HyMedPoly Newsletter

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"Drug-free antibacterial hybrid biopolymers for medical applications"

HyMedPoly

European Commission

MARIE CURIE ACTIONS

The overuse and misuse of antibiotics have led to the emergence of multi-drug resistant bacteria. Over the last years, drug-free therapies have been the focus of many research groups, including the development of antibacterial materials. The design of such materials includes loading biopolymers with antimicrobial molecules, performing chemical modifications with antibacterial functional groups, as well as developing materials possessing intrinsic bactericidal properties.

HyMedPoly project focuses on the development of such materials. The project is composed of universities and companies from across Europe and a cohort of 15 Early Stage Researchers from across the world.

HyMedPoly is part of the Horizon 2020 programme, a European Commission's initiative to develop European Industrial Doctorates with equal exposure to academics and industry, allowing them to combine research knowledge with business acumen.

Learn more by visiting the Official HyMedPoly Website, https://hymedpoly.eu/

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Heidelberg Meeting Highlights

The third HyMedPoly meeting was held on the last 9th to 11th November 2016 in the offices of Eurescom in Heidelberg, Germany.

The first day was dedicated to the internal meeting, during which the Early Stage Researchers (ESRs) shared their updates on the lab work and their training experience.

On the second day the Mid-Term Review took place. A Project Officer, Maria-Emma Campo-Cossio-Luhaces, and an External Expert, Prof. Miroslawa El Fray from West Pomeranian University of Technology, Szczecin, Poland, were present as representatives of the European Commission. In this context, the Scientific Coordinator, Prof. Ipsita Roy (University of Westminster), and Stuart MacLachlan (Lucideon) gave an overview of the project's activities to date. Each ESR presented the work to the Commission followed by a brief discussion. Both the research cohort and the partner representatives had meetings with the European Commission Project Officer and External Expert, separately.

The final day was dedicated to the Industry Training 3 – Forming Good Project Teams, run by Milon Gupta, Eurescom. After this, since some of the ESRs are focused on the development of medical devices and their coatings, Dr. Jochen Salber performed a demonstration on how to apply a central venous catheter. The demonstration showed how such catheters are applied in medical facilities, from the opening of the packaging that contains the catheter, followed by the insertion of the catheter itself until the cleaning procedure after the implantation is completed. The critical steps or potential stages that are likely to cause a bacterial infection were pointed out, and the aspects that should be considered when developing antibacterial coatings were discussed.

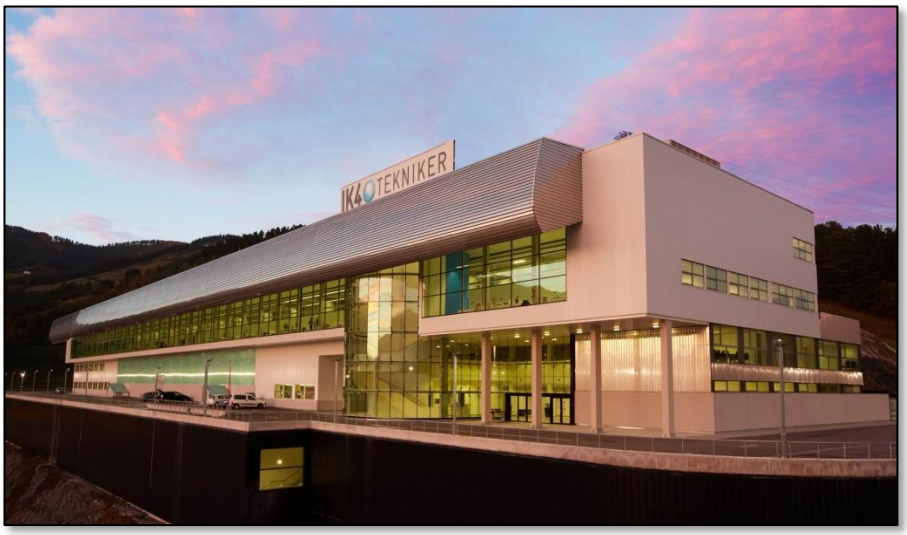
Bilbao Meeting Highlights

The fourth HyMedPoly meeting was held on 3rd and 4th May 2017 in the offices of Fundación TEKNIKER in Eibar, Bilbao (Spain).

During the first day, the partner representatives delivered short talks on the project and discussed some of the latest scientific challenges in the field of antibacterial materials.

