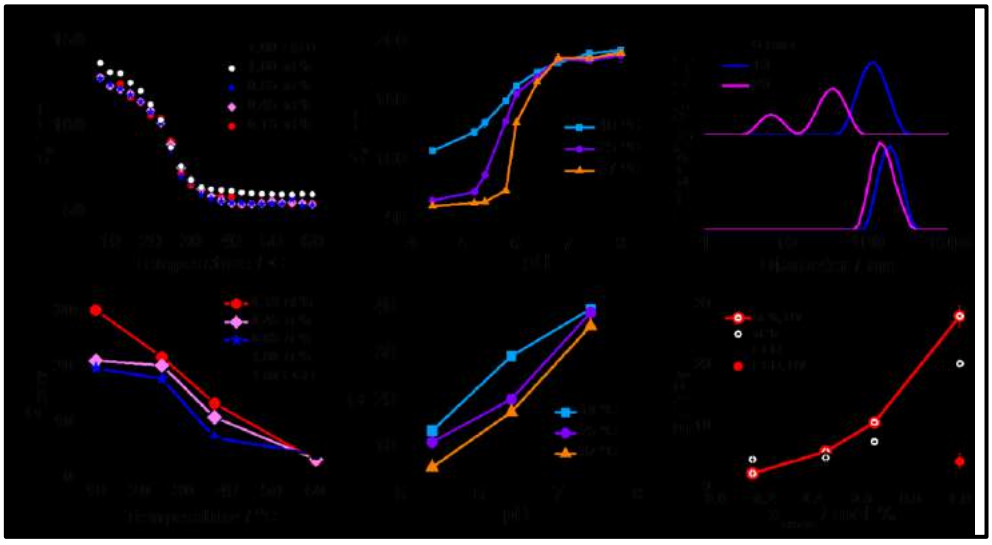

Figure 1. Temperature- and pH- responsibility of MG (A– B), UV-induced degradation of MG (C), pH- and Temperature- responsibility of DX MG (D– E), UV-induced mechanical enhancement of the DX MGs (F).

CONCLUSION

In this study, the relationship between new multi-responsive MGs and DX MGs was studied fully. The thermal- and pH-responsive behaviours of the DX MGs followed the parent MGs. However, the properties of the DX MGs do not simply follow those of the parent MGs and mechanisms account for the differences [2].

ACKNOWLEDGEMENTS

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Synthetic bone graft with potential application in oral and maxillofacial bone defects

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Oral ☐ Poster ☒

INTRODUCTION

Bone augmentation procedures using synthetic bone substitutes to surgically rebuild maxillomandibular complex defects whilst maintaining aesthetics and functionality is still a challenge. Although calcium phosphate-based materials have been shown to exhibit osseoconductivity and are biocompatible, the variable resorption rates and brittle nature limits application. To overcome the brittle nature and enhance surgical manipulation, hydrogel composites based on poly(vinyl alcohol) (PVA) and calcium metaphosphate (CMP) were recently reported with superior mechanical properties and in vitro cytocompatibility[1].

This study is aimed at developing the PVA-CMP composites with poly (vinyl alcohol) fibres, which will have a dual function of initial reinforcement of physical properties and subsequent dissolution of these fibres leading to channels within the scaffold to encourage vascularization and enable good transport of nutrients through the bulk of the composite. We report the findings of our initial study on the formulation of PVA-CMP-PVA fiber composites and selected physicochemical properties.

MATERIALS & METHODS

PVA (average molecular weight 145,000g/mol, degree of hydrolysis 98.0%, from Merck KGaA, Germany) were dissolved in distilled water at 121^{0}C to obtain solutions with concentrations 10w/v% and 20w/v%. CMP was synthesized by heat treating Calcium bi-(dihydrogen phosphate) monohydrate (MCPM) from Scharlab S.L, Spain, as reported earlier[2]. The hydrogel composites were formulated by freeze-thawing cycles with the incorporation of PVA short fibres (fineness 1.0 Denier, Diameter 11µm, cut length 4mm, supplied by Kuraray Japan).

The PVA fibres were incorporated during the manipulation of the constituents in different ratios. The scaffolds were characterized using infrared spectroscopy, mechanical tests, water uptake, degradation and scanning electron microscopy.

RESULTS & DISCUSSION

PVA-CMP-PVA fiber composites were obtained by repeated freezing and thawing cycles leading to the formation of crystallites which act as crosslinking sites, without any chemical crosslinkers. Since no crosslinking agents are used, no initiator, activator or residual monomers are present. The incorporation of PVA-fibres into the composites enhanced mechanical properties with potential application in critically sized bone defects.

CONCLUSION

The incorporation of fibres for the mechanical reinforcement of composite materials for bone tissue engineering, with simple and non-toxic methods can lead to clinically suitable scaffolds for bone grafts in oral, maxillofacial and other bone defects.

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Supramolecular Design of Cytoskeletal Protein-based Hydrogels, Characterization and Potential Applications in Regenerative Medicine

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Oral ☐ Poster ☒

INTRODUCTION

Tissue regeneration is a dynamic and complex process. The actin cytoskeleton is involved in cellular adhesion, contraction and motility all of which are key to regeneration processes.[1] Therefore, developing actin-based hydrogels with a three-dimensional (3D) network could be an amazing platform for probing how the interaction between cells and cytoskeleton proteins stimulates regenerative functions.

Supramolecular co-assembly holds great potentials as a strategy for engineering proteins in biomaterials design.[2,3,4]

RESULTS & DISCUSSION

Using the integrated principles of reaction-diffusion processes, supramolecular co-assembly and self-organization, we developed robust and viscoelastic hydrogels with 3D nanofibers networks based on supramolecular interactions between a cationic peptide amphiphile (PA) and globular actin (G-actin) (Figure 1). The hydrogels are characterized with high mechanical and self-healing properties. We have also demonstrated that the hydrogels are cell-friendly using stem cells.

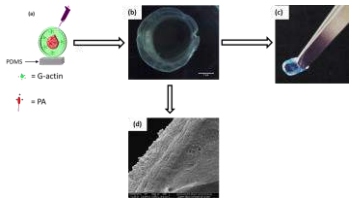

Figure 1: (a) Diffusion-driven co-assembly of G-actin and PA, (b) optical image of hydrogel formed, (c) hydrogel can be handled with a pair of twissors, and (d) SEM image of PA-actin gel.

CONCLUSION

We hope that this material will find potential applications in, for example, muscles regeneration and potentially revolutionized the field of regenerative medicine.

ACKNOWLEDGEMENTS

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Characterisation of oxidized alginate-gelatin hydrogels for *in vitro* models

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Oral ☐ Poster ☒

INTRODUCTION

An ideal biomaterial for tissue engineering should be adhesive, degradable and match the mechanical properties of the tissue of interest. Alginate is a biocompatible polysaccharide widely used in the biomedical field as scaffolding or encapsulating material; however, alginate on its own presents some important limitations in regenerative medicine due to the absence of adhesion moieties and lack of degradability. Partially oxidized alginate (OA) has been proposed as alternative to conventional alginate hydrogels with applications in myocardial and cartilage regeneration[1,2]. Here, we describe the use OA and gelatin to form cross-linked hydrogels with controlled mechanical properties and improved adhesion properties (gelatin). A library of hydrogels was formed by varying different gelling parameters, e.g. alginate/gelatin concentration, alginate oxidization degree. Cell response to stiffness and adhesion ligand density (gelatin concentration) was also studied.

MATERIALS & METHODS

Alginate was oxidized with $NaIO_4$ (aq.) under standard reaction conditions (mechanical mixing in the dark, 6 h, RT) to target oxidation degrees (OD) of 35% and 50%, followed by dialysis against water and freeze-drying. The OD was determined indirectly by quantifying unreacted $NaIO_4$ by triiodide-starch method; aldehyde groups (OA) were measured by hydroxylamine assay; amino groups (gelatin) were determined by ninhydrin assay. Hydrogels were formed mixing gelatin/HEPES buffered saline solution (HBS) into OA/HBS solution (37°C; sterile conditions), and then allowing gelation for 24h at RT. Hydrogel swelling and stiffness were measured for each hydrogel formulation. Preliminary biocompatibility was qualified by assessing the morphology and viability of MDA-MB-231 breast cancer cells cultured on selected hydrogels.

RESULTS & DISCUSSION

Hydroxylamine assay showed that 2% wt. solutions of OA 35%OD and OA 50%OD contained respectively 89 mM and 122 mM of aldehyde groups, available to cross-link with primary amines (gelatin). In this work, we used gelatin solutions of 5%wt., 7.5%wt. and 10%wt., respectively containing 4 mM, 6 mM and 8 mM of reactive primary amines. The stiffness of hydrogels was measured with compressive tests and found in the range of 0.5-10 kPa; stiffness values paralleled the concentration of both reagents and alginate OD. Preliminary live/dead assay results showed a good hydrogels biocompatibility, with higher cell survival seen on hydrogels with lower OD and higher gelatin content. Moreover, cells seemed to exhibit different morphologies among the different hydrogels, which may relate with the hydrogel stiffness.

CONCLUSION

We observed that the stiffness of OA-gelatin hydrogels was proportional to concentration of both polymers, as well as to alginate OD. Preliminary biocompatibility analyses showed biocompatibility of the majority of hydrogels. Cell morphology varied in response to hydrogel stiffness. Further investigation will be performed to de-couple the role of hydrogel stiffness and gelatin concentration. OA-gelatin hydrogel are promising biomaterials to investigate cancer cell response and invasiveness to stiffness.

ACKNOWLEDGEMENTS

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A biocompatibility study of a versatile ultra-short self-assembling peptide hydrogel for dental and soft tissue regeneration.

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Oral ☐ Poster ☒

INTRODUCTION

The primary challenge in treating small bone defects, where the mineral density is reduced, for example in an osteoporotic mandible, or in the case of a marginal alveolar bone loss, due to infection, for example, is finding adequate fillings or scaffolds which can stimulate increased bone growth. To date most fillings are performed with the use of ceramics and metals, however, while some ceramics may support low levels of remineralisation, metals often only fill the void, or contribute to further bone loss, without stimulating new tissue growth and resorption of the material. A number of potential membranes have been introduced into the dental regeneration field in recent years for evaluation. However, there have been calls to elucidate more clearly the properties of these materials, with the additional caveat of being able to stimulate new bone growth [1].

Ultra-short self-assembling peptides can be precisely, and repeatedly engineered to be biocompatible, non-immunogenic, and biodegradable, while providing a three-dimensional mimetic environment to guide cell growth and differentiation [2] for development of new bone, or soft gingival tissues.

MATERIALS & METHODS

We will assess the biocompatibility of the novel self-assembling peptide hydrogel, engineered to have of ultra-short repeating peptide sequences, with human dental pulp stem cells in-vitro for 7 days using Cell Titre Glo3D, and live dead imaging, for the potential use in dental, soft tissue, and other regenerative techniques.

In addition, we aim to study morphology, and behaviour of the cells in these novel versatile hydrogels, using a range of imaging techniques and the rate of cell proliferation with statistical methods.

