HyMedPoly

Drug-Free Antibacterial Hybrid Biopolymers for Medical Applications

Newsletter

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Issue no. 1

HyMedPoly received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 643050

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Introduction

The HyMedPoly project has been awarded a grant funded by the European Commission to train PhD researchers for the development of drug-free antibacterial materials for medical applications, such as wound care, implants, and biomedical devices.

The four-year long project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 643050. It forms part of the 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.

In the charming city of Turin, with fine wine, sumptuous meals, and stunning architecture, the participants and organisers of HyMedPoly met for the first time in Politecnico di Torino for the HyMedPoly Winter School 1, last February 8-10, 2016. Through a series of activities, the researchers were able to present their research plans and receive input that would help them improve on their work. It was a time to get to know everyone not only as researchers and scientists, but also as individuals.

To kick off this newsletter, let us meet the chosen early stage researchers.

Meet the ESRs

ESR 1

About the Research

The Goal: Synthesis of antibacterial functionalised copolymers and their applications in the wound healing sector

The research conducted in aims to synthesise a triblock polylactic-co-polyglycolic acid-polyethylene glycol- polylactic-co-polyglycolic acid (PLGA-PEG-PLGA) polymer in supercritical carbon dioxide (SCO_2) as a solvent. By using SCO_2, the need for polymer purification of the solvent is eliminated, making it an environmentally friendly process.

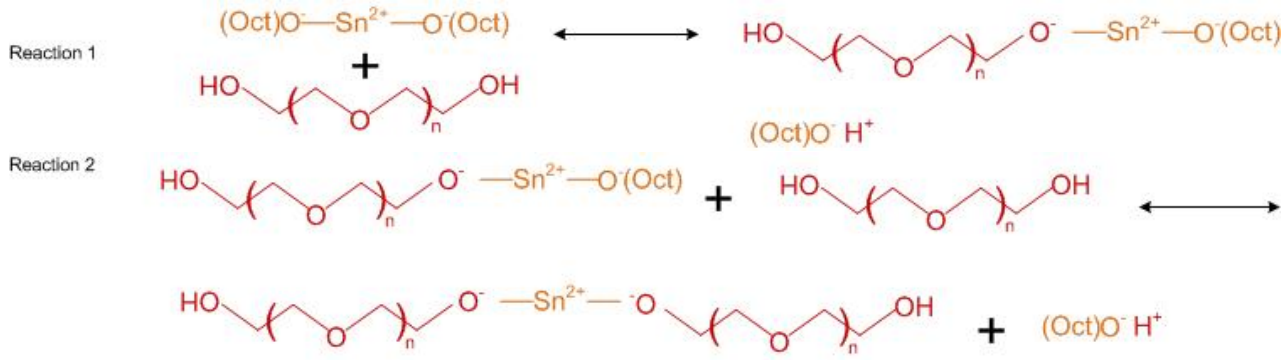


Figure 1. Polyethylene glycol (red) reacting with stannous octanoate (orange)

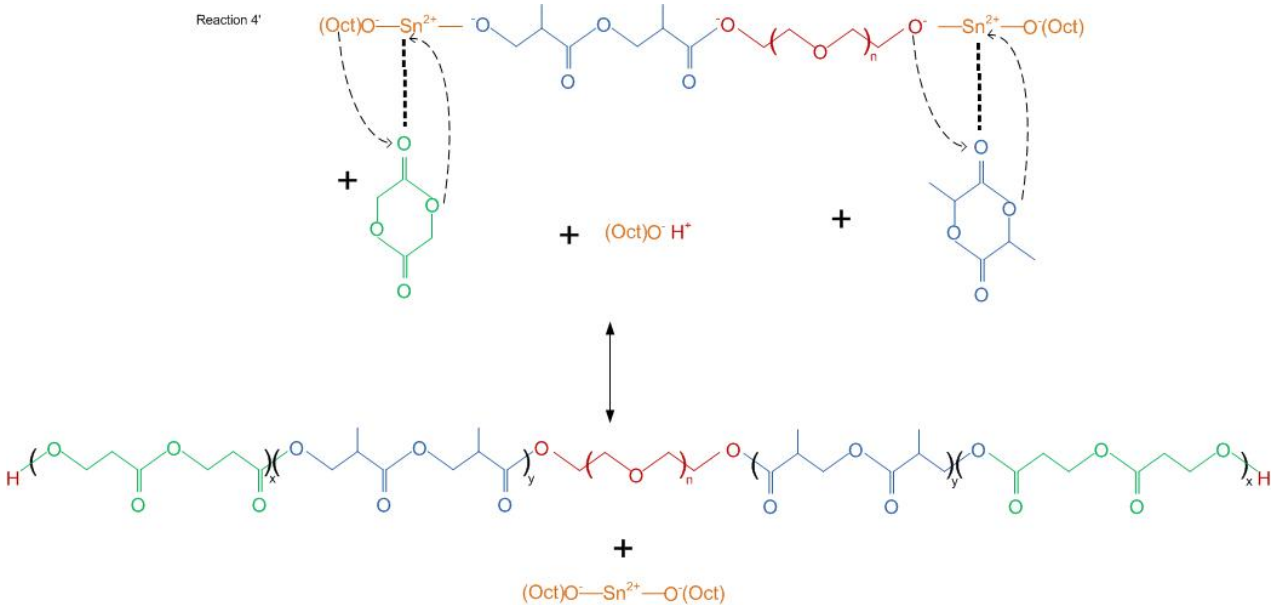


Figure 2. Reaction mechanism for triblock polymerisation from lactic acid (blue) and glycolic acid (green) monomers