Prof. Ipsita Roy (University of Westminster) gave a talk on Antibacterial Polymers of Bacterial Origin, with results from some of the ESRs. Prof. Valeria Chiono (Politecnico di Torino) presented an overview of the Antimicrobial Modification of Synthetic Polymers, focusing on the most innovative strategies investigated at the moment, including the latest work on AMPs and quorum sensing. Dr. Iban Quintana showed the technologies developed in Tekniker in the talk Antimicrobial Surfaces: Physical and Chemical Functionalisation, explaining two different approaches: passive, consisting of anti-biofouling and bacteriocidal, and active, involving coatings containing active compounds. Prof. Xiang Zhang (Lucideon) delivered a talk on Extending the Scientific Understanding and Practical Application of Newly Developed Antibacterial Materials, in which he emphasised the importance of innovation as well as the development of a product suitable for commercial application. Finally, Prof. Athul Bhaskar from University of Southampton discussed The Role of Modelling and Simulation in Understanding the Stiffness and Strength of Biostructures and Implants, where he proposed an insight in the engineering approach for the design of biomedical materials.

Stuart MacLachlan, from Lucideon, presented the Project Management Progress Since Mid-Term Review (November 2016-April 2017), where he talked about the successful feedback of the mid-term review and the website development, which now includes a description of each ESR and their background.



Bilbao Meeting Highlights/2

On the second day of the meeting, all the ESRs gave a ten-minute talk on the latest updates of their projects. Each presentation was followed by a brief discussion with the partner representatives, during which new ideas and suggestions were shared.

A tour of the laboratories of the company was then organised. The Research and Technology Centre work covers a wide range of technological solutions, including mechatronic systems, industrial maintenance, automation and industrial robotics, multifunctional surfaces, measuring and inspection, sensor devices and innovation and competitive intelligence. Tekniker collaborates with academic and industrial partners and it is involved in several international projects.

New Member: Faezeh Shalchy (ESR 12)

About the Project:

The research project is in the area of medical polymers for potential applications to biomedical implants and structures. It will look into the role of surface roughness and topography on the response of cell adhesion, proliferation and growth. There could be two possible applications in the longer terms – to maximise anti-microbial response and to enhance cell adhesion and growth for biomedical scaffolds. These could have important implications to healthcare in aging populations throughout the world.

The methodology envisaged would be theoretical and computational primarily, but some experiments are also planned. The use of computational elasticity and molecular modelling for multi-scale understanding of the structure-property relationship is proposed. The role of the elasticity of the solid surface on which cells grow will also be studied. Novel modelling techniques such as Dissipative Particle Dynamics are proposed for the understanding of the behaviour of matter at intermediate length scales.

About the Researcher:

Faezeh Shalchy is Early Stage Researcher 12 (ESR 12) from Hamedan, Iran. She received a gold medal in Chemistry Olympiad, 2005 and was admitted to the best University of Iran, Sharif University of Technology, without entrance exam. After her undergraduate studies in Mechanical Engineering, she was awarded a research/teaching assistantship to get her master's degree in the field of Civil Engineering at Worcester Polytechnic Institute, Worcester, MA, USA. Her previous research falls under the broad umbrella of studying mechanical behaviour of materials by the use of molecular modelling. The underlying science of all her research is mechanics and computational materials science with their application in engineering. She was always looking forward to using her chemistry and mechanics background in biology and biomedical engineering. She has experience with modelling different biopolymers and biological materials. Faezeh has also experience in finite element analysis of biological materials. Now, she is registered in PhD program at University of Southampton working under supervision of Prof. Atul Bhaskar.

Besides research, she is always passionate about art and design. She is always excited about experiencing new things and learning new skills. Knitting, swimming, cooking, painting, hiking and playing an Iranian musical instrument (Setar) are some of her favourite hobbies. Faezeh loves travelling to other countries, observing their culture, tasting their traditional foods and learning about their languages.

Experience at Clinical/Industrial Partner

Lucideon Limited

Agata

Agata Lapa, ESR 9, was located at Lucideon Ltd. , working there until the end of October 2017. The company based in Stoke-on-Trent, UK, has a long ceramic tradition. However, at the moment it is working on almost all types of materials for construction, industry and healthcare. Moreover, Lucideon is a specialist in bulk chemical and physical testing and advanced surface characterisation.