Keywords: Hydrogel, Bone Regeneration, Ultra-Short Peptides, Dental, Biocompatibility

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Rheological and recovery properties of self- assembly peptide hydrogels

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INTRODUCTION

Peptide hydrogel is a kind of biomaterial with great potential due to its good biocompatibility and degradability. And those advantages make hydrogel widely applicable to many areas, including tissue engineering, drug delivery devices, biosensors and actuators. For example, organ and tissue damage or dysfunction is one of the bad diseases that seriously affect the quality of patients' life, such as traumatic brain injury (TBI) and lower back pain (LBP) [1]. And tissue engineering is an important treatment. However, in application, the hydrogel materials required for different body parts need to have different stiffness, for example, hydrogel material applied to bone tissue is relatively hard and applied to brain tissue is relatively soft. Therefore, it is important to design hydrogels of different stiffness, especially, understand hydrophobic amino acids how to affect the attraction between individual fibres and the physicochemical properties of those hydrogels; and understand the relationship between peptide hydrophobicity and amino acid side chain structure based on the self-assembly [2].

MATERIALS & METHODS

In the first part of this study, five peptides: FEFKFEFK, LEFKFEFK, IEFKFEFK, VEFKFEFK and AEFKFEFK (F – phenylalanine, E – glutamic acid, K – lysine, L – leucine, I – isoleucine, V – valine, A – alanine) were designed at concentration were 15mg/ml and then diluted the gels twice to obtained gels at concentration were 10mg/ml and 5mg/ml.

In the second part, the secondary structure and recovery and mechanical properties of these self-assembled materials were charactered by fourier-transform infrared spectroscopy (FTIR) and rheometric techniques respectively.

RESULTS & DISCUSSION

All samples were found have β-sheet structure around 1625 cm^{-1} using FTIR, all samples have α-helix structure around 1526 cm^{-1} except LEFKFEFK; besides, the storage modulus of these peptide hydrogels were varied from 160 Pa to 475 Pa at the same pH value.

CONCLUSION

These hydrogels have different stiffness, which was defined through rheological properties. One challenge is that design an effective peptide hydrogel for special needs.

ACKNOWLEDGEMENTS

The authors would like to acknowledge funding from the Manchester Institute of Biotechnology

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Peptide-graphene oxide hydrogel nanocomposites for intervertebral disc tissue engineering applications

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INTRODUCTION

Intervertebral disc degeneration (IVDD) has been classified as a major contributor of global disability[1]. Current treatments are highly invasive and poorly efficient in the long-term. Cell-based therapies allow a minimally-invasive delivery of cell-seeded biomaterials at the injury site to promote regeneration. Among injectable biomaterials, self-assembling peptide hydrogels (SAPHs) represent potential candidates as 3D cell carriers, due to their tissue biomimicry and ability to support cell viability and differentiation[2,3]. Moreover, the advent of graphene-based materials has made the fabrication of graphene-hydrogel nanocomposites appealing, allowing graphene features to be exploited to direct cell fate[4]. In this study, we incorporated graphene oxide (GO) within a SAPH to develop novel peptide-GO nanocomposites as potential cell carriers for IVD repair.

MATERIALS & METHODS

Peptide-GO hydrogels were prepared by incorporating 0.5 mg/ml GO (mean size <5µm) into a FEFKFEFK (F8) peptide solution (10, 15 and 20 mg/ml). Hydrogel microstructures were assessed *via* atomic force and transmission electron microscopy (AFM, TEM), while rheological behaviour was studied *via* oscillatory rheometry. Nucleus pulposus cells (NPCs) were then encapsulated within the hydrogels for 3D cell culture and cell viability and metabolic activity were assessed over time.

RESULTS & DISCUSSION

GO flakes were homogenously dispersed in F8 hydrogels, revealing different levels of interactions with the peptide-based network. Incorporation of GO within F8 enhanced the mechanical properties of peptide hydrogels, achieving average storage moduli (G'~12.8 kPa) comparable with human NP tissue (G'~10 kPa). Moreover, hybrid hydrogels showed shear-thinning properties and injectability, making them suitable for minimally invasive applications. GO-containing F8 hydrogels resulted biocompatible for NPCs, preserving their characteristic rounded morphology, high cell viability and metabolic activity over time.

CONCLUSION

Results showed that GO can be added to SAPHs to create injectable and mechanically-reinforced scaffolds which are biocompatible for 3D culture of NP cells and appealing as cell carriers for IVD repair therapies.

ACKNOWLEDGEMENTS

The authors thank EPSRC & MRC (EP/L014904/1 & EP/K016210/1) for their financial support and the University of Manchester BioAFM and EM facilities for their technical support.

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Control of neuronal alignment and circuit formation in 3D hydrogel cultures

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INTRODUCTION

Within biological systems, neuronal circuitry is required to co-ordinate chemical environments and responses to stimuli across large volumes without reliance on spatial diffusion of signal molecules. Fabrication of 3D tissue engineered neuronal constructs has received widespread attention, however the presentation of defined circuitry within such constructs remains a serious technical challenge to be overcome. Here we present two hydrogel substrates for the support of 3D neuronal culture with tuneable mechanical properties.

MATERIALS & METHODS

Dilutions of collagen hydrogels were prepared by an acid-neutralization reaction of solubilized rat-tail collagen. Pre-polymer solutions of poly (ethylene glycol) methyl ether methacrylate (PEGMA) or hydroxypropyl methacrylamide (HPMA) were created by combing the monomer with N,N'-methylenebisacrylamide and Irgacure 184, for photoinitiation using UV light. These preparations were inoculated with SH-SY5Y cultures during and post gelation. Samples of cell-laden collagen gels were differentiated using 2μM retinoic acid and 50ng/mL BDNF, before being assessed rheologically, alongside acellular synthetic hydrogels. Cultures were stained for β-III-tubulin expression to qualitatively assess the extent of neuronal differentiation.

RESULTS & DISCUSSION

Higher concentrations of collagen and N,N'-methylenebisacrylamide resulted in gels with a greater storage modulus (G'). Conversely, a concentration of 0.5mg/mL and 0.05 wt% respectively, resulted in softer hydrogels. Qualitatively, less dilute gels correlated with greater expression of β-III-tubulin, producing larger cells with significant changes in cell morphology observed.

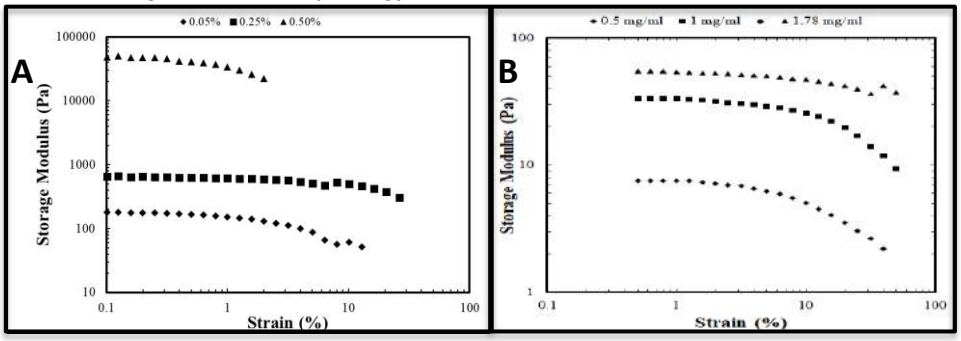

Figure 1: Strain amplitude sweep of tuneable synthetic (A) and collagen-based (B) hydrogels.

CONCLUSIONS

Substrate stiffness is widely implicated in guiding neural precursor cell differentiation[1], neuronal maturation[2], and neurite outgrowth and branching[3]. Even within chemically identical substrates, mechanical properties and physical conformation of the polymeric substrate of a hydrogel scaffold may have profound implications on cellular behavior. Design of a 3D substrate for controlled neuronal growth hence should consider the rheology of the chosen substrate as well as the underlying chemistry to optimize neurite growth and maturation.

ACKNOWLEDGEMENTS

Acknowledgements to the EPRSC for research funding, and to Dr. Sam Moxon of Manchester University for assistance with rheological analysis.

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Neuronal Alignment using Polymeric Micro-Hollow Fibres for Spinal Cord Injury Regeneration

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INTRODUCTION

Severe injury to the spinal cord results in some level of paralysis with little chance of significant improvement or return to motor function. The spinal cord is surrounded by an extension of the blood brain barrier that helps prevent further damage to the area, but also allows for the formation of the glial scar. This stops the regeneration and regrowth of neurons; thus, damage is permanent [1]. A distinct type of glial cells, namely Olfactory Ensheathing Cells (OECs), are known to regenerate central nervous system (CNS) nerves in the olfactory system after damage. Studies have shown that these cells also have potential to aid regeneration after spinal cord injury [2] by redirecting neurons and their extensions. However, recent research has shown that the mechanical environment is much softer than that of healthy spinal cord tissue [3] and, this leads to differences in cell responses due to the varying chemical and mechanical properties of the scar microenvironment [4]. This project aims to produce a model of spinal cord injury, initially using micro-hollow fibres (micro-HFs) to induce alignment of neurons with the aid of OECs. This will then be translated into a well-defined gradient within hydrogels to mimic the mechanical environment in the glial scar. Using this model, different regeneration agents could be tested, OECs amongst others.

MATERIALS & METHODS

Micro-HFs were fabricated using a polystyrene-polycaprolactone mixture and were produced with a phase inversion single orifice spinneret. NG108 cells, a motor neuron model, along with OECs were seeded onto the fibres, which were coated with PLL or Laminin, within a low attachment plate. The effect of cell seeding density, coating and length of culture were studied.

RESULTS & DISCUSSION

Both NG108s and OECs attached to micro-HFs became aligned along their length. NG108 cells extended neurites along the fibres to form connections with neighbouring cells, and OECs extended along the fibres appearing to increase the number of neurites extended from the NG108s (Figure 1B). Alignment of the cells along the fibres was quantified using a custom-made ImageJ macro plugin.

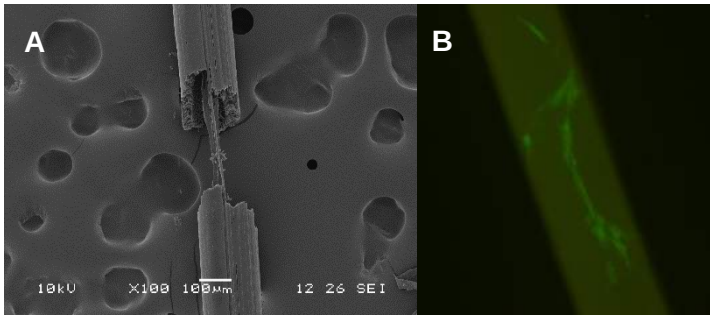

Figure 1: A) Scanning Electron Microscopy image of micro-HFs, showing the inner polycaprolactone and outer polystyrene, with the linear indents running parallel along the fibre. B) Live dead stain 6 days post-seeding of OECs and NG108s seeded at 20,000:1,000 cells/cm^2 respectively. Fibre was coated with Laminin.

CONCLUSION

NG108s aligned along the fibres with the help of OECs as opposed to their characteristic spread in a 2D culture. Further work with other cell types e.g. astrocytes will be conducted to determine its uses as a model.