After the polymer synthesis, it will be used to create a thermoresponsive hydrogel given its ability to be solubilised in water. This solution is intended to be liquid in room temperature (20-25°C) while form into a gel at body temperature (approximately 37°C). This thermosensitive property allows it to be used in wound dressing applications in conjunction with an antibacterial agent such as the enzyme glucose oxidase (GO). Under the reactive oxygen species mechanism, glucose oxidase will react with glucose to form hydrogen peroxide which stimulates wound healing and kills nearby bacteria.

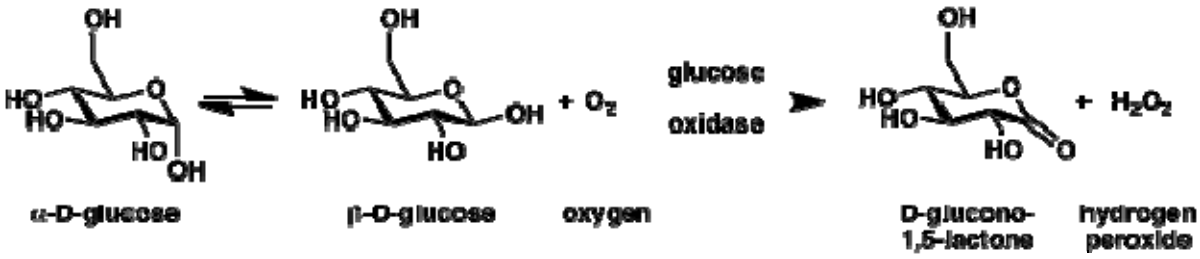


Figure 3. Enzymatic reaction of glucose oxidase with glucose to form hydrogen peroxide

Synthesis and characterisation of the polymer will be done in Vornia Biomaterials Ltd., (supervised by Dr. Wenxin Wang) and Politecnico di Torino (supervised by Dr. Gianluca Ciardelli).

About the researcher

Jeddah Marie (Jem) Vasquez, graduated from University of the Philippines – Diliman with a masters in Chemical Engineering last June 2015. For two months, she worked as an intern in Singapore's Nanyang Technological University's Department of Material Science Engineering. Her specialisations for the last two years were mostly focused on the synthesis of hydrogels from natural polymers such as cellulose, alginate, and chitosan. Her education in chemical engineering has also given her a background on reactor design, industrial plant design, chemical separation processes, environmental engineering, and biofuels.

Jem's birth was heralded by storm and lightning, from Typhoon Ruping which struck Philippines in the nineties. This chaotic backdrop served to foreshadow her restless and dynamic personality that moves from place to place seeking knowledge and adventure. Her interests include travelling, meeting new people, hiking, swimming, reading books, and playing RPG video games. The popular hashtag #YOLO (You only live once), has come to define her way of life.

ESR 2

About the Research

The main objective of ESR-2 module is to do synthesis of novel therapeutic polyurethanes. Biomimetic polyurethane will be synthesised mimicking antimicrobial peptides based on Ionic liquids monomers. FTIR, 1H NMR,13C NMR spectroscopic techniques will be used to perform the characterisation of the chemical structure and TEM, SEM, AFM, DLS, SAXS, SANS will be used to study the morphology. Further the charge density, size, morphology, sequence, biodegradability, amphiphilicity of the polymeric system will be optimised.

About the researcher

Subha Purkayastha is an Indian researcher pursuing his PhD in doctoral school of Bioengineering and Medical-Surgical Sciences, Politecnico di Torino, Italy under the supervision of Prof. Dr. Gianluca Ciardelli. He studied M.Sc in Polymer Science a joint master's program of the three universities in Berlin, Free University Berlin (FU), Humboldt University Berlin (HU), Technical University Berlin (TU) and the nearby University of Potsdam (UP).

He was a research student at Max Planck Institute of Colloids and Inerfaces, Golm from April 2012 to July 2013 in Department of Colloid Chemistry headed by Prof. Dr. Dr. h.c. Markus Antonietti and group of Polymer Dispersions headed by Dr. habil. Klaus Tauer.

