UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

CORSO DI DOTTORATO IN INEGNERIA DEI PRODOTTI E DEI PROCESSI INDUSTRIALI
Ciclo 32°

Proposta di progetto di dottorato

Il sottoscritto Prof./Dott. __ Giuseppina _____Luciani____

Nome *Cognome*

Professore IF ☐ Professore IIF ☒ Ricercatore ☐ Ricercatore a tempo determinato ☐

afferente al Dipartimento di Ingegneria Chimica, dei Materiali e della Produzione Industriale

chiede di essere inserito nell'elenco dei tutors per il 32° ciclo.

Tematica di ricerca proposta:
Design and fabrication of bio-inspired antimicrobial substrates: towards smart wound dressing solutions

Curriculum di riferimento:

☒ Ingegneria dei Materiali e delle Strutture

☐ Ingegneria Chimica

☐ Tecnologie e Sistemi di Produzione

N° di dottorandi con borse ministeriali dei quali il proponente è stato tutor nell'ultimo triennio
0

Curriculum del proponente (Max 500 parole. Indicazione di pubblicazioni, brevetti, responsabilità di o coinvolgimento in progetti di ricerca, esperienze scientifiche) con riferimento alla tematica proposta

Giuseppina Luciani, PhD

Education

Born in 1973, Giuseppina Luciani graduated in Chemical Engineering cum Laude at the University of Naples Federico II in 1996. She received her PhD in Materials Engineering in 2001 from the same University, with a thesis on "Phase transitions in inorganic amorphous systems".

Career

Associate Professor of Chemistry since October 2015. She is part of the Department of Chemical, Materials and Production Engineering of the University of Naples Federico II. She is also member of the Interdisciplinary Research Centre on Biomaterials of the University of Naples Federico II. In 2002 she was made assistant professor of Chemistry at the same university.

Scientific activity

Until June 2016 she appears as author in more than 50 publications in international high quality peer reviewed journals, receiving more than 200 citations, with an h index of 10 (Scopus).

Her research work has been focused on the design, synthesis and characterization of glasses, ceramics, glass-ceramics and nanostructured organo/inorganic hybrids, through wet chemistry routes. She is highly skilled in both synthesis and functionalization of ceramic nanostructures through sol-gel as well as hydrothermal processes. Mild synthesis conditions and accurate design of process parameters have been exploited to produce ceramic as well as hybrid nanostructures, tuning size, shape, and surface chemistry in order to obtain bioactive hybrids and nanocomposites, multifunctional coatings, smart drug delivery carriers, photoconductive TiO_2 based systems. She is appointed reviewer for international journals on chemistry of materials.

Prizes and Awards

2001 CCT PRIZE, 7th Ceramic, Cells and Tissue "Biomimetic Engineering: a New Role of Ceramics".

Commitments

Since 2013 she is member of the management committee for Cost Action MP1206 - Electrospun nano-fibres for bio inspired composite materials and innovative industrial applications.

2002-2012: Member of the commission of the PhD program "Ingegneria dei Materiali e delle Strutture" at University of Naples Federico II

Funded Competitive Projects

2000 -2001: PROGETTO GIOVANI RICERCATORI- "Hydroxyapatite deposition on bioactive glass and polymeric substrates from simulated body fluids under dynamic conditions".

Relevant Publications to the project

1. G. Vitiello, A. Pezzella, V. Calcagno, B. Silvestri, L. Raiola, G. D'Errico, A. Costantini, F. Branda, G. Luciani, Giuseppina, J. Phys. Chem C., 2016, 120, 6262−6268.

2. G. Vitiello, A. Pezzella, A. Zanfardino, M. Varcamonti, B. Silvestri, A. Costantini, F. Branda, G. Luciani, Titania as driving agent for DHICA polymerization: a novel strategy for the design of bioinspired antimicrobial nanomaterials, J. Mater Chem B, 3 (14), 2015, 2808-2815.

3. A. Pezzella, L. Capelli, A. Costantini, G. Luciani, F. Tescione, B. Silvestri, G. Vitiello, F. Branda, Towards the development of a novel bioinspired functional material: Synthesis and characterization of hybrid TiO2/DHICA-melanin nanoparticles, Mater.Sci. Eng. C 33 (1), 2013, 347-355.