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Schiff base new ligand derived from camphor with folic acid synthesizing and characterizing it with some metal ions.

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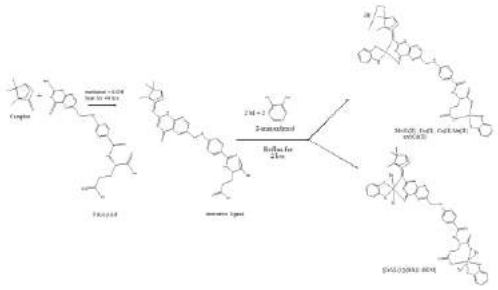
INTRODUCTION

Folic acid:- (pteroylglutamic acid) heterocyclic compound[1] is composed of three large sub-components. These are the pteridine ring, para-amino benzoic acid and glutamic acid. Glutamic acid is an amino acid that the body can actually synthesize by its self and found in proteins. **Camphor:-** is found in wood of the camphor laurel, a large tree found in Asia, as a white translucent crystals solid with strong aromatic odor [2], m.p (175-177 °C), it is soluble in water, acetone.

MATERIALS & METHODS

$[C_{29}H_{31}K_2N_7O_6]$ ligand has been formed from the reaction of (0.55 g) camphor with (2 g) folic acid by condensation reaction in methanol in the presence of calculated amount of KOH gave Schiff base ligand [L] in (85 %) yield as shown in the scheme below. The ligand and its complexes has been characterized by spectroscopic methods.



RESULTS & DISCUSSION

The sharp absorption bands at (1743 cm^{-1}) due to the υ(C=O) stretching vibration of carbonyl group of camphor **.** The spectrum of folic acid exhibits two sharp absorption bands at (3414 and 3547 cm^{-1}) assigned to the stretching vibration of υ_{sy}(N-H) and υ_{asy}(N-H) of the primary amine (R-NH_2) group**.**

CONCLUSION

The ligand and its complexes has been characterized by spectroscopic methods. The proposed structure for complexes are:- Tetrahedral and Octahedral structure is proposed for the metal complex

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Fast Synthesis of ZnMgO Nanowires by the Microwave-Assisted Hydrothermal Method

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Oral ☐ Poster ☒

INTRODUCTION

One-dimensional nanomaterials, with their unique properties, show enormous potential applications in electronics, electrophonics, composite materials, medical and others. Recently, the formation of ZnMgO nanostructures have reported in many papers with different methods such as thermal evaporation. microwave technology is a new technology for the development of the green chemistry and it is an important method for synthesis of nanostructures with uniform particle size distribution and versatile morphology. Microwave process has to be simple and easy to operate, rapid heating in comparison with the conventional one and reduce the time reaction[1-3]. In this work, we produced a performance ZnMgO nanotube via a facile microwave-assisted hydrothermal process with under considering the effect of processing parameters such as, time, temperature, and concentration of basic solution on the growth of nanocrystals since it is the deterministic factor in this process. Moreover, the structural of the produced nanoparticles performed using XRD, SEM and EDS.

EXPERIMENTAL

Synthesis of ZnMgO nanowires by directly as follows: 0.6 M of magnesium acetate tetrahydrate $Mg(CH_3OO)_2{\cdot}4H_2O$ and zinc nitrate hexahydrate $Zn(NO_3)_2\ 6H_2O$ was mixed with 0.4 M of urea in 100 ml distilled water. The mixture was stirred for 10 min and then transferred into Teflon-lined autoclave. The autoclave was sealed and maintained to 220°C for 2 h in Ethos 1, microwave furnace with a power 1000W, then allowed to cool down to room temperature. The precipitates were collected by centrifugation at 6,000 rpm for 5 min, and then we have a nomination with distilled water to reduce the agglomeration, and later dried at 80 C˚ for 3 h. Finally, we produce white powder.

RESULTS AND DISCUSSION

The reflection peaks characterizing ZnMgO were identified, these were indexed to the (0 0 2), (1 2 0), (1 1 -3), (1 0 1), (2 1 0) and (0 2 1) diffraction planes indicated from the typical X-ray diffraction pattern of synthesized ZnMgO nanotubes. Also, the crystallite size, as obtained from the Scherrers' formula, was 26.51 nm.

For the micro-structural analysis, the as-synthesized samples were directly transferred to the SEM chamber without disturbing the original nature of the products. Fig. 2 (a,b) show the low and high magnification SEM images of ZnMgO nanotubes. Fig. 3 demonstrates a typical EDX analysis of the as-grown ZnMgO nanotubes.

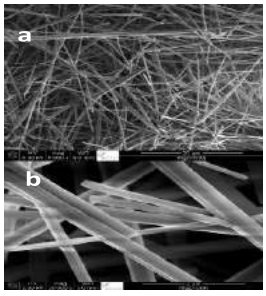

Fig. 2. Shows the typical (a and b) low and high-resolution SEM images.

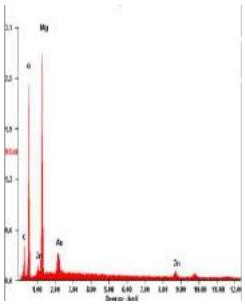

Fig. 3. EDX analysis confirming the existence of all elements

CONCLUSION

We describe a novel simple method to synthesize MgZnO nanotubes byusing microwave hydrothermal technique.

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Core–shell–shell cytocompatible polymer dot-based particles with near-infrared emission and enhanced dispersion stability

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Oral ☐ Poster ☒

INTRODUCTION

Polymer dots (PDs) are nanometre-sized particles prepared from semiconducting polymers, and are promising fluorescent probes for biomaterials applications, such as in vivo cellular imaging, tumour targeting, as well as biosensors and LEDs. PDs are attractive for biomaterials applications because they have reduced cytotoxicity compared to inorganic quantum dots. Of particular interest is including near-infrared (NIR) dyes into the PDs to enable NIR imaging, which is deeply penetrating in human tissue.

Unfortunately, nanoprecipitation though well-established, limits the morphologies available to a simple PD core with a stabilising shell [1].

MATERIALS & METHODS

Here, novel cytocompatible composite PD particles have been synthesised with a unique core–shell–shell morphology. PDs were prepared by nanoprecipitation of MEH-PPV, with an added near-infrared dye (NIR775), and PSMA surfactant. The pH of the system was then reduced in order to make the surfaces more hydrophobic, and a comonomer feed, consisting of ethyl acrylate (EA), methacrylic acid (MAA) and butanediol diacrylate (BDDA), together with ammonium persulfate (APS), was added and the mixture heated to 80 ^{o}C.

RESULTS & DISCUSSION

The PD aggregates acted as seeds for PEA–MAA–BDDA shell growth under starved feed emulsion polymerisation conditions. Additional PDs also adsorbed to the PEA–MAA–BDDA shell to give CSS composite particles.

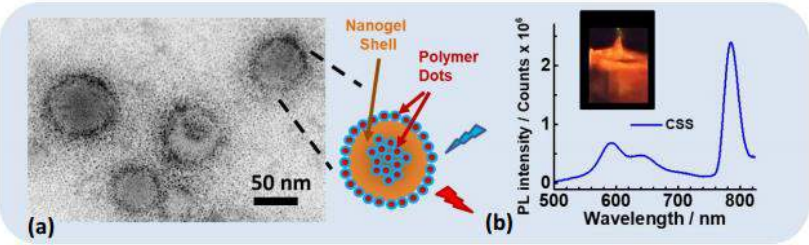

Figure 1: (a) Representative STEM image of CSS particles. Inset shows structure of the particles. (b) PL emission spectrum, and photograph (Inset), of CSS dispersion.

CONCLUSION

The resulting CSS particles show near-infrared emission, improved fluorescent brightness and enhanced colloidal stability compared to pure PDs. Furthermore, the particles also show non-radiative resonance energy transfer (NRET) with a model dye.

ACKNOWLEDGEMENTS

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Synthesis and optimisation of lipid-hybrid nanoparticles loaded with a mixture of two antiretroviral drugs for the treatment of HIV

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Oral ☐ Poster ☒

INTRODUCTION

The aim of this study is to synthesize lipid-hybrid nanoparticles (LPHNs) loaded with a mixture of two antiretroviral drugs for the treatment of human immunodeficiency virus (HIV). This system which is composed of a polymeric core and a lipid shell, combines the advantages of both polymeric nanoparticles and liposomes. These advantages include the synthesis of nanoparticles from biodegradable materials with high drug loading, relatively small size and low polydispersity. Adding ligands to the surface of the LPHNs for active targeting, the drug release can be easily be controlled and the produced particles have high stability.[1]

MATERIALS & METHODS

A nanoprecipitation method was used, where 1.5 mL of 2.5 mg/mL solution of poly (lactic-co-glycolic acid) (PLGA) in acetonitrile, is slowly added to a stirring preheated 4% ethanol solution of soybean lethicin (150 µg/ml), the mixture is then vortexed for 3 minutes and left stirring for 2 hours, the mixture is then freeze dried for further assessment.

RESULTS & DISCUSSION

[The synthesis method is reproducible and the Z-average of the produced LPHNs was around 120 nm with PDI of 0.3 before freeze drying, increasing the amount of the drug did not affect the size, even when the drug loading % increased from 0 % in case of the blank LPHNs to 50% in case of the drug-loaded LPHNs. Adding PEG (Mn 2050) as a cryoprotectant during freeze drying reduced the aggregation of the particles and made them easy to re-disperse. The drug loading and encapsulation efficiency were relatively high compared to other drug delivery systems].

CONCLUSION

This work illustrates a novel design of LPHNs to treat HIV, using a mixture of two antiretroviral drugs. The lipid nature of the surface of the particles may potentially enhance the uptake of the particles by Peyer patches to reach HIV reservoir sites.

ACKNOWLEDGEMENTS

[University of Liverpool / Schlumberger foundation]

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ACELULLAR GELATINE-ALGINATE SCAFFOLDS FOR DENTINE-PULP REGENERATION

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INTRODUCTION

Dental decay and poor long-term outcomes of traditional endodontic treatments have led the search for new dental tissue regeneration strategies. There is a lack of biomaterial approaches that harness the native dental pulp stem cells (DPSCs), which constitute one of the main agents responsible for the intrinsic regenerative capabilities of the pulp. To achieve this, a hybrid gelatine-alginate scaffold crosslinked via tetrazine-norbornene click chemistry incorporating bioceramic particles as an odontogenic moiety is proposed.

MATERIALS & METHODS

Sodium alginate (KIMICA, Japan) was modified with 2-norbornene (Sigma-Aldrich, UK) and gelatine (Nitta Gelatin Inc. Japan) will be functionalised with 5-(4-(1,2,4,5-tetrazin-3-yl)benzylamino)-5-oxopentanoic acid, which is being synthesised using nickel triflate as catalyst as described by Alge et al.[1] Proton Nuclear magnetic resonance (^{1}H NMR) will be used to characterise the tetrazine and confirm the functionalisation of alginate and gelatine with norbornene and tetrazine, respectively. Biphasic calcium phosphate (BCP), a mixture of hydroxyapatite (HA) and tricalcium phosphate (TCP) was prepared via wet precipitation and calcination at 1000 ºC. Bredigite ($Ca_7Mg(SiO_4)_4$) and ß-dicalcium silicate (ß-DCS; Ca_2SiO_4) were synthesised via a sol-gel process and calcination at 1150 ºC and 800 ºC, respectively. X-ray diffraction (XRD) was used to assess the crystallinity and formation of the bioceramics. Extracts of these were prepared via incubation at 37 ºC and 5 % CO_2 in DMEM for three days at 200 g/L. DPSCs were cultured in dilutions of the extracts (from 0 to 100 g/L) and MTT assays were performed after 1, 3 and 5 days to assess DPSC proliferation.