He wrote a research proposal which was accepted by the department director and the group leader therefore he was working on his own research project involving synthesis and characterisation of polysaccharide stabilised thermoresponsive core¬-shell porous colloidal particles via aqueous heterophase polymerisation. He was extensively trained in characterisation techniques like FTIR , 1H NMR , 13C NMR, TEM, SEM, AFM, DLS, Thermoporometry, Nitrogen adsorption-desorption measurement.

Afterwards, he worked as a Reasearch Associate at Federal Institute for Materials Research and Testing (BAM) under supervision of Dr. Katrin Hoffmann in Biophotonics group, Department 1:10 headed by Dr. rer. nat. Ute Resch-Genger. His main task was encapsulation of dyes in polymer beads, spectroscopic studies i.e. Absorption measurements, steady State Fluorescence measurements, time resolved fluorescence measurements free dyes in solution and dye loaded polymer particles. His research interests are synthesis and characterisation of polymer particles for biomedical applications, biomaterials, biomimetics, heterophase polymerisation, controlled radical polymerisation, spectroscopic techniques. In HyMedPoly project, he is part of ESR-2 module involving Politecnico di Torino and Vornia Biomaterials, Ireland.

"All our knowledge begins with the senses, proceeds then to the understanding, and ends with reason. There is nothing higher than reason."
— Immanuel Kant, Critique of Pure Reason

ESR 3

About the Research

Bioresorbable polyesters (such as polylactic acid) acidify their surroundings during hydrolytic degradation. As literature has shown, low pH can have an inhibitory effect on the growth of a number of bacterial strains. This research project, host by the Institute of Biomaterials at the University of Erlangen-Nuremberg and Lucideon Ltd, aims to tune and then successfully exploit this property. In second instance, polyesters will be coupled with natural polysaccharides (i.e. chitosan, heparin), in order to develop materials with a multi-strategy antibacterial action. These added species are meant to be metal ions carriers (e.g. silver), offering an additional drug-free strategy to fight bacteria. These developed materials will be fully characterised in terms of physico-chemical properties, antibacterial activity and biological compatibility in order to assess its suitability for soft tissue engineering and/or wound healing applications.

About the researcher

Lukas Gritsch studied biomedical engineering at the Polytechnic school of his hometown, Milano, in Italy. He graduated with a thesis on Crosslinked Gelatin Hydrogels as Heparin Controlled Delivery Systems as part of an international collaboration with the École Polytechnique de Montréal (Canada). His main professional interests include biomaterials, tissue engineering, biomedical research in general and intellectual property issues. Free time, on the other hand, is all about singing, playing guitar and travelling adventures.

"You don't see things as they are, you see things as you are"

ESR 4

About the Research

In the aim of the project "Biodegradable and bioresorbable polyester", dendritic compounds, such as Polyethylenimide (PEI) or Polyamidoamine (PAMAM) dendrimer, might be interesting. It is well-known that quaternised amine groups exhibit significant antibacterial resistance. A typical example of amine – functional hyperbranched polymers is that the quaternised branched PEI showed the most effective antimicrobial activity in the acidic pH range of 4.5 – 6. Interestingly, during the degradation period, polyesters can create acidic environment leading to suppression of bacterial growth. Thus the hypothesis is combining hyperbranched polyamines/polyamidoamines with biodegradable polyesters to achieve a new material which possesses both of above advantages (Figure 1). Their high density of positive charges and specific dendritic structure of dendrimers with biodegradable chains of polyesters may not only change the degradation rate but also strengthen the intrinsic antimicrobial activity of both of low-generation dendrimers and polyesters. Furthermore, we could avoid the inconvenience of bulkier size in dendrimers with elevated number of generations while still elongating the circulation time of the material in the body. Nevertheless, this kind of structure opens a wide range of positive modifications, for example, varying the components or their contents, increasing the generation of amine – dendron, incooperating other antibacterial agents as nano-metals.

