HyMedPoly Newsletter

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Drug-Free Antibacterial Hybrid Biopolymers for Medical Applications

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THE AIM OF HYMEDPOLY

Infection has become one of the toughest problems in the medical world, and as bacteria become more resistant to drugs there are fewer effective antibiotics to fight against pathogens. Biomedical polymers have been widely used in combination with drugs in medical settings but a challenge has arisen to develop new materials that have an intrinsic antibacterial functionality.

To meet this need, **HyMedPoly** *was formed.* **HyMedPoly** *is a partnership of 10 universities and companies from across Europe aiming to design new therapies based on antibiotic-free antibacterial polymeric and inorganic materials for the development of novel antibacterial and biofilm preventing technologies used for medical applications, such as wound care, scaffolds and implants.*

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, hymedpoly.eu .

LONDON WORKSHOP HIGHLIGHTS

- Last July, 18-20th, the members of the HyMedPoly consortium got together for the second meeting of the project. The meeting, hosted by **University of Westminster**, was blessed with three days of wonderful summer that broke the monotony of English infamous weather.

- Achievements, bottlenecks and goals of single projects and of HyMedPoly as a whole have been presented and discussed during internal talks among consortium members.

- The HyMedPoly meeting was also a chance of learning thanks to the interesting workshop intitled:

"*Biomaterials in Medicine: New concepts of drug-free antibacterial therapies*"

The workshop was organized and chaired by Prof. Ipsita Roy and saw the participation of many eminent speakers: Prof. Aldo Boccaccini, Ian Campbell, Prof. Sian Harding, Prof. John Haycock and Dr. Jochem Salber.

- The next summit of the HyMedPoly consortium is planned for the beginning of November 2016 in Heidelberg, Germany

In this new issue of HyMedPoly newsletter we will first introduce three new young scientists that recently joined the team. Moreover we will also quickly report, one by one, the research progresses and the most relevant achievements that the host institutes achieved in the last months.

ESR 5 – Elena Marcello

Novel Natural Polymers with Antibacterial properties

UNIVERSITY OF WESTMINSTER

The aim of this project is the production of natural polymers with antibacterial properties and their modification and functionalization to allow their use for wound healing applications.

The project is divided into two parts. The first one will be carried out at the University of Westminster and focuses on the production of natural polymers with antibacterial properties. The natural materials chosen are polyhydroxyalkanoates (PHAs), polyesters obtained through bacterial fermentation in nutrient limiting conditions, e.g. excess carbon source and nutrients limitation. In particular, the production of Sulphur containing PHAs will be investigated as these polymers have shown antibacterial properties. The addition of antibacterial molecules and possible functionalization will also be evaluated to enhance antibacterial properties.

The second part of the project will be carried out at Vornia Ltd, where novel supercritical carbon dioxide based green technology will be used and adapted for the purification of the produced PHAs.

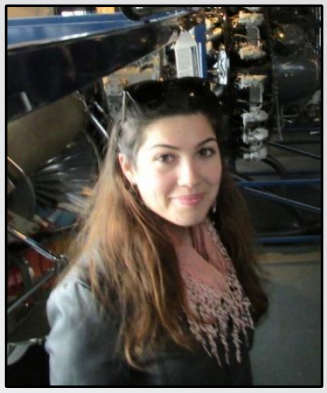
Elena Marcello is from Milano, Italy. She obtained both her Bachelor and Master Degree in Biomedical Engineering at Politecnico di Milano, with specialization in cell, tissue and biotechnology. Her Master thesis title is "Development of Biohybrid Polysaccharides/Proteins Hydrogels". She focused on the production of alginate/gelatin device for the release of local anesthetics for pain management after abdominal surgery, in collaboration with the University of Pavia. She also worked on an additional research to produce innovative injectable gels based on the combination alginate and decellularized tissues. During her Master Degree, she participated in the Erasmus Exchange Program at the University of Twente, The Netherlands. Besides academic life, Elena loves sports (especially volleyball), travelling and visiting new countries.