RESULTS & DISCUSSION

XRD spectra confirmed the formation of BCP with a high ß-TCP/HA ratio (approximately 80/20), pure bredigite and ß-DCS after calcination. A more prevalent ß-TCP phase is considered desirable as BCPs with higher ß-TCP/HA ratios have been described to be more odontogenic, presumably due to the higher bioresorbability of ß-TCP.[2] Ceramic extracts displayed no significant DPSC cytotoxicity against control (media without extract), except for BCP extracts for which DPSC viability greatly decreased at the highest concentrations, (2x and 4x dilutions) but remained high at the lowest concentrations (16x and 64x dilutions). Polymer modification with tetrazine and norbornene moieties allows for bio-orthogonal crosslinking which will enable encapsulation of bioactive molecules such as growth factors and cytokines to engineer endogenous DPSCs.

CONCLUSION

In this work, preparation and characterisation of the main components of an acellular scaffold for dentine-pulp regeneration is presented. The hybrid scaffold combines the tuneable mechanical properties of alginate with the pro-attachment moieties and biodegradability of gelatine. Future work includes optimisation of hybrid scaffold parameters such as porosity and Young's modulus to support DPSCs in-vitro and incorporation of bioceramics and other odontogenic elements for differentiation of endogenous DPSCs.

ACKNOWLEDGEMENTS

We would like to thank the Department of Bioengineering at Imperial College London for providing the funding and resources to carry out this work.

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Developing a novel ocular adhesive for corneal perforations

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Oral ☐ Poster ☒

INTRODUCTION

Corneal scarring and vascularization is a major cause of blindness worldwide, second only to cataract [1]. This study aims to develop a novel biodegradable adhesive to be used in the treatment of corneal damage and perforations, eradicating the need to use toxic materials such as cyanoacrylates. Owing to its excellent biocompatibility, optical clarity and viscoelastic behaviour, silk fibroin (SF) is a promising material for ocular tissue engineering. In order to achieve an adhesive which may be polymerised *in situ,* this work focuses on SF methacrylation using glycidyl methacrylate (GMA).

MATERIALS & METHODS

Briefly, degummed SF was dissolved in 9.3M lithium bromide solution at 60°C. GMA was added to the SF solution at a rate of 0.5 mL/min, and allowed to react for 3h at 60°C. Methacrylated-silk fibroin (SF-MA) was then dialysed against deionised water for 5 days. Finally, the solution was lyophilised for 2 days to generate a white porous foam. The degree of methacrylation (DM%) was quantified by proton nuclear magnetic resonance (^{1}H-NMR).

RESULTS & DISCUSSION

Being a structural protein, fibroin contains amino and carboxylic groups that can be modified with several functional groups. In this study, fibroin was methacrylated through the reaction of GMA with the free amines in the lysines, introducing vinyl groups in the polymer chain. This modification was confirmed by the lysine signal decrease at δ = 3 ppm and the appearance of the vinyl group signal at δ = 6.2 ppm (Fig. 1). SF-MA with low (5.4 $\pm$ 0.6%) and medium (10.6 $\pm$ 0.2%) were obtained by varying the amount of GMA added from 6 to 10 % (v/v).

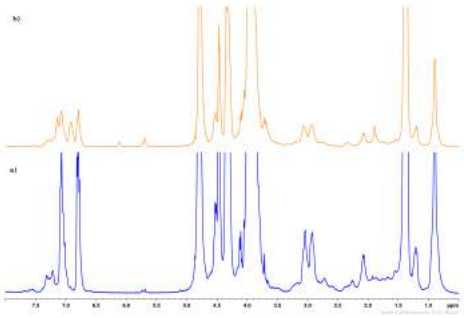

Figure 1: ^{1}H-NMR spectra of raw silk fibroin (a) and SF-MA (b).

CONCLUSION

In situ forming adhesives are very attractive materials due to their ability to adapt to the perforation before being cured, avoiding potential leakages. Importantly, the mechanical properties of SF-MA are controllable by changing the DM% and the polymer concentration. In the future, the application of biocompatible adhesives could reduce the demand of human corneal transplants, and the use of cyanoacrylates and sutures.

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Control of Mesenchymal Stem Cell and Articular Chondrocyte Morphology using Large-Area Chemical Nanoarrays by Polymer Pen Lithography

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Oral ☒ Poster ☐

INTRODUCTION

It is well established that cells sense and respond to changes in stiffness, topography and material chemistry. In parallel, recent advances have proven that cells can sense and respond to stimulus at the sub-micron/nano scale. Here we report on the use of polymer pen lithography (PPL), to reproducibly fabricate large-area chemical nano-arrays, that are designed to control the spatially defined interaction, at the nano-scale, between selected chemical groups (-NH_2 and -CO_2H) and human mesenchymal stem cells (MSC) and human articular chondrocytes. The data presented defines the ability of selected chemical groups to control initial cell adhesion, and focal contact formation of both MSC and chondrocytes. Distinct differences in initial cell adhesion between MSC and chondrocytes on selected nanoarrays were observed. A definitive relationship between spatial orientation of integrins/focal contacts and presenting chemical group is presented.

MATERIALS & METHODS

16-mercaptohexadecanoic acid (MHA/-CO_2H) or 11-amino-1-undecanethiol (AUT/-NH_2) was patterned using PPL with formation of square arrays on large-area gold surfaces (2 cm x 2 cm). Each array consisted of a feature size (modified area) 300 nm ± 5 nm, with variations in the spatial distribution of adjacent features ranging from 1-3 μm. Arrays were passivated with (11-mercaptoundecyl)hexa(ethylene glycol) (m-PEG) enabling controlled interactions with the chemical groups of interest at the point of contact. MSCs (Lonza, UK) were cultured in contact with selected surfaces in basal medium for up to 28 days. Human articular chondrocytes (Lonza, UK) were subcultured for 3 passages using DMEM supplemented with 10% FCS. Levels of adhesion, and phenotype expression were defined using immunofluorescence.

RESULTS & DISCUSSION

Data obtained has demonstrated that changes in the nano-scale resolution of presenting –NH_2 and –CO_2H groups has distinct ability in controlling initial MSC and chondrocyte adhesion. Selected MHA chemical arrays induced clustered cell morphology whilst in contrast AUT patterned surfaces with identical topography design showed little to no MSC adhesion but supported chondrocyte adhesion. However, AUT chemical nanoarrays with reduced spatial distribution and increased amount of features led to widely spread MSC and chondrocyte morphology.

CONCLUSION

We demonstrated that defined chemical nanoarrays with various presenting end groups combined with feature size and spatial distribution have successfully controlled and demonstrated distinct initial integrin binding of MSCs and chondrocytes. Research shows that both chemistry and associated spatial distribution of cell adhesive areas are essential design criteria in controlling MSC and maintaining terminally differentiated chondrocyte morphology.

ACKNOWLEDGEMENTS

This project is sponsored by the Leverhulme Trust.

Magnetic hydrogels: Tissue engineering constructs with switchable stiffness

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Oral ☐ Poster ☒

INTRODUCTION

When engineering a specific tissue, multiple factors dictate the design process, especially when attempting to create a clinically viable regenerative medicine. For example, the ability to '*switch*' the material properties of a scaffold from a 'soft' *in vitro* model, to a temporary 'stiff' material to enable transport/ implantation, is a unique and advantageous characteristic that this study aims to explore. In this work we target this reversible switch of stiffness to the application of neural tissue regeneration. By crosslinking hybridized magnetic nanoparticles into a tunable and biocompatible synthetic hydrogel, a scaffold that is analogous to the target tissue can be manipulated for clinical applications. Here we report the synthesis, surface modification and incorporation of magnetic nanoparticles into polymer networks to afford a magnetically stimulated gel.

MATERIALS & METHODS

Hybridised magnetic nanoparticles (HNPs) were synthesised according to previous work.[1,2] Briefly, gold-coated iron oxide nanoparticles containing a poly(ethylenimine) (PEI) intermediate layer (2 mL) were stirred with allyl methyl sulphide (0.5 mL) and sonicated with a pre-polymer solution of either poly(ethylene glycol) methyl ether methacrylate (PEGMA) or hydroxypropyl methacrylamide (HPMA). The resultant mixture was injected into moulds and cured using UV light for 35 minutes. Scanning electron microscopy was used to visualise the internal morphology of each gel.

RESULTS & DISCUSSION

Hydrogels that could be influenced by magnetic fields were synthesised (Figure 1). The introduction of HNP's into the polymer network resulted in a crosslinked hydrogel that could be manipulated using a neodymium magnet when in close proximity (Figure 1 A-B).

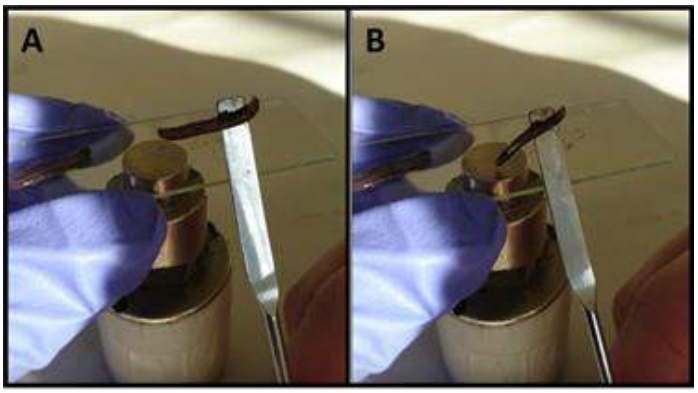

Figure 1: A PEGMA hydrogel containing HNPs responds to the magnetic field of a neodymium magnet. At rest (A), the hydrogel does not experience a magnetic force powerful enough to disform the hydrogel from it's natural shape. In close proximity (B), the hydrogel is drawn towards the magnet as a result of the encapsulated HNPs.

CONCLUSIONS

Preliminary observations indicate that the encapsulation of HNPs into the synthetic polymers results in a hydrogel that can be influenced by a magnetic field. However, magnetorheological studies are required to quantify the change in storage/elastic modulus.

ACKNOWLEDGEMENTS

The authors would like to thank the ESPRC for funding, the Loughborough Materials Characterisation Centre (LMCC) for their facilities, and Dr Claire Hoskins of Keele University, for help in synthesising the HNP's.