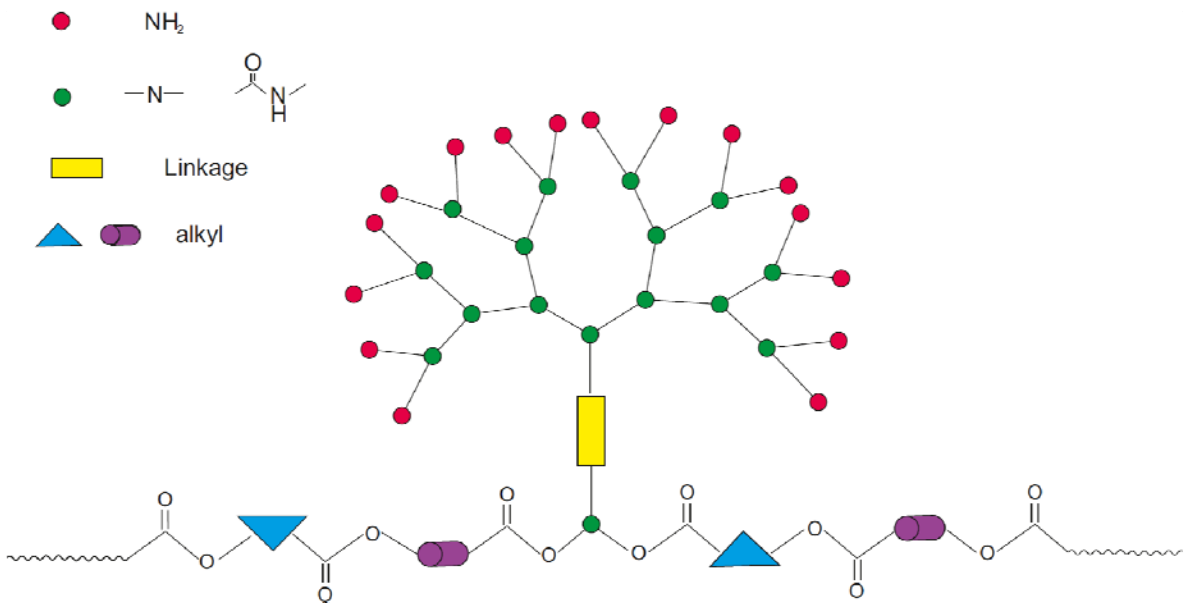


Figure 1. Prospective structure of dendrimer – polyester copolymer

About the researcher

Binh Thi Thanh Phan (Hana) – Department of Biomaterial – Friedrich Alexander University Erlangen – Nürnberg. She obtained her Bacherlor of Chemistry in Hanoi University of Science and Master of Engineering in Osaka Prefecture University. She is concentrating in biomaterials, i.e. polymers and nanomaterials for bioapplications. Her favourite quote is "Research is what I'm doing when I don't know what I'm doing"(Wernher von Braun). Also, she is fond of watching sports, cooking and traveling to discover natural beauty, exploring different cultures and the diversity of cuisines."

ESR 6

About the Research

"Drug-Free Antibacterial Hybrid Biopolymers for Medical Applications"

In the context of the HyMedPoly project, the position number 6 is focused on the production of a drug-free antibacterial hydrogel. The aim of the work is to realize a medical device with suitable properties to be used in the field of wound dressing: if a wound occurs, one of the most important thing is to provide a moist environment so that new tissue can generate; furthermore, the humidity can avoid the pain during the change of the dressing due to dryness of the skin. Infections can occur during the wound healing process, for example after an accident, a surgery or after implantation of a biomedical device, leading to prolonged hospitalisation time or even implant failure. Polymeric hydrogels are gaining importance because of their unique properties: a hydrogel is generally known as a hydrophilic three-dimensional network containing chemical or physical cross-links. Due to its structure, a hydrogel can absorb a huge amount of water and hence ensures a moist environment necessary for new tissue to generate. If a cationic polymer is involved in production of the hydrogel, it has been observed that the material shows antibacterial activity by altering the physiological equilibrium of the bacteria through electrostatic interactions with their membranes. Biopolymers are an interesting starting point for the development of such wound healing hydrogels because of their high degree of biocompatibility and biodegradability; for this reason, γ-polyglutamic acid will be produced through bacterial fermentation and used as a biocompatible material for the development of antibacterial wound healing patches based on the principle of a polyelectrolyte complex. In addition, the production of bacterial cellulose via bacterial fermentation and its chemical functionalisation will also be investigated for the same purpose. Finally, synthetic hyper-branched PEG based wound healing patches will be developed in collaboration with Vornia Ltd, the industrial host for this position.

About the researcher

Isabel has always studied chemistry, so the work involved in the project is a bit different from her background. She has studied Industrial Chemistry at the University of Bologna, Alma Mater Studiorum, where she graduated in October 2013 with a thesis on bioorganic synthesis focused on the production and characterisation of 9-hydroxystearic acid derivatives with antiproliferative activity against human colon cancer cells. She also gained the master degree in October 2015 in the same faculty, where she carried out a 950 hours training on the synthesis of biologically active thiazoles, benzothiazoles and indoles whose properties have been tested in collaboration with the Department of Biochemistry.

Isabel changes her mind like the weather in London, so she doesn't have one quote that inspires her life. She is inspired by a quantity of different things and sometimes by nothing, but she is trying to understand what she wants to do in her life, and what she wants to do, as a chemist or as something else.

ESR 7

About the Research

In this project topic, the synthesis of highly ordered mesoporous silicate bioactive glasses with changed surface charge potential in order to prevent bacteria growth will be done. The development of biodegradable and bioresorbable silicate bioactive glasses with different ion release rates will be the aim to be obtained. The methodology to produce highly ordered mesoporous silicate bioactive glasses will be the sol-gel technique in combination with surfactant-templating and evaporation-induced self-assembly (EISA) processes. These glasses will be doped with several antibacterial ions to increase their resistance to the bacterial infections. After successful production of the mesoporous glasses, several investigation techniques will be performed to study their properties. These techniques will be: biological testing, characterisation studies i.e. nano/microscopy, surface science and x-ray analysis before and after biological testing, the evaluation of antibacterial effect by a series of in vitro testing methods and the testing of cytotoxicity potential. Finally, undoped and doped mesoporous silicate bioactive glasses will be compared in terms of their antibacterial properties. The partners which will be involved in this project are, University of Erlangen-Nuremberg (Germany) and Lucideon Limited, UK.