ESR 10 – Alexandra Paxinou

Novel Antibacterial Agents for Innovative Antibacterial Polymers

UNIVERSITY OF WESTMINSTER

The aim of this project is the development of novel antibacterial agents which can be used as additives to create innovative antibacterial polymers. Most current antibacterial materials contain drugs or active factors which then induce the development of antibiotic resistant bacteria. The main aim of this project is to develop antibacterial agents with a relatively novel mechanism of antibacterial activity. These will then be used to modify and functionalize biocompatible polymers in order to produce a new family of antibacterial materials.



This project will be carried out by Early Stage Researcher (ERS) Alexandra Paxinou from Greece. Alexandra did her Bachelor Degree in Materials Science at the University of Patras, School of Natural Science, Department of Material Science, with a thesis of "Production, Transfer and Characterization of Graphene". She gained her Master Degree in the same faculty in co-operation with ICE-HT/FORTH, (Institute of Chemical Engineering Sciences/Foundation for Research and Technology, Hellas) by carrying out her Master thesis "Development of Nanostructured $PtTiO_2$ and Pt/CeO_2 Catalysts for Hydrogen Production from Methanol".

Besides science, she enjoys travelling, music and sports.

ESR 13 – Loris Domenicale

Mechanics of Porous and Structured Materials

UNIVERSITY OF Southampton

ESR13 works the supervision of Prof. Atul Bhaskar. His project addresses the problem of the use of polymers in combination with 3D-printing for biomedical applications. One possible application area is the development of synthetic bone materials from mechanics and manufacturing standpoints.

The wish is to understand structure-property relationships for a class of architectured materials and to translate this understanding to a tangible biomedical product. It would be interesting to control the way an object is 3D-printed and use this to control its mechanical properties. A complete control on the toolpath would allow us to create geometries with the architectures of desired shapes and topology. The manufacturing process will be FDM (Fused Deposition Modelling); this kind of 3Dprinting works by depositing a filament of fused polymer one layer at a time.

Development of these topics may result in the examination of mechanical properties of functionally graded materials, the study of the role of filament overlap on the bulk stiffness, and the investigation of contact mechanics of porous structures. These topics will be developed both from the theoretical and the manufacturing points of view. Experiments are planned and being carried out to reconcile theory with measurements.

Loris Domenicale, Early Stage Researcher 13, was born in Italy. He received his Bachelor and Master degrees at Politecnico di Torino, Italy. His BSc in "Mathematics for Engineering" gave him a solid background in mathematics, yet with an engineering attitude. During his Master degree in "Mathematical Engineering", he specialized in Fluid Dynamics (Continuum mechanics). The topic of the Master thesis was "Travelling Waves Vorticity and Enstrophy Transient Dynamics in Couette and Poiseuille Flows". It was collaboratively developed at the Department of Mechanical and Aerospace Engineering of Politecnico di Torino, and at the Massachusetts Institute of Technology (MIT), in the Department of Mathematics.

Hobbies are his most effective way to relax and get his mind ready for the next day of hard work. For this reason, there are many activities in Loris' collection. Running, together with speedcubing (Rubik cube solving), learning languages, cooking, and reading Astronomy books, to name a few. Sports have always been in Loris' life: karate, volleyball, beach volleyball, parkour, motocross, climbing, and running, depending on what his studies allowed him to do.

"*Anyone who has never made a mistake has never tried anything new*"

- A. Einstein

FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG

Three ESRs are currently working at the FAU facilities in Erlangen, Germany, under the supervision of Prof. Boccaccini. Two projects (ESR3, Lukas Gritsch, and 4, Binh Thi Thanh Phan) are currently developing antibacterial biodegradable and bioresorbable polyesters. The antibacterial strategy that this project aims to develop is the conjugation of the bacteria inhibition effect that bioresorbable polyesters (BPE) have as a consequence of their degradation with the antimicrobial activity of a second specie, coupled with the BPE. Experimental work in this direction focused on chitosan.