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Poly(acryloyl-hydrazide) as a versatile scaffold to induce bacterial aggregation

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Oral ☐ Poster ☒

INTRODUCTION

About 99% of the world's population of bacteria are found in the form of a biofilm at various stages of growth. Biofilm could be described as a consortium of bacteria attached to a surface and embedded in a matrix of extracellular polymeric substance. In this stage, the bacterial community behaves more like a supra-cellular organism rather than a unicellular one, showing off traits that individuals lack.

Our aim is to synthetize polymers that induce biofilm formation in *Escherichia coli*. We chose to synthetize Poly(acryloyl-hydrazide)[1], every monomer unit is easily modifiable with functional groups that carry ketones or aldehydes, these groups will be positively charged, or able to interact with membrane receptors. We used the RAFT polymerization technique, this allow control over the average length of the polymer chain

MATERIALS & METHODS

We were able to successfully synthetize the backbone and eight different modifications. Polymers were characterized by NMR and GPC, and tested against *E. coli* PHL 644 and its effect measured via: spectrophotometry, flow cytometry, optic microscopy, confocal microscopy and metabolic assays.

RESULTS & DISCUSSION

Three polymers were able to induce aggregation on *E. coli* PHL644: protonated Poly(acryloyl hydrazide), Poly(acryloyl-hydrazide-glucopyranose), Poly(acryloyl-hydrazide-mannopyranose). Clusters appear between the first 3 hours and aggregates can be seen with the naked eye, this aggregation is stable after applying dissociative forces. As clusters turn bigger and denser we measure a drop in optic density, as bacterial aggregates fall to the bottom of the culture. Optic microscopy pictures of bacterial samples inoculated with these polymers show clusters of bacteria embedded into a extracellular substance

CONCLUSION

Poly(acryloyl hydrazide) is a versatile scaffold that can be easily modified and is successful at aggregating and clustering bacteria.

ACKNOWLEDGEMENTS

Thanks to the University of Birmingham and John Evans fellowship of Nanotechnology for the funding of this project.

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Investigation of the anticancer activity of electron-deficient organometallic complexes

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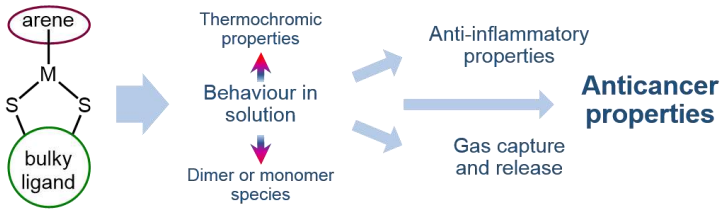
Oral ☐ Poster ☒

INTRODUCTION

Ruthenium and osmium organometallic complexes are an attractive alternative to platinum-based anticancer agents[1,2] since many compounds have demonstrated promising properties such as anticancer and antimetastatic activity, low toxicity and good selectivity.[3,4] Electron-deficient metal complexes have been isolated as air- and water-stable compounds which possess unique properties, for instance high symmetry, stability, robustness, anticancer activity, and can be easily functionalised to alter the overall activity of the complex. Here, we will discuss the efficient synthesis of four 16-electron metal complexes, their antiproliferative activity towards HCT116 *p53*+/+ and HCT116 *p53*-/- cells, and their effect on regulation of genes related to DNA damage repair processes, growth arrest, and apoptosis.[5]



MATERIALS & METHODS

Ruthenium and osmium complexes have been synthesised according to known procedures and characterised by ^{1}H NMR and UV-vis spectroscopies. Antiproliferative activity of the complexes in HCT116 *p53*+/+ and HCT116 *p53*-/- cell lines has been determined by an MTT assay. Gene expression studies include RNA extraction, synthesis of cDNA and qPCR assays.

RESULTS & DISCUSSION

The electron-deficient complexes reported here have demonstrated different results in terms of cytotoxicity and gene expression studies and this provided an indication of what the activity of the complexes might be and what processes they induce in HCT116 *p53*+/+ and HCT116 *p53*-/- cancer cells.

CONCLUSION

Based on gene expression studies, complexes appear to be cytotoxic or cytostatic. The natures of the metal ions and ligands influence the overall activity of the complexes.

ACKNOWLEDGEMENTS

We thank The Royal Society (University Research Fellowship No. UF150295), and the Academy of Medical Sciences (Springboard Award SBF003\1170).

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A novel pH/strain sensing blue-emitted nanogel probe and hydrogel application

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Oral ☐ Poster ☒

INTRODUCTION

Conventional hydrogels are fragile because of the uneven distribution of elastic chains. Common means such as TEM, SANS, etc. are expensive and inconvenient in order to be able to study the changes in the internal structure of the hydrogel. Here, we have developed an easily constructed novel nanogel probe based on NRET to report changes in the internal environment of the three stimulated ''host'' hydrogels.[1]

MATERIALS & METHODS

Ph and An fluorophore pairs are copolymerized into Poly(MMA-MAA-EGDMA) nanogel ($NG_{Ph/An}$) by emulsion polymerization. Afterwards, the $NG_{Ph/An}$ nanoprobe were incorporated into the doubly crosslinked nanogel, Poly(acrylamide) (PAAm) hydrogel and a tough nanocomposite gel.[1] Data were mainly characterized by PL.

RESULTS & DISCUSSION

Blue-emitting nanogels ($NG_{Ph/An}$) can transforms sensitively nanoprobe in the environment pH, which is designed on account of the notion of pH-responsive Non-radiative resonance energy transfer (NRET) induced by swelling configuration (Fig 1a). Furthermore, the assembled pH-responsive doubly crosslinked polyacid hydrogel (DX NG($NG_{Ph/An}$)) that displayed blue-emitting ability, pH-sensitive swelling-shrinking ability, and the apparently transformational NRET signal can be used to probe calcium ion concentration and served as drug carrier to model pH-triggered release (Fig b-d). Meanwhile, poly(acrylamide) hydrogel containing nanoprobe (PAAm-MBAAm($NG_{Ph/An}$)) and (PAAm-Lap($NG_{Ph/An}$)) also exhibited remarkable NRET compatibility of nanoprobe in composites with changed pH and compressive strain respectively (Fig e-f). [1]

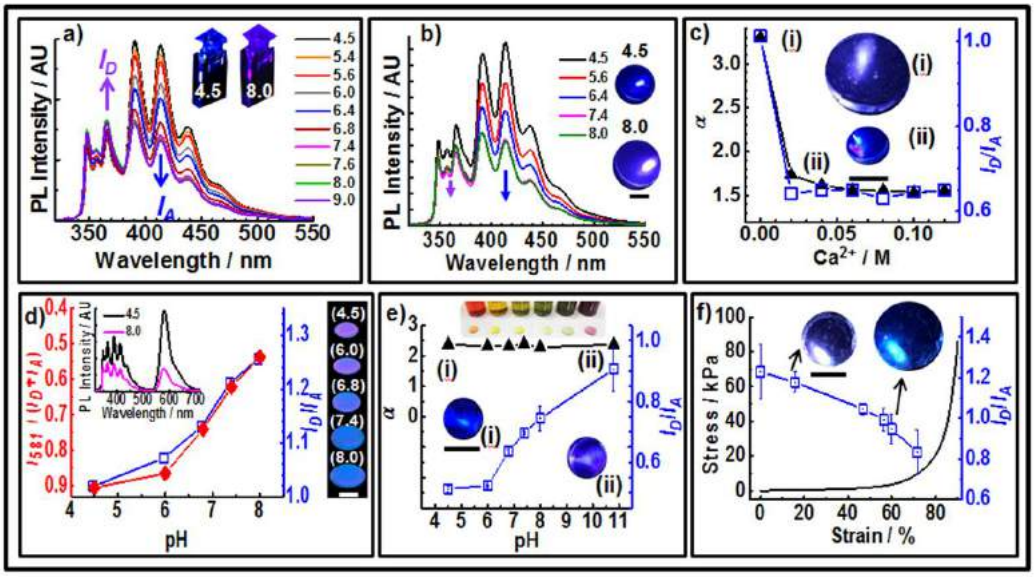

Figure 1 *PL of pH-responsive swelling $NG_{Ph/An}$ nanogel probe (a), DX NG($NG_{Ph/An}$) gels (b). Ca^{2+}-triggered collapsed in DX NG($NG_{Ph/An}$) gels (c). Molecules monited in DX NG($NG_{Ph/An}$) gels (d). pH-sensing PAAm-MBAAm($NG_{Ph/An}$) gel (e). Compressive-strain sensing in PAAm-Lap($NG_{Ph/An}$) gels (f).*

CONCLUSION

This study has introduced a versatile nanogel probe ($NG_{Ph/An}$) and the prospects for the $NG_{Ph/An}$ probe composites may have potential application as biological diagnosis or stimuli drug delivery or intervertebral disc repair.[1]

ACKNOWLEDGEMENTS

This work was supported by a 5 year EPSRC Established Career Fellowship awarded to BRS (M002020/1).

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A novel calcium chelating agent for the treatment of corneal mineralisation

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Oral ☐ Poster ☒

INTRODUCTION

Trauma, inflammation or systemic chemical imbalance can result in a build-up of mineralisation in the corneal tissue in both animals and humans. Corneal mineralisation can occur with corneal ulcers, or in band keratopathy. Current treatments to remove mineral build-up involve mechanically or chemically removing the epithelial layer and dousing the affected area with 1% EDTA solution, normally performed as an out-patient procedure under local anaesthetic. Although this method has shown high efficacy, the trauma to the epithelial layer leaves patients at risk of further complications. If other chelating agents with enhanced penetrative ability could be used to remove the mineralisation, without the associated trauma to the epithelial layer, the invasiveness of the treatment could be reduced. In this study, we investigated the capacity of sodium hexametaphosphate to mediate this de-mineralisation process.

MATERIALS & METHODS

The influence of clinically relevant concentrations of sodium hexametaphosphate and EDTA solution on the surface of the cornea were compared using *in vitro* and *ex vivo* models. *In vitro* cell toxicity of both solutions on primary human corneal fibroblasts and epithelial cells were investigated using cell proliferation (CyQuant) and cell metabolism (MTT) assays. For the *ex vivo* assessment of corneal penetration and tissue damage, both chelating agents were applied to the anterior surface of porcine corneal samples. The sectioned samples were then stained using H+E and DAPI to assess the health and structure of the cell layers and compare to chemical damage (sodium hydroxide) controls. Corneal penetration was assessed using fluorescein staining and post-test extraction. The demineralising effect of both chelating agents was assessed *in vitro* using a nanohydroxyapatite sol, and the potential demineralising effect of the extracted HMP and EDTA from the *ex vivo* model was compared

RESULTS & DISCUSSION

HMP was shown not to compromise the viability of human corneal fibroblasts at concentrations of up to 2mM as determined using the MTT assays. This concentration did not change the pH value of the media sufficiently to modify the colour of the culture media, while enabling demineralisation of the HA sol. Importantly, the HMP was shown to have superior and safer corneal penetration compared to EDTA, with EDTA causing chemical insults to the epithelial layers.

CONCLUSION

HMP demonstrated suitable hydroxyapatite demineralisation, corneal penetration and superior cell and tissue viability compared to EDTA. HMP presents as a possible alternative chelating agent to EDTA in the treatment of corneal calcification, which may prevent epithelial trauma whilst still maintaining effective levels of demineralisation.