About the researcher

Seray Kaya was born in 09/09/1990 in Ankara, Turkey. She obtained her bachelor´s degree in 2011 from the Department of Materials Science and Engineering, Anadolu University (Turkey). During her undergraduate studies, she was an Erasmus exchange student for six months in the Technical University of Hamburg-Harburg (TUHH). Before finishing her bachelor´s, she made two industry internships in companies involved in ceramics and aviation & defence industries. Her Master´s degree was obtained in 2014 from the Department of Metallurgical and Materials Engineering, Middle East Technical University (Turkey). The title of her thesis was "Magnetic and Electromagnetic Characterisation of Barium Hexaferrite Ceramics & Their Polymer Matrix Composites". Since November, 2015 she has been pursuing her PhD in the Department of Materials Science and Engineering, Institute of Biomaterials, University of Erlangen-Nuremberg (FAU-Germany) with the thesis topic of "Mesoporous Silicate Bioactive Glasses as Antibacterial Materials". Her hobbies are, watching and doing sports like tennis, basketball and athletics, voluntary work and travelling.

ESR 8

About the Research

Title of Project: Substituted Hydroxyapatite with Antibacterial Applications

The aim of this project is to develop and characterise substituted Hydroxyapatite for antibacterial applications by optimisation of series of multiple substituents in hydroxyapatite (Single element substitution as well as combination of multi-elements substitution). Novel synthesis route will be developed for controlled release of ions in multi-substituted hydroxyapatite for antibacterial applications. This substituted hydroxyapatite will be fully characterised in terms of physicochemical properties, antibacterial functionality and biological compatibility in order to assess its suitability for antibacterial applications.

About the researcher

This project will be carried out by an Early Stage Researcher (ESR) Muhammad Maqbool from Pakistan. His academic background consists of Masters in Material Sciences and Engineering from Institute of Space Technology Islamabad Pakistan (2012-2014). He research experience in biomedical materials includes working in Interdisciplinary Research Centre in Biomedical Materials IRCBM, COMSATS Lahore Pakistan (2014-2015). His research curiosities comprise of synthesis, characterisation, mechanical testing and biological evaluation of bioactive ceramics for tissue engineering applications. Apart from academia, his extracurricular activities include playing football and badminton. He is always eager to occupy his leisure time in visiting new places, observing different cultures and linking to new people from diverse nations.

ESR 9

About the Research

The aim of research project is to manufacture new bioactive phosphate glasses with antibacterial properties for medical application due to the increased prevalence of antibiotic-resistant. For almost 100 years phosphate bases glasses have been widely used in industrial because of their good optical properties. They may be manufacture both by melting quenching technique and, since last years, also by sol gel. However, in last year's they have been investigated as materials for medical application especially in bone tissue engineering, wound healing or nerves regeneration. Phosphate based glasses consist mainly from pattern of the linkages between PO4 tetrahedra, they are soluble which allow them to degraded in human organism and that degradation rate can be modifying by changing glass composition. Additionally they are bioactive which allows them to bond with bone and support hard tissue regeneration. Incorporation of new elements may improve biological response, enhance proliferation or reinforce materials. In this project the researcher will focus on antibacterial phosphate glasses based on quarternary system P2O5-CaO-Na2O-MgO.

Academic part is carried out at Institute of Biomaterials, Department of Materials Science and Engineering University of Erlangen-Nuremberg under supervision of Prof. Dr.-Ing. habil. Aldo R. Boccaccini. First 50% of time research activities will be taken part in industrial partner Lucideon Ltd. UK and with a strong collaboration with other academic and industrial partners in HyMedPoly. During this studies novel glasses will be characterised using technology including nano/microscopy (SEM, TEM, AFM), surface science (SXP, SIMS, contact angle, Zeta potential, BET) and X-ray analysis (XRF, XRD, SAXS, WAXS). The antibacterial effect will be evaluated by a series of in vitro testing methods. The project is co-supervised by Dr Mark Cresswell at Lucideon Ltd. UK

About the researcher

Agata Lapa from Poland is a PhD Student at Institute of Biomaterials, Department of Materials Science and Engineering University of Erlangen-Nuremberg, taking part in ESR9 HyMedPoly project. She graduated AGH University of Science and Technology in Krakow, where she was living for 5 years. Agata finished as MSc Eng. of Biomedical Engineering with specialisation on Biomaterials. Her master thesis was realized in cooperation with Gent University Belgium under supervision of Dr Timothy EL Douglas and Prof Elzbieta Pamula. Biomaterials interested her from very beginning of her studies, both master and bachelor theses were focused on ceramic-polymer composition for bone regeneration.