Working in a material consultancy is an important experience that corresponds well with academia by complementing it. Despite the different approach, this placement helps to understand the market needs and business approaches providing services and offerings for those market places. Students from the HyMedPoly project can observe and learn while working on their own projects inside this industrial environment. Participation in meetings and brainstorming for new project ideas is a great experience to understand the needs of potential clients and the process of developing appropriate solutions to their requests. Material development in a state-of-the-art facility such as Lucideon provides broader experience and expanded knowledge about materials.

Lucideon Limited is open to work with universities in many ways through programmes such as the MSCA and H2020 projects to individual placements. For example, every year students from like Queen Mary University of London (QMUL) can take part in a one-year placement at the company. Moreover, PhD students from HyMedPoly were present during a students' outreach exhibition hosted by the School of Engineering and Materials Science at QMUL. The HyMedPoly students were able to talk about their experiences on the joint academia-industry PhD programme in an informal environment and were also able to answer questions from the students present.

Experience at Clinical/Industrial Partner/2

Universitätsklinikum Knappschaftskrankenhaus Bochum

Ayesha

Ayesha, ESR 14, is currently working with the clinical partner of her project, namely "Universitätsklinikum Knappschaftskrankenhaus Bochum", Germany. The University Medical Centre "Knappschaftskrankenhaus" is an affiliate of the University Hospital Ruhr-University Bochum (RUB). Several clinical disciplines have research units and labs in the Centre of Clinical Research at the Ruhr-University. The "Medical Biomaterials" research unit of the Centre is involved in this project.

The development of new antimicrobial polymers with medical applications is a challenge, but it is even a bigger task for these polymers to eventually reach to clinic. The clinical experience gives an understanding of clinical aspects and clinician's preferences. Ayesha finds this experience as a very valuable factor for the successful training of industrial doctorates. Clinical experience is highly recommended, first to understand the challenges on practical grounds and then to develop the strategies to really implement the antibacterial materials produced.

Wounds, especially chronic wounds, have become a main therapeutic challenge. The clinical experience provides biological as well as clinical training in implant-associated infections. Realising the concept of clinical requirement for wound care is only possible by this practical connection at healthcare reform. This is to establish a thought and a framework for consideration that focus primarily on clinical demands and applications.

Patricia

Patrícia Varela, ESR 15, joined her clinical partner (Clinic of Surgery, Knappschaftskrankenhaus Hospital of the Ruhr-University Bochum) on January 2017. Already the contact with this clinical partner has been definitely influencing the scientific way of thinking of Patrícia. To listen and to understand how the current treatments are performed on various real patients with chronic wounds, which is her main focus on the project, is changing completely the perspective on how to proceed in laboratory investigation. There are so many specific aspects that we do not imagine to include in our research, if there is no contact with specialists that work in hospital environments.

Another advantage of this partnership is the possibility to perform studies that are closer to reality. Moreover, the ESRs with a clinical partner have the opportunity to participate in practical clinical courses about their matter of study. In Patrícia's case, she will be able to observe how the management of normal and complex wounds is done. Besides that, the procedure for changing wound dressings on patients in the Intensive Care Unit and/or in an operation theatre (clinic/hospital) is also planned.

Experience at Clinical/Industrial Partner/3

This experience has been rewarding mainly because it is possible to understand better the reality of the problem. This is extremely important to give motivation and to perform laboratory work in the most proper way to find solutions that can have a direct application on biomaterials related infection problems or to overcome existing infections with new treatments in human patients.

Vornia Biomaterials

Jem

Jem has received training in Vornia Biomaterials Ltd., Ireland, for eighteen months. Her work schedule provided her with the opportunity to grow and improve.

As far as the industrial training is concerned, she finds it a challenge to go out of the comfort zone of basic academic experience and learn all the detailed tasks required to run a biomedical company on a day-to-day basis. She has started to know about the different ISO and ASTM standards that have to be complied with for medical devices. She has experienced what it was like to take part in company meetings and plan out things efficiently for different people involved in the company. Jem learned how to design attractive logos and brochures, promote strategies to get people interested in the products the company is selling, improved her skill with computer-aided design software.

She was able to participate in organising meetings that Vornia hosted for their different research projects, which has led to knowing the different research partners and people involved aside from the HyMedPoly project. Taking part in such events broadened her view on the different areas in biomedical research she could work in in the future as well as the institutions and companies involved.

Also, she was trained on how to operate a high pressure supercritical carbon dioxide to synthesise polyesters in a way that does not need solvent and purification, so it is safe for both biomedical use and for the environment. Jem also learned how to synthesise hyperbranched polymers using the traditional methods.