Mechanical Properties of Gelatin-GO hydrogels for biomedical applications

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Oral ☐ Poster ☒

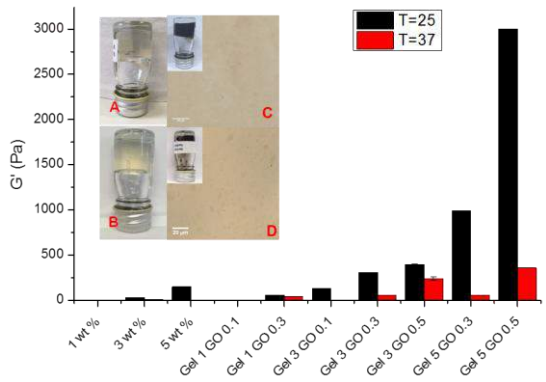
INTRODUCTION

The development of injectable hydrogel systems for biomedical applications is limited by their poor mechanical stability in-vivo. Graphene oxide (GO) has been shown to improve the mechanical properties of a wide range of hydrogel forming materials including peptides and gelatin.[1,2] Here, we present the enhancement of the mechanical properties of gelatin hydrogels at physiological temperatures using GO as a reinforcement agent.

MATERIALS & METHODS

Gelatin-GO gels (pH=7) of various compositions were made by a simple solution mixing technique. Oscillatory rheology was used to obtain the shear elastic modulus (G') to evaluate the mechanical properties of the hydrogels. Furthermore, the fibre morphology and chemistry of the hydrogels were investigated by AFM and ATR-FTIR respectively.

RESULTS & DISCUSSION



GO improves G' at 25 and 37°C which can be seen in Figure 1. This is due to favourable intermolecular interactions between GO sheets and gelatin fibres.

The value of G' increases with increasing GO and gelatin concentration with the maximum at 3003 Pa which was achieved with a composition of 5 wt% Gelatin, 0.5 wt% GO. This particular hydrogel composition also increased G' by 3 orders of magnitude at 37°C when compared to the control.

Figure 1: G' of gelatin-GO hydrogels obtained by oscillatory frequency sweeps measured at v= 1 Hz, γ=0.1 % (inset: Optical Images of hydrogels **A)** 3 wt% Gelatin **B)** 5 wt % Gelatin **C**) Gel 3 GO 0.5 wt % **D)** Gel 5 GO 0.5 wt %).

CONCLUSION

GO improves the storage modulus of physical gelatin hydrogels at 25 and 37 °C although improvements are seen at lesser extent at 37 °C

ACKNOWLEDGEMENTS

EPSRC and Graphene NOWNANO CDT

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Polymer scaffolds for 3D biocatalysis

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Oral ☐ Poster ☒

INTRODUCTION

This project is on developing robust biocatalysts in the form of enzymes expressed in biofilms. The aim is to design polymer scaffolds onto which bacteria adhere in a controlled manner, to form biofilms that can be used in biotechnology. Poly(acryloyl hydrazide) has been chosen as the polymer scaffold, due to easy post-polymerization modification resulting in highly functional polymers[1] that are predicted to interact with biofilm forming *Escherichia coli* K-12 strain.

MATERIALS & METHODS

Poly(acryloyl hydrazide) has been functionalized with a range of nitrogen heterocyclic aldehydes predicted to interact with bacteria. A range of experiments have been designed to analyse polymer-induced *E. Coli* K-12 clustering and subsequent biofilm formation. Biofilm factors have been probed with specific fluorescent stains, and bacterial viability and metabolism have been analysed.

RESULTS & DISCUSSION

It is thought hydrophobicity and charge interactions between the polymers and cells are the main drivers towards polymer induced clustering and we have shown that their viability and metabolism can be reliably tuned using specific polymers in optimised growth culture. Furthermore, data suggests that day old clusters have developed many of the traits of a biofilm; crystal violet and lectin staining have suggesting the presence of extracellular polymeric substances, a reporter gene has been used to monitor amyloid fibre production with the intensity of these traits being specific to the different polymers.

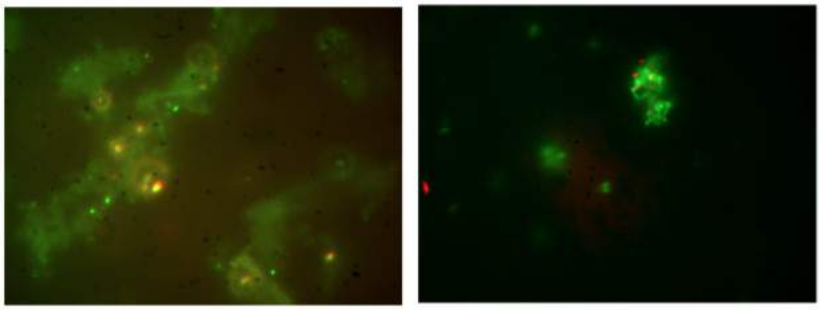

Figure 1: Fluorescence microscopy image of a day old polymer induced cluster in different media predicted to change the hydrophobicity of the polymer – poly(acryloyl hydrazide) functionalised with 2-Amino 3-Formylpyridine.

CONCLUSION

Now that we have developed conditions for polymer-induced bacterial clustering and biofilm formation, a deeper understanding of biofilm formation, metabolism, and expression factors will allow us to manipulate the resulting phenotype for industrial purposes.

ACKNOWLEDGEMENTS

BBSRC, MIBTP, IMI

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Next-generation 2.5D tissue culture surfaces to study cancer cell aggregation.

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Oral ☐ Poster ☒

INTRODUCTION

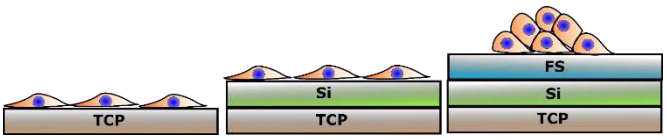
Cancer cell metastasis involves detachment from the extracellular matrix, ability to thrive as anoikis-resistant aggregates in blood or lymph vessels, and extravasate at secondary metastatic site. Investigating the dynamics of cancer cell aggregation could reveal important factors affecting metastasis and highlight novel players involved in epithelial to mesenchymal transition (EMT).

Studies have shown that by changing the surface topography and functionality, one can influence cellular behaviours such as proliferation, differentiation and morphology.[1] However, currently available tissue culture platforms involves culturing cells as 2D monolayers on tissue culture polystyrene (TCP), or grown as 3D spheroids that require advanced and expensive culturing techniques, and also the need to constantly change substrates to study the aggregation-disaggregation behaviour.

MATERIALS & METHODS

Our laboratory has developed 2.5D silica-modified surfaces: super-hydrophilic silica (Si) surfaces[2] (TCP functionalised with Tetramethyl orthosilicate) and hydrophobic Fluorosilane (FS) surfaces[3] (TCP functionalised with 1H,1H,2H,2H-Perfluorodecyltriethoxysilane).

RESULTS & DISCUSSION



Different cancer cell lines show unique aggregation-disaggregation profiles on these modified surfaces. On FS surfaces, most cell lines, such as SHSY5Y neuroblastoma cells seem to initially aggregate, then disaggregate after 24-48 hours. Although some cell lines such as A549 lung carcinoma cells remain aggregated on FS surfaces. Whereas on Si surfaces, most have reduced adherence and/or growth.

These aggregation profiles could be result of the Vroman effect. This protein adsorption theory describes that higher affinity proteins (such as fibronectin) replace the initially adsorbed high-mobility but low-affinity serum proteins (such as albumin). The differences in these profiles between different cancer cell lines could be because of variances in the extracellular matrix proteins that they secrete.

CONCLUSION

Establishing a 2.5D surface model with clinically relevant nanotopographic parameters could be important for revealing new factors of EMT and metastasis. These 2.5D approaches are becoming valuable, facile and inexpensive options to study cellular behaviour in more clinically relevant settings.[1]

ACKNOWLEDGEMENTS

I would like to thank my supervisors, members of the Biomolecular Materials and Interfaces Research Group, and John Van Geest cancer research centre.

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A dentine adhesive with remineralising potential

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Oral ☐ Poster ☒

INTRODUCTION

Resin-dentine bonding consists of etching to expose dentinal collagen followed by infiltration of adhesive resin. This interface between the dentine and resin composite restoration is termed the "hybrid layer". Hydrolytic and enzymatic degradation of collagen fibrils within the hybrid layer are major factors thought to destabilise the resin-dentine interface[1]. Recent strategies have incorporated acidic functional monomers with phosphate groups capable of interacting with tooth hydroxyapatite, stabilizing the dentine-bonded interface[2]. Our previous studies have shown that ethylene glycol methacrylate phosphate (EGMP) and 2 hydroxyethylmethacrylate (HEMA) based hydrogels enable precipitation of hydroxyapatites on interaction with simulated body fluids. Since copolymers of HEMA-EGMP show evidence of mineralisation, this study investigates adhesives with EGMP and reports initial physical properties towards a remineralising dentine adhesive.

MATERIALS & METHODS

An experimental dentine adhesive containing HEMA, Bis-GMA, UDMA, GDMA and TEGDMA with ethanol as a solvent was formulated with 0, 5 10 or 20 wt% of EGMP. The degree of conversion (DOC), thermal analysis, polymerization exotherm, surface free energy (YS) and water sorption (W_{sp}) and solubility (W_{sl}) were determined. The etch pattern on enamel and dentine was viewed under scanning electron microscopy (SEM). Results were statistically analyzed with a significance level set at $p<0.05$.

RESULTS & DISCUSSION

Incorporation of EGMP into experimental adhesives resulted in a significantly more hydrophilic formulation without significant changes in DOC, polymerization exotherm, glass transition (Tg) or melting temperatures (Tm). SEM images showed distinct etch patterns on enamel and dentine due to low pH of EGMP. Since the physical properties remain unaffected with inclusion of EGMP, this system with polar phosphate groups tethered to the polymer backbone within the hybrid layer may potentially enable higher affinity to tooth tissue and remineralisation.

TABLE 1: Mean (SD) YS and DOC, as well as median (IQR) Tg and Tm of the experimental adhesives (DBA)

Concentration of EGMP in DBA (%)	YS	DOC (%)	Tg (°C)	Tm (°C)
0	97.59 (4.3)	94 (3.4)*#	63 (3)	141 (6)*
5	99.88 (4.5)	98 (1)#	65 (2)	119 (5)ϒ
10	96.73 (5.2)	90 (1.5) *	65 (2)	135 (8)*ϒ
20	107.6 (4.8)*	85 (3.6)ϒ	67 (1)	126 (9)*ϒ
Different characters indicate significant differences within columns				

CONCLUSION

The potential of incorporating EGMP into a dentine adhesive is promising. Future work will focus on dentine bond strengths, hybrid layer degradation and remineralisation.

ACKNOWLEDGEMENTS

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Polyions complex and mesoporous silica nanoparticles for the fluorogenic detection of endotoxin and the delivery of Polymxin B.