Sintesi del Progetto di Ricerca (Max 500 parole. Stato dell'arte, breve programma previsto per le attività e obiettivi)

The skin is the largest multifunctional organ of the human body and the first line of defense against harmful physical or chemical environments, as well as the invasion of microorganisms. Therefore, wounding that frequently results from trauma, surgery or any pathological diseases rises a major healthcare issue.
Wound dressing materials actually play a key role in the healing process, hence they represent the fastest growing segment of the medical market.
Electrospinning has emerged as a cutting edge technique for fabrication of dressings with high performance in wound healing process, because of the peculiar morphology and structure, mimicking extra cellular matrix, high specific surface allowing good draining, nutrient exchange and air permeability, as well as easy incorporation of suitable drugs.
Although, significant efforts have been made towards the development of smart tissue-engineered constructs for wound care, relevant shortcomings such as scar formation, poor tissue integration and bacterial infection are still to be overcome. The incorporation of antimicrobial agents into the polymer materials is an effective approach to overcome this limitation. Nevertheless, commercially available antibiotics show toxicity and narrow therapeutic efficacy especially towards drug-resistant bacteria.
Eumelanins, negatively charged, hydrophobic natural pigments show intrinsic antimicrobial activity [1-3]. Following a bioinspired approach, we have recently proposed a novel synthetic strategy whereby a TiO_2 sol acts as a catalyst and a templating agent for 5,6-dihydroxyindole-2-carboxylic acid (DHICA) polymerization to eumelanin [1,2]. The hybrid TiO_2–DHICA melanin nanostructures show intrinsic potent antimicrobial activity even under environmental light [2]. Unique biocide properties as well as non-toxic and bio-friendly nature of both organic and inorganic components make these materials very promising as a synthetic platform to produce antimicrobial formulations for biomedical applications. These stimulating achievements prompted submission of the present proposal that aims at designing **novel antimicrobial textiles for wound healing**. This objective will be pursued through a global **bioinspired approach** based on materials simulating the extracellurar matrix (ECM) (**electrospun dressings**), thus providing structural and biochemical support to tissue regeneration while, at the same time, mimicking nature's strategy against pathogens infection (**melanin based systems**).
As a key contribution to the fundamental research in the field, the projects aims to:

- Assess the mechanisms through which melanins and TiO_2-melanin hybrids perform their antimicrobial activity;
- Elucidate the role of melanin composition and structure, as determined by the nature of its precursors and their ratio to TiO_2, in defining the efficacy of their biological properties.

Addressing these still open issues will allow significant breakthrough to the knowledge of structure-properties-function relationships of melanin based hybrid systems endowed with antimicrobial properties, thus providing a useful guide to tune their biological properties and opening the way to their application as active phase in **woven non woven constructs** .
Exploring these technological potentialities, as integral part of the present project, we plan to:

- design novel bio-interfaces for wound healing, based on electrospun hydrogel (polylactic acid) nanocomposites.
- test their biocompatibility and their antimicrobial activity.

Both research strategy and breakthroughs of the proposal target priorities of RIS3 strategy as well as the Horizon 2020 pillars as an interdisciplinary research with a focus on human health and a primary commitment to advancement of knowledge, innovation and enabling technologies.

Informazioni sintetiche relative a: attrezzature/software disponibili, disponibilità finanziaria, collaborazioni con altri enti di ricerca italiani e ed esteri (eventualmente anche con aziende) potenzialmente rilevanti con riferimento specifico alla tematica proposta.

Equipment and Facilities:

- FT-IR spectrometer for attenuated total reflectance (ATR), diffuse reflectance (DRIFT) and transmittance mode experiments
- Thermogravimetric Analysis apparatus (TGA)
- Thermogravimetric/Differential Scanning Calorimeter (TG/DSC) simultaneous analyzers equipped with gas analysis through FT-IR spectrometry
- Controlled atmosphere high temperature ovens
- Spin-coater
- Dip-coater
- Electrospinning apparatus

Straight access to:

- X-Ray diffraction (XRD) measurements
- Electronic Paramagnetic Resonance (EPR) Spectroscopy
- UV-Vis Spectroscopy (Liquid and Solid)
- Neutron scattering (SANS, NR) spectroscopy

Achievement of the project goals is realistic in view of the synergy among a multidisciplinary team with complementary expertise in the design of hybrid materials, physical chemistry of supramolecular/nanocomposite structures, biochemical and microbiological systems, as detailed in the following:

- Dept. of Chemical Sciences, University of Napoli Federico II, Dr. Alessandro Pezzella, Prof. G. D'Errico
- Dept. of Biology, University of Naples Federico II, Prof. M. Varcamonti

Strategic for a positive outcome of the PhD project will be also cooperation with:

- Boston University School of Medicine, Prof. V. Falanga
- Dept. of Civil, Environmental and Mechanical Engineering, University of Trento, Prof Matteo Leoni
- Dept. of Industrial Engineering, Prof. M. Modesti, Ing. M. Roso

In particular, the letter of support by Prof. Vincent Falanga, an outstanding worldwide kown dermatologist, proves the real involvement of key users.