In parallel, ESR7, Seray Kaya, is working on inorganic systems based on mesoporous silicate bioactive glasses (MBGs) used as carriers of antibacterial agents. These novel glasses are currently under characterization.

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FAU early stage researchers are currently producing papers reviewing the research literature of interest. They also represented their Institute participating in the following scientific events with poster presentations:

- **International Workshop on Advanced Ceramics (IWAC-07)**
  26-28th September 2016.
  Limoges, France

  Processing and Characterization of Mesoporous Bioactive Silicate Glasses Doped With Biologically Active Ions (poster)

- **International Workshop and Summer School on Advanced Materials Challenges for Health and Energy Solutions (AMAES/NanoMed)**
  31st August-3rd September 2016
  Cologne, Germany

  *** Awarded 2nd best poster *** 

  Fabrication of Chemically-Modified Chitosan Films and Preliminary Characterization (poster)

  Development and Characterization of Therapeutical Ion Doped Mesoporous Bioactive Silicate Glasses (MBGs) (poster)

At Prof. Ciardelli's laboratory at Politecnico di Torino (PoliTo), Italy, ESR2 Subha Purkayastha is synthetizing new polyurethanes mimicking the structure of antimicrobial peptides (AMPs), a class of proteins that act as a first line of defense in the human body. Hydrophobic domains and electrostatic interaction stemming from their amino acid composition, cationic charge and size, allow them to interact with the bacterial membrane forming pores and consequently disintegrates the structure. Detailed investigation regarding the chemical structure and the characterization of the size and morphology of the particles in dry state were performed. The long term objective of the work is to reach a balance between the compatibility and ability to kill desired bacteria.

ESR15, Patricia Varela, is also currently based at PoliTo, collaborating to the development of "Drug-Free Antimicrobial Polyurethane for Wound Care" using a biology-based approach. The aim of the project is to establish novel optimal cell viability assays and to study the biofilm formation of the principal bacterial strains found on skin infections in order to eventually test the *in vitro* compatibility of antibacterial materials.

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The ESRs currently at PoliTo were members of the first HyMedPoly summer school held in Torino last February, featuring talks by Prof. Paola Petrini (Politecnico di Milano), Ipsita Roy (University of Westminster) and Pietro Favia (Università di Bari). Moreover, they disseminated their early results and planned future work at the following event:

- **Congresso Nazionale Società Italiana Biomateriali (SIB) 2016**
  13 - 15th July 2016
  Ischia Porto (Naples), Italy

  Novel polyurethanes mimicking antimicrobial peptides (TALK)

Moreover, an upcoming symposium entitled "*New Advancements in Drug-Free Antibacterial Biomaterials for Medical Applications*" proposed by PoliTo has been accepted for presentation at TERMIS-EU 2017 (Davos, Switzerland, June 2017).

UNIVERSITY OF WESTMINSTER

The group of Prof. Roy, based at University of Westminster (UoW), is specialized in the synthesis of polymers from bacterial sources. Two ESRs are working on the production of bacteria-derived polymers, such as bacterial cellulose and polyglutamic acid (ESR6, Isabel Orlando) or polyhydroxyalkanoates (ESR 11, Sheila Piarali), subsequently functionalized with antibacterial species. Bacterial cellulose is highly biocompatible and an ideal candidate for application as wound healing hydrogel, because of its ability of retaining a large volume of water in its interstitial spaces. The other synthetized materials are designed and optimized for other biomedical applications, such as tissue engineering scaffolds among others.

The properties of the newly developed material have been already investigated using a spectrum of techniques. Among them: spectroscopic analyses (FTIR), mechanical testing and preliminary testing with antibiotic resistant bacterial cultures of *S. aureus* and *P. aeruginosa*.