The two places she spends her time in are in the manufacturing facility/cleanroom, which is located in the Institute of Technology – Tallaght (ITT), and the research laboratory facility inside University College Dublin (UCD). She spends more time working in the research laboratory in UCD, where she presents her research work updates twice a month to her colleagues. Here, she started being trained on how to operate the different analytical instruments (e.g. GPC). Jem loves this environment, where people can share their ideas, get improvements and help from each other.

Work Progress

ESR 1: Jeddah Marie Vasquez

Due to increasing antibiotic resistance, alternative antimicrobial strategies are under exploration, such as the use of plant based products like honey. This investigation was aimed at the preparation of a quick forming, biocompatible hydrogel able to mimic the antibacterial property of honey, which was achieved by the production of reactive oxygen species (ROS) in the form of hydrogen peroxide, using two components found in honey: glucose oxidase enzyme and glucose.

Glucose oxidase was added to a solution of hyperbranched polyethelene glycol diacrylate (HB-PEGDA) while glucose was added to a polymer solution of thiolated hyaluronic acid (HA-SH). The two polymer solutions rapidly formed a hydrogel via thiole-ene click chemistry.

Different concentrations of enzyme and glucose were studied. A 10 mM hydrogen peroxide (H_2O_2) concentration produced at a daily constant rate was targeted because it enhances angiogenesis. However, 160 mM H_2O_2 concentration retards wound closure. Results suggested that a hydrogel containing glucose oxidase enzyme and glucose at the optimum level produces 9.35 ± 0.76 mM H_2O_2 after 24 hours.

Publications

- McMahon, S., Kennedy, R., Duffy, P., Vasquez, J.M., Wall, J.G., Tai, H. and Wang, W., 2016. Poly (ethylene glycol)-Based Hyperbranched Polymer from RAFT and Its Application as a Silver-Sulfadiazine-Loaded Antibacterial Hydrogel in Wound Care. *ACS Applied Materials & Interfaces*, *8*(40), pp.26648-26656.

- Sigen, A., Xu, Q., Zhou, D., Gao, Y., Vasquez, J., Greiser, U., Wang, W., Liu, W. and Wang, W., 2017. Hyperbranched PEG-based Multi-NHS Polymer and Bioconjugation with BSA. *Polymer Chemistry*.

Work Progress/2

ESR 2: Subha Purkayastha

A library of novel amiphiphatic polyurethanes mimicking the antimicrobial peptides was synthesised by ESR 2. Redox initiated aqueous heterophase polymerisation was used to graft the desired monomer from an amphiphilic polyurethane backbone. The redox system was established by redox couple of oxidant ceric ammonium nitrate and reductant amphiphilic thermoresponsive polyurethane. The first approach concerned grafting of the hydrophobic ionic liquid containing QA moieties from the NHP407 (polyurethane) backbone resulting in formation of NHP407-g-HDPIL colloidal particles. The hydrophobic anion was subsequently exchanged with desired counter anion in order to impart hydrophilicity and potential antimicrobial activity. In another approach, thermoresponsive core-shell colloidal particles were synthesised where *N*-isopropylacrylamide monomer (NIPAM) was grafted from the amphiphilic NHP407 backbone and subsequently it was decorated with either cationic polyionic liquid or zwitterionic polymeric shell. Chemical and structural characterisation were performed with nuclear magnetic resonance (NMR) spectroscopy, Cryo-transmission electron microscopy, dynamic light scattering and zeta potential measurements.

Dissemination Activities

- European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society (TERMIS), June 2017, Davos (Switzerland)
  Oral presentation *"Novel amphiphatic antimicrobial polyurethanes design and development of new biomaterials with instrinsic antimicrobial properties"*;

- Società Italiana Biomateriali 2017, 24th-26th May 2017 - Politecnico di Milano, Italy
  Oral presentation *"Functional mimetics of antimicrobial peptides: Novel amphiphatic polyurethane to combact gram positive bacteria"*

Publications

Subha is drafting a manuscript on synthesis and characterisation of polyurethane grafted polyionic liquid colloidal particles by redox initiated aqueous heterophase polymerisation.

Work Progress/3

ESR 3: Lukas Gritsch

The project continued following the strategy of combining the advantages of bioresorbable polyesters matrices with chitosan-based antimicrobial agents. Several fabrication techniques are currently under investigation. At the same time, the promising results of physico-chemical and biological characterisations performed so far encourage further developments.