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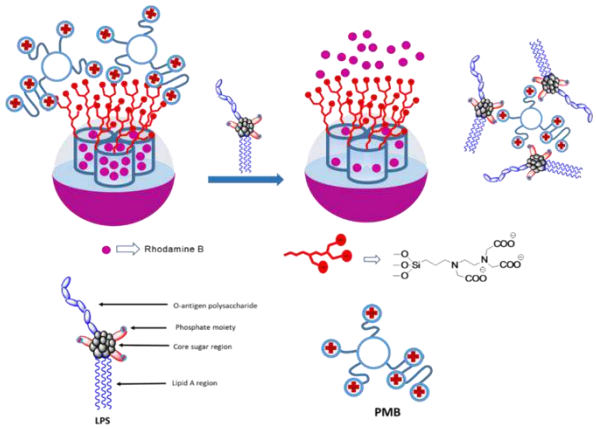
Oral ☐ Poster ☒

INTRODUCTION

[Give a brief background to the research being presented in this abstract, including any references to the literature in superscript format[1]] Endotoxin is a component of the outer cell membrane for all gram negative bacteria which is known biochemically as lipopolysaccharide (LPS) according to its component. The immune response of endotoxin depends on LPS structure which contains lipid A and polysaccharide which give it toxicity and immunigicity features respectively. In addition, LPS released by gram negative bacteria after death to the environment that leads to several health problems such as respiratory difficulties, pulmonary inflammation, asthma, fever, diarrhea and vomiting.[1] In parallel to that, Polymyxin B (PMB) is a natural cyclic cationic peptide active against gram negative bacteria, contain lipophilic part, has high affinity to bind and neutralize lipid A in LPS.[2] Taking into account the above mentioned facts, we prepared hybrid nanomaterial that was able to detect LPS using mesoporous silica nanoparticles (MSNs) loaded with rhodamine B and capped electrostatically using PMB. The designed MSNs keep blocked without rhodamine B release in the absence of LPS while undergo selectively uncapping when LPS is present, which lead to the release rhodamine B (Scheme 1).



Scheme 1: Schematic representation of nanoparticles **S1** in the presence of endotoxin.

MATERIALS & METHODS

For the same purpose, in my new fellowship in university of Birmingham, new nanoparticles for the detection of LPS and even the delivery of PMB in order to achieve antibacterial effect will be prepared. This new nanoparticles will based on the Polyion complex nanoparticles (PIC) which are enzyme responsive. This PIC will composed of poly charged polymer contain peptide sequence that interact electrostatically with PMB. The peptide sequence is specifically degradable with pathogenic bacteria enzyme which finally led to delivery of PMB close to pathogens that could cause highly toxicity effect.[3]

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Plasmonic and colloidal stability behaviours of Au-acrylic core–shell nanoparticles with thin pH-responsive shells

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Oral ☐ Poster ☒

INTRODUCTION

The localised surface plasmon resonance (LSPR) of Au nanoparticles (NPs) as well as its interaction with nearby entities provides a wealth of fundamental and practical information at the nanometre scale. Precipitation polymerisation is a scalable method and here we establish such a method to synthesise pH responsive Au-poly(methyl methacrylate) copolymer core–shell NPs without the need for pre-functionalisation. The comonomers used were methacrylic acid (MAA) or 2-carboxyethyl acrylate (CEA) and the shells were crosslinked with ethylene glycol dimethacrylate. A series of five core–shell systems with collapsed shell thicknesses less than 30 nm are studied. The LSPR properties of the core–shell NPs were dependent on the shell thickness and were successfully simulated using finite difference time domain (FDTD) calculations. The further study includes the enhanced colloidal stability and reversible pH-triggered aggregation of these core-shell NPs.

MATERIALS & METHODS

Au NP dispersion (20 mL, 2.97 M) was transferred to a three-necked flask and stirred magnetically (290 rpm). An aqueous SDS solution (1.0 mL, 4.12 mg mL^{-1}) was added and purged with nitrogen for 30 min. The solution was heated to 80 °C. A comonomer mixture (49.5 mg) containing MMA (80.5 wt%), MAA (17.5 wt%) and EGDMA (2.0 wt%) was added to water (5.0 mL). K_2HPO_4 (80 µL, 1.0 M) and APS (100 µL, 19 mM) were added which gave a pH of 5.3. The comonomer solution was then fed into the flask at a uniform rate (0.083 mL min^{-1}) using a syringe pump over a period of 1.0 h. The reaction was allowed to proceed for further 3.0 h and then quenched in an ice bath.

RESULTS & DISCUSSION

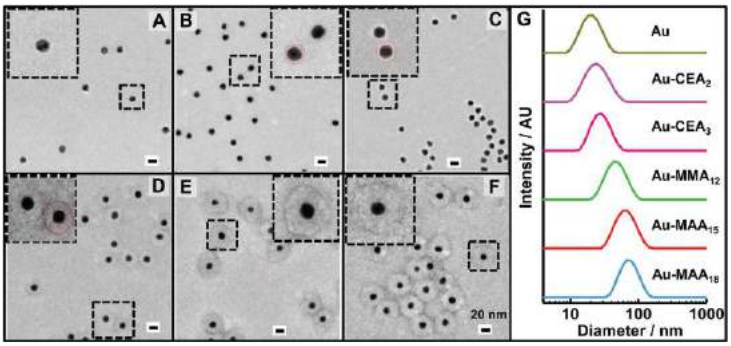

Figure 1: TEM images and DLS result of Au or core-shell NPs

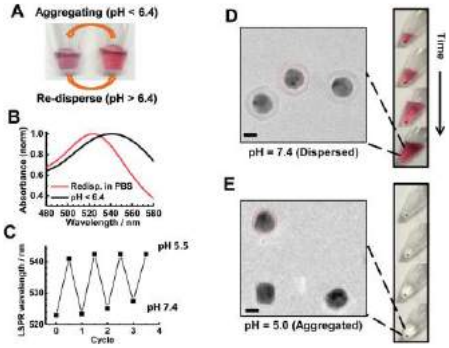

Figure 2: The reversible pH triggered aggregation

CONCLUSION

The Au-CEA NPs had the thinnest shell of any core–shell Au-copolymer system prepared using precipitation polymerisation, showed pH-triggered and reversible aggregation in the physiological pH region. This system demonstrated potential for being taken up within HeLa cells and reporting the local pH.

ACKNOWLEDGEMENTS

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Design and Test of self-assembling peptide systems for target cancer drug delivery

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Oral ☐ Poster ☒

INTRODUCTION

Cancers are still incurable and most of available therapies on clinic are not efficiently in modern society. Some of the effective components of antineoplastics might be degraded by enzymes or accumulate on off-target sites which decrease the efficacy of cancer drugs and in the case increase adverse side effect[1]. There is a necessity to make a delivery system which not only keeps the protein/peptide drugs from enzymatic degradation but also support in enhancing its absorption without changing its biological activity. Peptide-based hydrogels are excellent candidates for biomedical application due to their best outcomes in functional diversity, structural mechanical, high bio binding recognition, biodegradability, biocompatibility, tuneable mechanical properties and controlled release at target site[2]. Thus, using peptide hydrogels as nano-carriers are capable carrier systems for delivery of protein/peptide drugs.

Stemming from this, the study proposes to design the peptide nanoarchitectures and study the effects on anti-cancer activity of the modified peptide-drug hydrogel. Ultimately, the research aims to contribute to this field by conveying that the modified peptide is expected to be beneficial for the delivery of anti-cancer drugs.

MATERIALS & METHODS

1. Peptide powders was purchased from Biomatik (UK) and used without further purification.
2. Using FTIR to confirm the secondary structure of the peptide.
3. HPLC was used for purification analysis.
4. Shear Mixer was employed for making the peptide hydrogel.
5. Rheometer was used for detecting the mechanical properties of peptide hydrogel.

RESULTS & DISCUSSION

The results from FTIR shown that both of the peptide powder and peptide hydrogel are able to form β-sheet structures because there was an absorbance peak at around 1615cm^{-1}. Meanwhile, the peptide was purity enough through HPLC analysis. Besides, the stiffness of this peptide hydrogel could be changed at different pH, which was defined through rheological properties.

CONCLUSION

As a conclusion, much work should be done on the study of peptide hydrogels, discovering some novel properties of peptide hydrogels for the development of biomedical and biotechnology applications. Peptide hydrogels are capable of forming varies networks under specific environmental stimulus which might have different functions yielding a vast of interests in this research.

ACKNOWLEDGEMENTS

The authors would like to acknowledge funding from the Manchester Institute of Biotechnology.

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Towards the development of a mechanically and biologically relevant oral mucosa model to evaluate tissue integration approaches for dental implants

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Oral ☐ Poster ☒

INTRODUCTION

The oral cavity is lined by a mucous membrane known as the oral mucosa, an important tissue for dental implant integration. Attachment of the oral mucosa to the implant is essential to prevent bacteria migrating into the jawbone, potentially causing chronic infections with debilitating effects on patients and large cost implications[1]. Novel materials and antimicrobial approaches are continuously being developed, but these are difficult to translate into clinical practice due to a lack of sufficiently representative models. This work aims to develop a model of the oral mucosa, including 3D tissue culture and bacterial colonisation, to study integration of cells with different biomaterials surfaces. It is critical that we can test biomaterials in physiologically relevant environments. Therefore, this study will compare the mechanical properties of native tissue (porcine and human) with alginate and collagen-based hydrogels in order to select a model that is mechanically and biologically relevant.

MATERIALS & METHODS

Alginate solutions of 1, 2, and 3 % w/v were prepared and added to circular stainless steel moulds. Crosslinking of the hydrogel was performed with $CaCl_2$, with a gelation time of 10 minutes. The alginate hydrogel constructs were washed and placed in a 24-well plate for cell viability studies. 5 mg/ml rat tail collagen type I was diluted to 1, 2, and 3 mg/ml. 1 ml of each concentration was used to assess cell viability. The plate was incubated at 37ºC for 1 hour to allow the collagen to crosslink. A human keratinocyte cell line was added to the surface of both hydrogels. Cell growth was measured at 3, 7 and 9 days.

To assess the mechanical behaviour of the hydrogels utilised in the model, stress relaxation tests (30% strain) were performed on alginate gels. Dynamic mechanical analysis (DMA) was used to determine the frequency-dependent (0.1 – 1 Hz) viscoelastic properties of alginate gels and porcine/human oral mucosa. E’ and E’’ were calculated for each specimen tested. For the collagen gels, rheology was performed instead of DMA to determine its mechanical properties.

RESULTS & DISCUSSION

Preliminary mechanical testing has been conducted on alginate and collagen hydrogels. The findings are being compared to the properties of human/porcine oral mucosa to determine the most mechanically representative model. Here we will present our data comparing human/porcine tissue to *in vitro* constructed tissue models.

Furthermore, preliminary cell viability studies have been conducted on the hydrogel models. These showed that collagen gels supported significantly higher cell numbers than alginate gels, however, collagen hydrogels do not have the elastic properties of the oral mucosa.