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UoW-based ESRs took part to the organization of the HyMedPoly meeting and workshop, held in in London last July. Moreover, they attended the following scientific events:

- **15th UK Society of Biomaterials Annual Meeting (UKSB)**
  (also members of the organization committee)
  30th June - 1st July 2016
  London, UK

  Drug free antibacterial hybrid biopolymers for medical applications (poster)

  Antibacterial material for biomedical applications (poster)

- **15th International Symposium on Biopolymers (ISBP)**
  26th September - 29th September 2016
  Madrid, Spain

  Drug free antibacterial hybrid biopolymers for medical applications (TALK)

  Transfer of CVD-grown graphene on TiO2, Teflon and NiTi (poster)

In the framework of the close collaboration between Lucideon Limited and the University of ErlangenNuremberg (FAU), two ESRs are now carrying out part of their research at their industrial partner. The two projects are investigating two inorganic systems to deliver an antibacterial activity: substituted hydroxyapatite (Muhammad Maqbool, ESR8) and phosphate based glasses (Agata Łapa, ESR9).

The intention of the first project is to synthesize substituted hydroxyapatite (HA) with certain novel compositions to attain versatile antibacterial properties against both Gram positive and Gram negative bacteria. These innovative compositions will comprise of both single ion substitutions and multi ion substitutions. At present, preparation, compositional and crystallographic analysis of cosubstituted HA is ongoing.

The aim of the second project is to design and manufacture phosphate based glasses (PBG) with antibacterial capabilities for medical application. The solubility of phosphate based glasses can be modified and they have been used as materials for hard and soft tissue regeneration. Both the mechanical and biological properties of PBG may also be controlled by changing their composition. These changes can not only provide antibacterial activity but also improve mechanical properties and support cells adhesion and proliferation as a scaffold for tissue regeneration. Moreover various shapes of phosphate glass fibre (PGF) were investigated. All glasses have shown an ability to pull a fibre or be sintered as porous structures in order to obtain composites for medical application.

The two ESRs based at Lucideon will represent the Lucideon/Erlangen/MSCA Scheme at an upcoming undergraduate event at Queen Mary University, London in November 2016.

UK RUB UNIVERSITÄTSKLINIKUM DER RUHR-UNIVERSITÄT BOCHUM

The aim of the study of ESR14, Ayesha Idrees, is the bio-evaluation of antimicrobial biomaterials intended for wound dressings. As a wound dressing will be in direct contact with the wound and therefore the skin cells, it should not only be antibacterial to prevent infection at wound site but also be non-toxic to the surrounding tissue. For this purpose, testing of the newly developed biomaterials will be performed using in vitro assays based on 2D & 3D cell culture systems as well as testing against microbial biofilm formation.

The 3D culture preparation depends on the application and thus on the knowledge of the specific tissue. Therefore for testing of biomaterials for wound dressings, a skin model is required. Initially, a preliminary model system was developed using fibroblast and keratinocyte cell lines. The evaluation of this system for the cytotoxicity assays was performed using cell viability and cytotoxicity assays. For this purpose different factors were optimized including test assay format, incubation time, color development, viability of cells inside the matrix over time, effect of frequent media changes and repeated exposure of reagents on cell viability. This knowledge will now be used to develop a system using actual skin cells (human primary fibroblasts and keratinocytes). Eventually this model can serve as a testing system having more *in-vivo* like relevant complexity.

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ORNIA BIOMATERIALS

The major objective of the work of ESR1, Jem Vasquez, is the design, synthesis and characterization of novel biodegradable hydrogels containing advanced degradable additives adding physical advantageous performance which will be designed to have inherent antimicrobial properties for wound healing applications. The study aimed to create a quick forming, biocompatible hydrogel that will imitate the antibacterial property of naturally occurring substances.

Investigations performed so far focused on the assessment of the release of different concentrations of antibacterial agents. The main challenge is to tune the actual release from the hydrogels in order to reach the proper release concentration of active species that allows the prevention of bacterial adhesion, enhancing angiogenesis without retarding the closure of the wound. Results achieved so far have showed that the produced hydrogels diffuse the antibacterial species in the same range of interest as stated in literature.