Recently the project was relocated from the University of Erlangen-Nuremberg (Germany) to Lucideon Ltd (UK) as part of the joint training between Academia and Industry.

Dissemination Activities

- 5th Syntactic and Composites Foams (SCF-V), 26th-31st March 2017, Siracusa, Italy
  Member of the organisation committee
  Poster presentation *"Antimicrobial chitosan foams with and without polyester blending as tissue engineering scaffolds*"
- 28th Annual Conference of the European Society of Biomaterials, 4th-8th September 2017, Athens, Greece
  Poster presentation *"Fabrication and characterisation of a new promising biomaterial based on chitosan chelating copper ions"*

Publications

A research paper describing the successful results obtained during the first year of the project is to be published soon. Two reviews on the use of polyesters in tissue engineering are in preparation. Furthermore the following title is in press at the moment:

Gritsch L., Meng D., Boccaccini A. R., Nanostructured Biocomposites for Tissue Engineering Scaffolds. In: Biomedical Composites 2nd Edition, Elsevier. In press

Work Progress/4

ESR 4: Binh Thi Thanh Phan

Since the previous report, composites of synthetic polyesters and natural polymers were studied. First, polymer films with different relative contents of polymers were produced by solvent casting method. Secondly, the investigation of solvent was carried out in order to determine the possibility to use a safe solvent for biomaterials purposes. Finally, essential oils, such as cinnamon and tea tree oils, were incorporated as antimicrobial agents. As a result, the encapsulation method improved the solubility and decreased the volatility of essential oils during film formation. In addition, nanospheres of polymer encapsulated essential oils were obtained. The presence of essential oils in the matrices requires further characterisation due to their low content. In the near future, the preparation of films will be optimised, and the essential oil release profiles and the antibacterial properties of composites with different combination of synthetic polyesters, natural polymers and essential oils will be studied.

Work Progress/5

ESR 5: Elena Marcello

The aim of this project is to produce inherently active antibacterial polyhydroxyalkanoates. To achieve this goal two strategies are being investigated. The first is the production of sulphur containing PHAs (S-PHAs) through bacterial fermentation. Currently the optimisation of the production of thioester containing PHAs is being analysed using *Pseudamonas putida* KT2440 and a co-feeding experiment with decanoic acid to support bacterial growth and 6-acetylthiohexanoic acid for polymer production. Preliminary antibacterial studies have been conducted showing activity against *Staphylococcus aureus* strains. In the future, other substrates containing sulphur will be investigated to produce a range of antibacterial S-PHAs. The second strategy involves the chemical functionalisation of mcl- and scl- PHAs through radical graft polymerisation to introduce antibacterial groups in the polymer side chains. The materials produced will be used for the development of 2D and 3D structures for bone and cartilage tissue engineering applications.

Dissemination Activities

- European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society (TERMIS), June 2017, Davos (Switzerland)
  Oral presentation "*Antibacterial Polymers derived from bacteria*", in collaboration with ESR 11.
  Poster presentation *"Novel natural polymers with antibacterial properties"*
- Post graduate fair, 27th April, University of Westminster, London (UK)
  Poster presentation *"Novel Natural Polymers with Antibacterial Properties"*

Publications

Elena is writing a review on natural antibacterial polymers for medical applications in collaboration with her colleagues from University of Westminster, which will be submitted soon.

Work Progress/6

ESR 6: Isabel Orlando

In the context of bacterial derived polymers, bacterial cellulose (BC) is a promising material for the development of wound dressings thanks to its unique mechanical and structural properties. In this project, BC was produced by *Gluconacetobacter xylinus* in static conditions. The pellicles obtained were purified to remove the biomass and chemically modified to achieve antibacterial activity. The reaction was performed under base catalysis and the modified material was fully characterised by solid-state techniques such as Energy-dispersive X-ray Spectroscopy (EDX) and Fourier-Transformed Infra-Red (FT-IR) spectroscopy.

The activity of the antibacterial groups was evaluated by studying the inhibitory effect against Gram positive bacteria *Staphylococcus aureus*. Different methods were investigated such as direct contact test and colony forming assay, which showed promising results for the functionalised samples. Scanning electron microscopy (SEM) performed on modified BC after incubation with the bacteria confirmed a cell lysis based antibacterial activity. Biocompatibility of the functionalised material is also under study by evaluation of indirect cytotoxicity and direct biocompatibility at different time points using the HaCat cell line, a human keratinocyte cell line.