For 2 years Agata was a member of Students Scientific Association "Nucleus" at AGH University of Technology and Science in Krakow and until May 2014 she had been continuing research under PhD Justyna Pawlik supervision. Results of her studies were presented twice on Student Scientific Conferences at AGH University of Technology and Science in 16th May 2013 and 8th May 2014 when her presentation entitled "Improving the Method for Formation Bioactive Polymer Composites" was awarded (2014).

Agata´s hobbies are all kinds of outdoor activities: skiing, swimming, climbing and sailing however her greatest passion is scuba diving. For 3 years she was a board member of nonprofit student organisation AKP KRAB AGH which goals are to popularise diving and organise diving courses or trips. During that time she was able to meet a lot of inspiring people, visit outstanding places and taking part with many both cultural and charity events.

ESR 11

About the Research

Antibacterial materials for tissue engineering scaffolds

Bacterial infection has become one of the major problems in the medical world as it represents a major cause of morbidity and mortality. Current approaches to treat infections are becoming less effective mainly because of the presence of drugs or active factors which induce the development of antibiotic resistant bacteria or have no effect in antibiotic-immune patients. Additionally, the number of multidrug-resistant bacteria is increasing along with an ageing population. Thus, it is necessary to develop alternative strategies in the field of non-antibiotic therapeutics to overcome this problem and to develop an effective way to fight infections.

The main aim of this research project is to develop "drug-free" antibacterial materials based on the combination of biopolymers and novel antibacterial agents for tissue engineering applications.

The project is divided into two parts. In the first part, the work will be carried out in the University of Westminster, London, where the objective will be to produce polyhydroxyalkanoates (PHAs), biocompatible and biodegradable polymers through bacterial fermentation. Both SCL-PHAs and MCL-PHAs are going to be produced. In addition, novel antibacterial agents such as antimicrobial peptides will be isolated and characterised with respect to their antibacterial properties.

The second part of the work will be performed in the Universitätsklinikum Knappschaftskrankenhaus Bochum, and in this case, the selected antibacterial agents will be used as an additive to PHAs, which in turn will be processed to form 2D and 3D tissue engineering scaffold structures and assessed for their use in various biomedical applications, thereby promising a new family of antibacterial materials.

About the researcher

Early stage researcher 11 is Sheila Piarali, a Portuguese student who comes from Lisbon.

Sheila did her Bachelor degree in Biochemistry at the University Nova de Lisboa in the Faculty of Science and Technology. Due to her interest in genetics she did her Bachelor project on this area, more specifically she studied the effect of cofactors in polymerisation reactions carried out by the enzyme Terminal deoxynucleotidyl transferase (TdT). Then she began her Master degree in Biotechnology in the same faculty. For her Master thesis she decided to focus on Systems Biology and in this case her aim was to develop process control strategies, namely medium optimisation for MDCK suspension cells. During this period she was able to do part of her thesis in Magdeburg, Germany at the Max Planck Institution for Dynamics of Complex Technical Systems.

Besides academic life, Sheila is a football lover and she is a strong adept of Sporting Clube de Portugal. Other of her interests includes tennis, music, cinema and cooking.

Quote: “Struggle is the meaning of life. Defeat or victory is in the hands of God. But struggle itself is Man’s duty and should be his joy.” — Aga Khan III

ESR 14

About the Research

ESR 14 will focus on the bio-analyses of antimicrobial biomaterials synthesised in this project and thus preventing microbial infectious diseases. For this, she will be doing biocompatibility analysis through established and novel methodologies to evaluate antimicrobial properties. Polymer films and scaffolds with different topography and porosity will be manufactured to show the effect of material surface morphology on bacterial growth and biofilm formation. Her work will be carried out in Politecnico di Torino, Italy under the supervision of Prof. Valeria Chiono and Universitätsklinikum Knappschaftskrankenhaus Bochum, Germany under the supervision of Prof. Jochen Salber.

About the researcher

Ayesha Idrees is from Lahore, Pakistan. She did her graduation in Microbiology and Master's in Virology & Immunology from National University of Science & Technology (NUST) Islamabad, Pakistan in 2013. Her Master's research was mainly focused on the effect of a drug to unveil the underlying molecular and biochemical mechanisms to elucidate the new strategies for the treatment of neuro-toxicity and inflammation.

Her interest in this area evoked during her work in a hospital (SKMCH&RC) in 2011, where the healing problems of serious infections were because of rapidly emerging antibiotic-resistant bacterial strains. Later, her research in Interdisciplinary Research Centre (IRCBM) linked these challenging questions with biomedical materials.

Other than academics and research, she enjoys doing art work and visiting new places. "Be yourself, believe in yourself and stay happy!"