CONCLUSION

It is imperative to ensure that a novel model is both biologically *and* mechanically relevant. Collagen-based hydrogels have been shown to have a higher cell viability, however they have poor mechanical properties. The mechanical properties of alginate-based hydrogels are more closely aligned to the elasticity of the oral mucosa, but alginate has poor cell adhesion and therefore reduced cell numbers. In future, the here tested gels can be used in a combination model to achieve a hydrogel model that has both mechanical and biologically desirable properties.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge financial support from the EPSRC through a studentship from the Sci-Phy Doctoral Training Centre at the University of Birmingham.

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A Comparison of Lattice Designs to Optimise Mechanical Properties in a Novel Lattice Hip Spacer Implant

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Oral ☐ Poster ☒

INTRODUCTION

Hip implant failure due to infection is a major problem with over 8000 patients in the UK receiving a revision due to infection in 2017[1]. The gold standard for revising these failed implants is a two stage procedure, including thorough debridement of the soft tissue and the use of a temporary hip spacer that elutes antibiotics, along with systemic administration to clear the infection[2]. These temporary hip spacers are often made of bone cement and so are not load bearing leading to long periods of bed rest for patients who are usually elderly[2].

Reinforcement of these temporary cement spacers may enable patients to load bear during this 6 – 8 week period. It may also be possible to use this supporting secondary phase to tailor release of the embedded antibiotic. The focus of this project is to develop a novel composite hip spacer comprising of a porous metal lattice filled with an antibiotic loaded cement capable of supporting the weight of the patient. Conventional implant manufacturing techniques, such as casting are unable to create the complex structures required. Selective laser melting is a metal additive manufacturing technique that allows significantly more design freedom through layer-by-layer manufacture. A number of different lattice structures have been investigated for use in orthopaedic applications and this work looks to investigate which offers the greatest strength while maintaining sufficient void volume to house an efficacious dose of antibiotic loaded bone cement. As a consequence all lattices were produced as 30% by volume metal to leave 70% of the volume for antibiotic eluting bone cement.

MATERIALS & METHODS

Various lattices designs, in the form of cylinders (12mm diameter, 15mm height) were generated in Element (nTopology, New York, USA), and built on a Renishaw AM500M (Renishaw PLC, Wooten-Under-Edge, UK) from gas atomised Ti-6Al-4V powder using optimised in-house parameters. After removal from the build substrate, the lattices were ultrasonically cleaned for three minutes to remove loose powder. Five different lattice designs were produced in triplicate (n=3). Compression testing was performed on the lattices in accordance with BS ISO 13314:2011. The testing was performed under displacement control at a rate of 0.6 mm per minute until the first of either; 50% total strain, or a maximum load of 100 KN was reached.

CONCLUSION

This preliminary study demonstrates the possibility to exploit additive manufacturing technologies to enhance the value of medical devices. More specifically, the design freedoms of these bottom up techniques have been exploited to generate porous lattice structure intended to structurally reinforce antibiotic bone cements for use in two-stage revision of infected hip arthroplasty.

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RGD-peptide functionalised Highly branched Poly(N-isopropylacrylamide)- *Synthesis and Cell-Lifting application*

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Oral ☐ Poster ☒

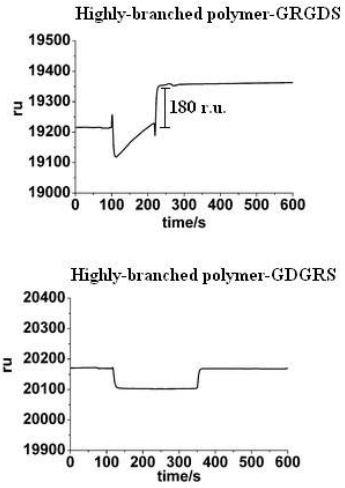
INTRODUCTION

RGD (in fibronectin) promotes cell adhesion in mammalian tissues through binding *cell surface integrins*. The highly-branched polymer, poly(N-ispropylacrylamide) ('HB-PNIPAM'), chain-end functionalised with RGD peptides and synthesised in our laboratory[1], was studied to assess the binding of *RGD*S groups with $\alpha_5\beta_1$ Integrin immobilised on CM5 SPR chips. A range of HB-PNIPAM-(GXG*RGD*S) hepta-peptide conjugates were also assessed by SPR, where it was revealed that when X=Proline (P) significant binding occurred between the polymer-peptide unit and the immobilised integrin.

MATERIALS & METHODS

Highly branched PNIPAM was synthesised *via* RAFT polymerisation of NIPAM with 4-vinylbenzyl-1-pyrrolecarbodithioate to give the polymer in high yield. The N-pyrrole-dithioate end groups were then converted to carboxylic acid chain-ends using a large excess of 4,4'-azobis-(4-cyanopentanoic acid). Following purification of the HP-PNIPAM (COOH) polymer using ultrafiltration, the chain-ends were modified by peptide coupling to a range of 'RGD' peptides, involving a final purification *via* ultrafiltration. The hepta-peptides were synthesised using solid-phase peptide synthesis (*Chemspeed Technologies*).

RESULTS & DISCUSSION



- RGD (in fibronectin) promotes cell adhesion in mammalian tissues through binding *cell surface integrins* (Dermal fibroblast cells express $\alpha_5\beta_1$Integrin receptors on their surface)
- Integrin was immobilised on a *Biacore* chip and highly branched PNIPAM polymers modified with cell-adhesive peptide GRGDS were eluted over the surface: *HB-PNIPAM-GRGDS binds* receptor (*via* RGD)
- No response in SPR using scrambled peptide chain-ended GDGRS highly-branched polymer

Polymer particles bind cell surface integrins on *dermal fibroblasts* and *endothelial cells* and at T>LCST (34^{0}C) particles collapse, *lifting cells* from culture substrates for transfer to new substrate.

Figure 1: *Surface Plasmon Resonance (SPR) results showing the binding of HB-PNIPAM-GRGDS highly branched polymer to immobilised $\alpha_5\beta_1$Integrin (Analysis carried out on Biacore 3000 instrument).*

CONCLUSION

After brief cooling of particle–cell dispersion to T< 34^0 C cells can grow on new substrates. No *trypsinisation* is required to detach cells/no centrifugation to collect cells post-detachment,facilitating *delivery to wound bed*

ACKNOWLEDGEMENTS We are grateful to the EPSRC (UK) for providing a studentship for Hopkins and a post-doctoral fellowship for S.Carter (GR/T19773/01).

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NOVEL ANTIMICROBIAL EMULSIONS: FORMULATION OF A TRIGGERED RELEASE REACTIVE OXYGEN® DELIVERY SYSTEM

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Oral ☐ Poster ☒

INTRODUCTION

Experts have predicted that by 2050 antimicrobial resistance (AMR) will kill more people than cancer, with deaths upwards of 10 million per year. With very few products in the research and development pipeline it is essential that research in novel antimicrobial treatments is undertaken [1].

The presence of glucose oxidase in honey enables the production of reactive oxygen species (ROS), such as hydrogen peroxide, a known antimicrobial. Currently, honey is an adherent, highly viscous product and with ROS production initiated by water, clinical usability is limited. SurgihoneyRO™ (SHRO) is a chemically engineered honey and it has been shown to eradicate drug resistant bacteria, such as Methicillin-Resistant Staphylococcus Aureus (MRSA) [2].

This study aims to improve delivery of ROS by formulating W/O emulsions that contain SHRO and phase inverts through addition of water and shear to become active in-situ.

MATERIALS & METHODS

Emulsions were created using a T18 Ultra Turrax® disperser (IKA, UK). An AR-G2 Rheometer (TA Instruments, UK) was used to determine the viscosity of the emulsions. Droplet size was characterised by use of a Malvern 3000 Mastersizer (Malvern Instruments, UK). Conductivity was measured using a HI99300 conductivity test meter (Hanna Instruments, UK). The presence of hydrogen peroxide was detected using a fluorescence hydrogen peroxide assay (Sigma Aldrich, UK). Zones of inhibition were used to test the *In vitro* antimicrobial activity against Staphylococcus Aureus, Pseudomonas Aeruginosa and Escherichia Coli.

RESULTS & DISCUSSION

Paraffin oil continuous emulsions formulated using the emulsifier polyglycerol polyricinoleate displayed shear-thinning and pseudoplastic behaviour. Viscosities ranging from 1.4 Pa.s to 19.3 Pa.s at a shear rate of 4.1 s^{-1} were achieved by changing the volume of the dispersed phase allowing for future application-specific modifications to be made.

The emulsion undergoes catastrophic phase inversion, evidenced by a change in conductivity from 0 μS in the non-aqueous state, to 220 μS in the sheared, inverted state. These emulsions generated, in most cases, sufficient levels of ROS to inhibit growth of clinically relevant bacteria.

CONCLUSION

This study demonstrates the development of innovative Reactive Oxygen® products that may be used as alternatives to current antibiotic-based treatments. These emulsions allow the controlled release of a water-sensitive active - an approach other actives with similar reaction initiators could take.

ACKNOWLEDGEMENTS

This research was supported by the EPSRC and undertaken in association with Matoke Holdings Ltd.

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Rapid Screening of Polymeric Transfection Agents for the Treatment of Glaucoma

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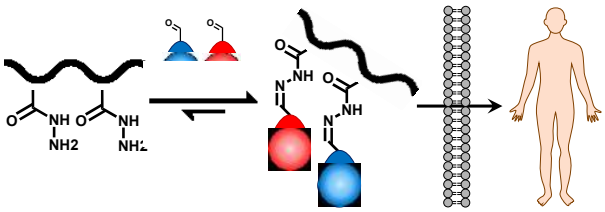
Oral ☐ Poster ☒

INTRODUCTION

Polymers aid in a variety of medical applications by enhancing the pharmacological properties of single molecule, including their cell penetration properties.[1,2] The secondary structure is particularly important for cell penetration into the eye for treatment of glaucoma due to delivery to the back of the eye requires the cornea to be overcome, which itself is a highly complex network of protective cell, membranes and barriers.[3,4] In comparison to intravitreal injection, the most common method of treatment,[5] eye drops are more acceptable to patients, who may self-administer outside of the clinic, however, the penetration issues need to be overcome. Thus, a polymer system may be designed and produced in order to navigate the cornea allowing eye drops to become a viable delivery method for a wider range of drugs than are currently available by topical administration.

MATERIALS & METHODS

New polymer formulated with click-able side chains, as described in the figure right and a controlled helical secondary structure, utilising documented rhodium catalysed reactions for a novel monomer. The polymer has been characterised via both chemical and biological methods, this includes but is not limited to 1H nmr, GPC, MTT assay and a novel cornea penetration assay.



RESULTS & DISCUSSION

The polymer has been synthesised and full characterised chemically with results denoting the structure; all characteristically broad peaks in the relevant region. Average $Đ_{GPC}$ = 1.44. Qualitative penetration through the cornea fluorescent data, showing that the polymer makes it through the cornea layers. Toxicity data describing non-toxic nature of the naked backbone polymer which is the excretion product

CONCLUSION

We have demonstrated that the new polymer system can be synthesized with a regular size and a low distribution of chain lengths. Furthermore we have shown that the polymer can pass through the multicellular layers of the cornea allowing for it to pass into the eye.

ACKNOWLEDGEMENTS

EPSRC through a studentship from the Physical Science for Healthcare Centre for Doctoral Training (EP/L016346/1).

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