Dissemination Activities

- 6th World Congress on Biopolymers, September 7th-9th 2017, Paris
  Oral presentation *"Drug-free hydrogel based antibacterial hybrid polymers for wound healing applications"*
- Doctoral Conference, University of Westminster, 27th April 2017, London
  Poster presentation *"Hydrogel based antibacterial hybrid polymers for wound healing applications"*

Publications

A review on antibacterial natural polymers for biomedical applications has been written with other ESRs working at University of Westminster and is being edited before submission.

A manuscript for the work on bacterial cellulose is currently in progress and will be completed soon.

An abstract for writing a book chapter entitled "Cellulose-based hydrogels for wound healing" has been submitted.

Work Progress/7

ESR 7: Seray Kaya

After the first mid-term review meeting of the project, which was held by EURESCOM in Heidelberg in November 2016, some experiments and characterisation studies were performed.

The synthesis of mesoporous silicate bioactive glasses (MBGs) doped with antibacterial ions (Ag, Zn, Cu) with and without surfactant assisted sol-gel method were continued. The bioactivity of the obtained MBGs were tested by keeping them in simulated body fluid (SBF). SEM, EDS, FTIR and XRD analyses were performed for these MBGs. After successful production of the MBGs, their resistance against *E. coli* and *S. carnosus* bacteria was started to being investigated *via* the disk diffusion test. Future work will include carrying on the antibacterial tests on the synthesised MBGs, ion release measurements from the MBGs and cell culture studies.

Dissemination Activities

- European Congress and Exhibition on Advanced Materials and Processes, 17th-22nd September 2017, Greece
  Oral presentation *"Processing and Antibacterial Characterisation of Therapeutic Ion-DopedMesoporous Bioactive Silicate Glasses (MBGs)"*

Publications

A review article covering the studies done in this field is being worked on too.

Work Progress/8

ESR 8: Muhammad Maqbool

The title of this project is 'Substituted Hydroxyapatite with Antibacterial Applications'. The intention of this project is to synthesise substituted hydroxyapatite (HA) with novel compositions to attain versatile antibacterial properties against both Gram positive and Gram negative bacteria. These innovative compositions consist of both single ion substitutions and multi ion substitutions. The current approach encompasses incorporation of novel metal ions in HA lattice with varying doping concentration to attain successful antibacterial efficiency. In up to date experiments, silver, zinc, strontium, cerium, selenium and copper substituted hydroxyapatites with several concentrations have been prepared by wet chemical precipitation method.

The structural properties and chemical composition of these hydroxyapatites were investigated by X-ray diffraction (XRD), X-ray fluorescence (XRF) and energy dispersive spectroscopy (EDX). Morphological properties of hydroxyapatites were studied by scanning electron microscopy (SEM). Zeta potential measurements were attained in a bid to know whether the net surface charge of hydroxyapatite particles impacted on anti-bacterial activity.

Crystallographic and compositional analysis proved the doping of these metallic ions in HA lattice. XRD results showed that doping of metallic ions in the HA lattice produced changes in a- and c-axis lattice parameters. EDX results revealed that substituted hydroxyapatites comprise of calcium or/and respective substituted ion, phosphorous and oxygen. Zeta potential tests indicated that the surface charge of doped hydroxyapatites was changed as compared to pure HA. Antibacterial properties were investigated by a zone inhibition method which revealed that, compared to pure HA, Ce-HA, Cu-HA and Zn-HA had substantial antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*.

On the basis of reported antibacterial mechanisms of metallic ions described in literature, specific combinations of metallic ions were chosen for the co-substitution in HA lattice to intensify antibacterial activities as well as improving other biological properties for example osteoblast cell adhesion. In above mentioned experiments, preparation, compositional and crystallographic analysis of these co-substituted HA is carried out in Lucideon Research Laboratories, Stoke-on-Trent, UK. Morphological and EDX analysis was performed in Institute of Biomaterials Erlangen Germany. This project is being carried out under supervision of academic supervisor Prof. Dr.-Ing. habil. Aldo R. Boccaccini (FAU Erlangen Germany) and industrial supervisor Dr. Mark Cresswell (Lucideon, Stoke-on-Trent, UK).

Work Progress/9

ESR 9: Agata Lapa

Soluble Phosphate-based glasses (PBG) are interesting materials from a medical point of view. It is proposed that PBG can be formulated to offer hard/soft tissue regeneration and anti-bacterial performance.