ESR 15

About the Research

The ESR 15 phD research will focus on developing optimal sterilisation methods depending on the material and to perform antibacterial testing of polymers synthesised throughout the project. Moreover, biocompatibility will be studied aside exploring basic molecular and cellular mechanisms to develop a greater understanding of the immune system in the presence of these new materials. Finally, all the technical documents for the validation of novel polymers will be prepared. These tasks will be achieved into two institutions: first in the Politecnico di Torino (Italy) under the supervision of Prof. Gianluca Ciardelli and later in the clinical partner Universitätsklinikum Knappschaftskrankenhaus Bochum (Germany) with Dr Jochen Salber.

About the researcher

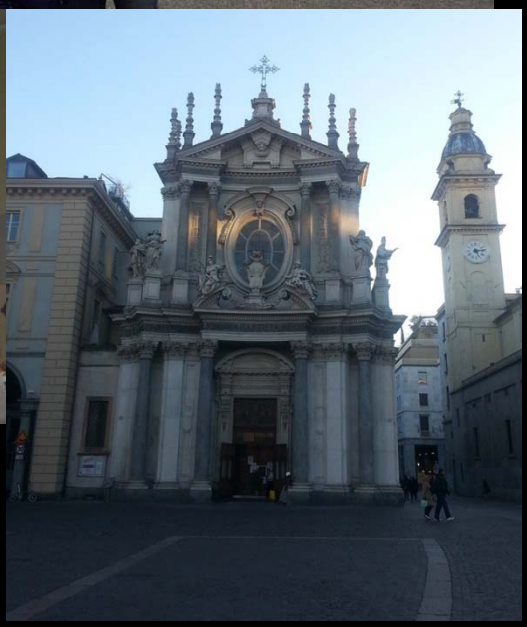
Patrícia Varela is a Portuguese Biologist that in 2012 obtained her Master's degree in Cell Biology and Biotechnology in the Faculty of Sciences, University of Lisbon.

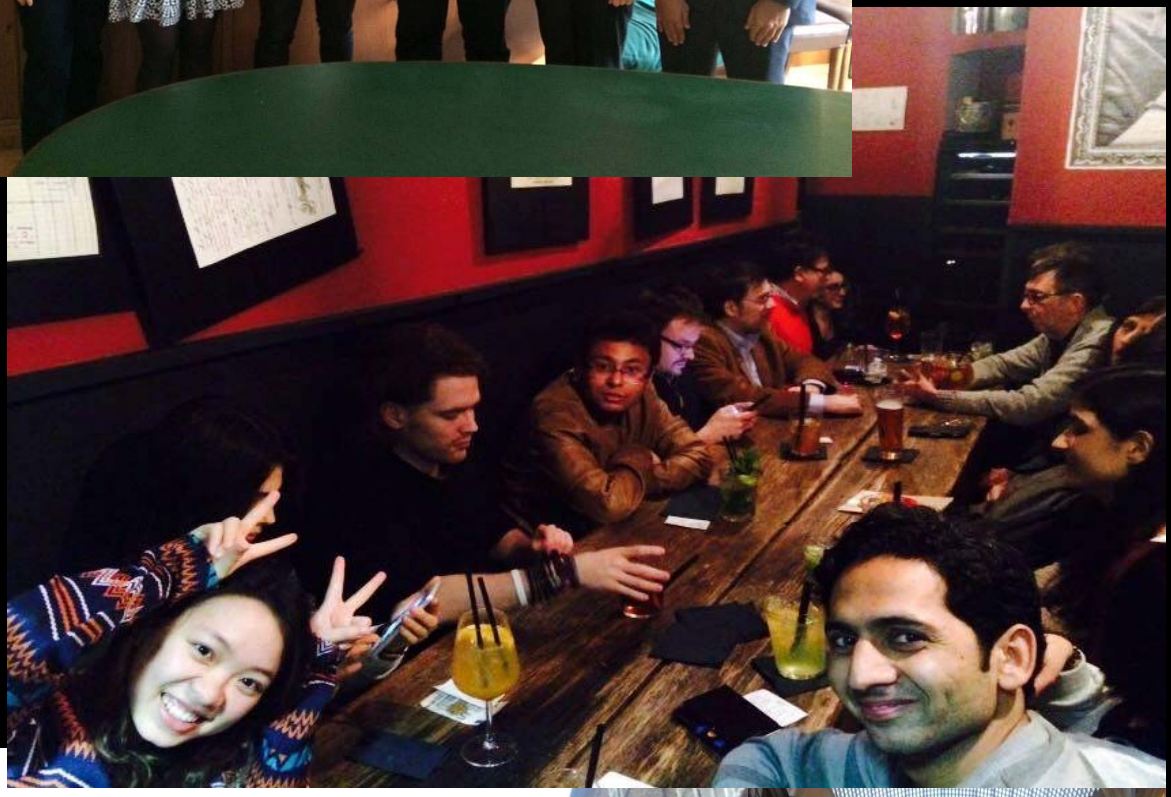
Her interest in Microbiology started as an undergraduate student by doing a curricular internship in which she studied the phenotypic resistance to antibiotics of Gram-negative bacilli isolated from mackerel. Later in the Institute for Molecular and Cell Biology (IBMC) she associated this area with Nanomedicine in projects that explored the efficacy of drug delivery systems as therapeutic solutions to diseases such as sleeping sickness and leishmaniasis. More recently, she found a new curiosity in immunotherapeutic approaches in ICVS Life and Health Sciences Institute, where she studied metabolic reprogramming of Macrophages in the presence of different pathogenic microorganisms (e.g. Aspergillus fumigatus).