Soluble quaternary phosphate glasses were obtained by fusion. Correlations between composition and dissolution rate were observed. Two glass compositions were then chosen for the next step, in which anti-bacterial ions (Cerium and Gallium) were incorporated. The dopants influenced both the solubility and surface charge of glasses in aqueous media. The most negatively charged surface was reported for the gallium containing glass due to lower electronegativity.

Bioactivity studies performed in simulated body fluid (SBF) for three weeks showed apatite-like precipitate formation on all doped glasses; the effect was especially notable with the gallium containing samples. It suggests that addition of antimicrobial dopants also enhances the bioactive properties of glasses. Scanning Electron Microscopy studies aimed at understanding re-mineralisation phases deposited on the glass surface when immersed in SBF.

Early-stage antibacterial evaluation for both Gram positive (*Staphylococcus aureus*) and Gram negative (*Escherichia coli*) bacteria strains suggests a superior antibacterial effect for *E. coli* bacteria than for *S. aureus*.

Dissemination Activities

- One-Day Research meeting on Advanced Ceramics (1DRAC), 5th December 2016, Kingston University of London
  Oral presentation *"Influence of antimicrobial dopants on phosphate based glasses for medical application"*
- 7th Royal Society of Chemistry Biomaterials Chemistry Special interest Group Annual Conference, 11th - 12th January 2017, Ulster University, Belfast, Northern Ireland
  Oral presentation *"Phosphate based glasses with antimicrobial resistance for medical application"*
- 28th Annual Conference of the European Society for Biomaterials (ESB), 4th-8th September 2017, Athens, Greece.
  Poster presentation *"Phosphate Based Glasses and Phosphate Glass Fibres with Antimicrobial Properties for Medical Application"*, in collaboration with Dr. Ifty Ahmed from Nottingham University

Publications

Agata is preparing a review article about Phosphate Glass Fibres which is expected to be submitted soon.

Work Progress/10

ESR 10: Alexandra Paxinou

In this research project Polyxydroxyalkanoates (PHAs) will be used to develop antibacterial nerve conduits. Nerve injuries are responsible for nerve damages which can affect the neuronal communication between the central nervous system (CNS) and the peripheral organs. The disadvantages of the conventional treatments, end-to-end repair and nerve grafts have led to an alternative approach. Nerve conduits act as a bridge between the two ends of an injured nerve, allowing them to regrow. In this context synthetic and natural polymers have been used in order to develop these conduits. So far there are only five FDA approved products based on PLCL, PGA, PVA and collagen polymers. In vitro studies have shown that these conduits are promising materials for their use in nerve conduits. Although in vivo studies have revealed limitations such as relatively poor biocompatibility, degradation rate and swelling. These drawbacks have led to the discontinuation of some of these products. An alternative solution could be the use of Polyxydroxyalkanoates. These natural polyesters, which are produced from bacterial fermentation, possess high biocompatibility, biodegradability and range of mechanical properties, which can be varied. In this context, short chain length (scl) and medium chain length (mcl) PHAs have been produced. Blends of these polymers have been developed and their mechanical and thermal properties have been tested, in order to obtain the best candidate for the production of the nerve conduit. Antibacterial agents of organic and inorganic origin will be loaded into the selected composition and antibacterial tests as well as biocompatibility tests will be performed with respect to neuronal cells.

Dissemination Activities

- Doctoral Conference, 27th of April 2017, London, University of Westminster
  Poster presentation *"Development of antibacterial nerve conduits"*
- 9th European Symposium on Biopolymers (ESBP), 5-6th of July 2017, Toulouse, France
  Poster presentation *"Antibacterial nerve conduits"*

Publications

A draft of a review article "Natural drug-free antibacterial polymers for biomedical applications" has been prepared along with her colleagues and the article will be reviewed for submission soon.

Work Progress/11

ESR 11: Sheila Azim Piarali

The development of antibacterial materials based on the combination of "drug-free" agents and Polyhydroxyalkanoates (PHAs) is the main focus of this project.

Short chain length Polyhydroxyalkanoates (scl-PHAs) and medium chain length Polyhydroxyalkanoates (mcl-PHAs) are continuously being produced and characterised to ensure that the physical, as well as the chemical properties remain the same for every batch.

Simultaneously, natural agents were shortlisted to be incorporated into PHAs based on their activity against pathogenic bacteria. The agents were selected taking into consideration three promising classes of antibacterial agents, namely, essential oils, bacterial protease inhibitors (BPI) and antimicrobial peptides (AMPs). As a starting point, trans-cinnamaldehyde (TC), an essential oil, was chosen and characterised with respect to its antibacterial activity by performing the disc and agar well diffusion assay. The minimum inhibitory concentration was estimated for TC using the broth dilution method. Based on the results obtained, different concentrations of TC were added to both MCL- and SCL-PHA films. Finally, the physical properties and the antibacterial activity of the final materials were evaluated against *S. aureus* ATCC® 6538P™. Further antibacterial tests will be performed against *E. coli* ATCC 8739. The antibacterial activity of a BPI and three AMPs are also under investigation.

Dissemination Activities

- European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society (TERMIS-EU), 26th – 30th June 2017, Davos, Switzerland
  Oral presentation *"Antibacterial Polymers derived from bacteria"*
- Doctoral Conference, University of Westminster, 27th April 2017, London
  Poster presentation *"Drug-free antibacterial PHAs, a new generation of biomedical materials"*

Publications

A review on antibacterial natural polymers for biomedical applications has been written with other ESRs working at University of Westminster and will be soon sent for corrections.

A manuscript of the work with PHAs incorporated with trans-cinnamaldehyde is currently in progress and will be completed soon.

Work Progress/12

ESR 13: Loris Domenicale

This research project focuses on a novel technique that allows the users of conventional 3D printers to obtain functionally graded architectures (FGAs): these are characterised by a non-uniform distribution of properties throughout their mass, as chosen by the user. In the last twenty years, also thanks to the advent of additive manufacturing (AM), these structures have shown great potential, especially in the biomedical field.

When designing a bio-scaffold, three main choices are made: which manufacturing process to choose, which material to use and which internal architecture to adopt. The correct combination of these factors allows to tweak the mechanical properties. For bio-scaffolds, titanium alloys are usually adopted. These materials, though, have a much higher elastic modulus than human bone; this leads to stress shielding: the load is absorbed by the implant, not transferred to the bone. This causes the activation of osteoclasts, which breaks down bone tissue resulting in bone resorption. The use of polymers could result in implants with a modulus closer to that of bone, possibly reducing this effect; additionally, FGAs can be achieved with cheaper and easier techniques, like the one developed here.

Dissemination Activities

A novel manufacturing process, based on fused deposition modelling, has been developed for functionally graded polymeric materials. The application for the IP to protect this new methodology is in progress. The idea, though, cannot be disclosed until the IPR are in place (hopefully, in a year time).

A research paper is in preparation. It will be submitted after having the initial IP protection. Conference presentations are planned, in order to attract the attention of possible industrial collaborators.

Work Progress/13

ESR 14: Ayesha Idrees

The aim of this study is the bio-evaluation of antimicrobial biomaterials intended for wound dressings. For this purpose, testing of the newly developed antimicrobial biomaterials will be performed using in vitro assays based on 2D & 3D cell culture systems as well as testing against microbial biofilm formation.

For the evaluation of newly developed antimicrobial biomaterials on 2D system, cytotoxicity assays were optimised for human primary cells.

The skin model based on human primary fibroblasts and keratinocytes was prepared by optimising the 3D culture system. Eventually this model can serve as a testing system having more *in-vivo* like relevant complexity.

Publications

Ayesha worked on the review article "Drug-free antibacterial polymers for biomedical applications" with her colleagues and the article will be reviewed for submission process soon.

ESR 15: Patricia Varela

Currently, Patrícia is working at the clinical partner of the project 'Universitätsklinikum der Ruhr-Universität Bochum (UK RUB)'. The main focus is to perform antimicrobial tests and cytocompatibility assays of materials produced in the project. In addition, a strategy is being developed to overcome the strong inflammatory response in chronic wounds and to promote wound healing.

Dissemination Activities

- Italian Society for Biomaterials, July 2016,
  Oral presentation *"Novel Polyurethanes Mimicking Antimicrobial Peptides"*, in collaboration with ESR 2
- PhD day, October 2016, Politecnico di Torino
  Poster presentation *"Antibacterial evaluation of polymers"*
- European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society (TERMIS), June 2017, Davos (Switzerland)
  Contribution to oral presentation *"Novel amphiphatic antimicrobial polyurethanes design and development of new biomaterials with instrinsic antimicrobial properties"*, in collaboration with ESR 2.