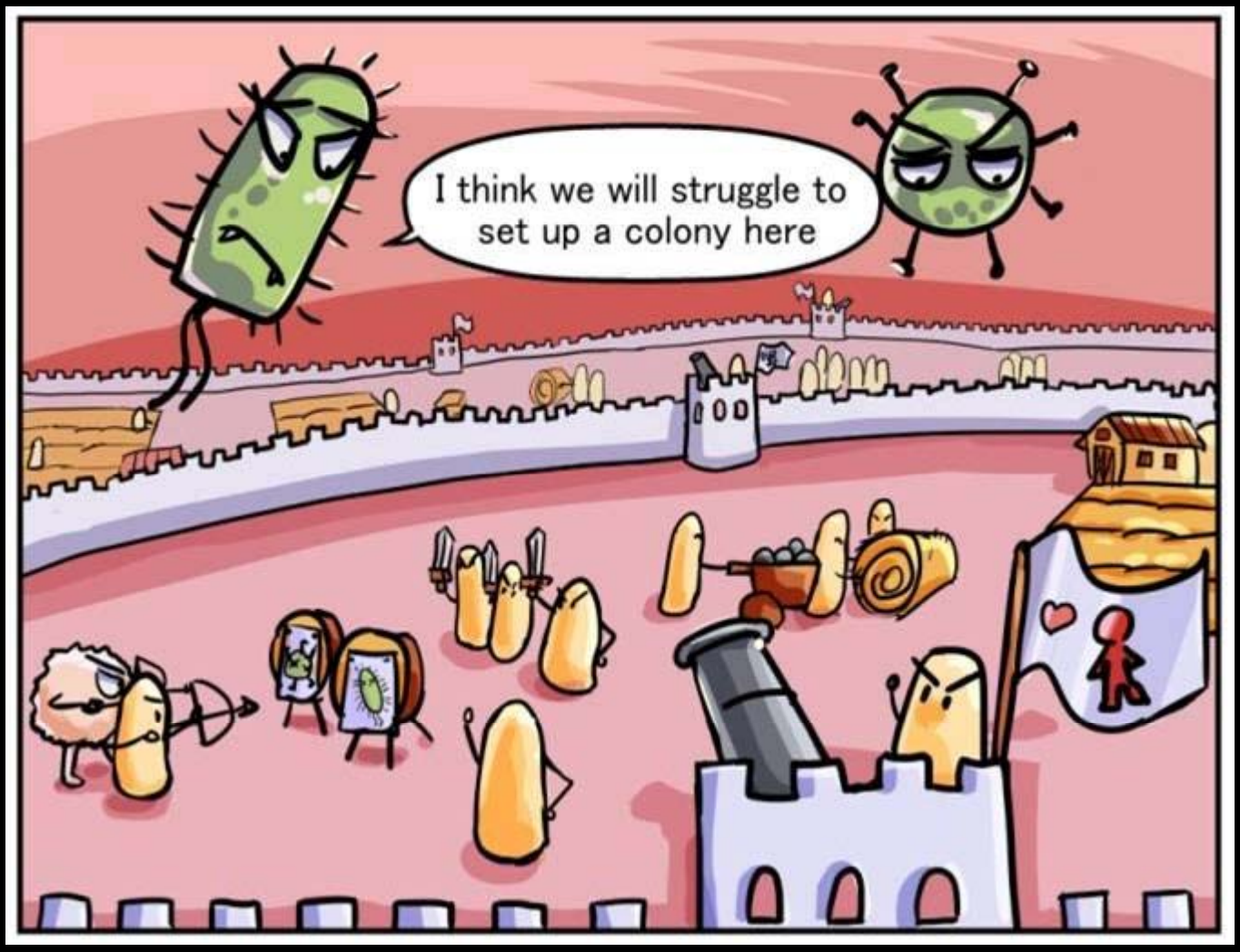
Besides science, she enjoys many activities such as travels, music, books, series, movies, sports and to be with friends and family. A famous quote that represents her is 'I have no special talent. I am only passionately curious.' by Albert Einstein.

The HyMedPoly Winter School in Photos


HyMedPoly
Project – No.: 643050
Marie Skłodowska - Curie Actions
Early Stage Researcher (ESR) 14
Bio-Analyses of Antimicrobial Biomaterials and Beyond -
Next Level of Preventing Microbial Infection Diseases
Ayesha Idrees







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