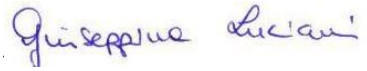
Finally, the tutor of PhD project, as a member of the management committee, can rely on the support of Cost Action MP1206 - Electrospun nano-fibres for bio inspired composite materials and innovative industrial applications.

Informazioni sintetiche relative ad eventuale periodo all'estero previsto per il dottorando (periodo, gruppo di ricerca, Università, ente di Ricerca….)

The PhD student is expected to spend a training and research period abroad in one of the following Universities or Research Institute:

- Spanish Council for Scientific Research (CSIC), Paterna, SPAIN, Novel Materials and Nanotechnology Group, Leader Dr. Jose M. LAGARON. Aim of the training: gaining skills in electrospinning processes.
- Boston University School of Medicine, Boston, USA, Prof. Vincent Falanga. Aim of the training: gaining deep insight in biochemical processes underlying skin regeneration.
- Ecole Nationale Supérieure des Mines de Saint Etienn Centre Microélectronique de Provence, Department of Bioelectronics, Gardanne, FRANCE, Prof. Róisín Owens. Aim of the training: gaining skills in biological evalutation of produced systems.

Il sottoscritto garantisce, sotto la propria responsabilità, di poter accedere a risorse tecniche e finanziare adeguate a supportare le attività necessarie al corretto sviluppo del progetto di ricerca proposto.

Napoli, 18/07/2016____ Firma del richiedente: 

Vincent Falanga, M.D., F.A.C.P.
The Barbara A. Gilchrest Professor of Dermatology
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March 10, 2016

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RE: BioDressMel – "Design and fabrication of bio-inspired antimicrobial substrates: towards smart wound dressing solutions"

Dear Dr. Luciani,

I have analyzed your proposal in detail and, with this letter, I confirm my definite agreement to collaborate with you and your team. In addition to our expertise in studying extracellular matrix in experimental models, we also have well-documented clinical and clinical trial experience with both acute and chronic wounds. As a collaborator and advisor for your project, I strongly believe that we can be of substantive help in this innovative and exciting proposal.

As you so well detailed in your proposal, there is an immense need to develop improved and innovative "smart" and state of the art materials that have the capability to act as both an extracellular matrix generator and antimicrobial agents. The major problem with non-healing wounds, in addition to their often-ischemic component, is frequent bacterial contamination and colonization of the wound bed. The excessive bacterial burden is now a well-established pathological problem which has a number of complications: a) infection; interference with wound closure; and recurrence. These critical pathophysiological aspects are particularly inherent to the challenges of chronic non-healing wounds, which suffer from poor/inadequate matrix deposition, impaired epidermal migration, and even wound contraction. These issues affect ulcers due to pressure, to diabetes, venous insufficiency, and burns, among others. Increasing evidence now points to a persistence of tissue bacteria and other pathogens, surprisingly even after complete wound closure. In the context of the latter component, one should also recognize the importance of biofilms, which are inherently resistant to traditional antibiotics. It has often been stated that, while achieving healing is so very essential, and desirable, the recurrence of wounds is the major driver in both patients' suffering and tremendous economic consequences. For example, in our FDA-approved studies of living bioengineered skin for chronic wounds, we found that the recurrence rate was not altered by achieving wound closure. In the case of venous ulcers, the recurrence rate remained at 21% after one year (Falanga et al, 1998 and 1999, Wound Repair and Regeneration). The diabetic ulcer epidemic we are seeing could also benefit from your approach, given the pathophysiology of those wounds (Falanga, Lancet, 2005)

In assisting you with the clinical and wound healing basic science implications of your project, we feel quite enthusiastic. In studying your proposal, I was personally also impressed by the incorporation of melanin. It's not generally recognized that, even upon healing, the neo-epidermis lacks melanin deposition. Therefore, I regard your proposal as addressing an aspect of antimicrobial activity that has not been properly studied before. As you perform your promising work, and depending on your findings, we would also be pleased to study your material by using in vivo studies. We have developed a unique mouse full-thickness tail wound model that is virtually independent of contraction and relies mainly on epithelial migration for wound closure (Falanga et al, Wound Repair and Regeneration, 2004). This published model is also unique in that complete healing requires approximately 21 days, compared to the more typical dorsal wounds, which heal in 7-8 days. This prolonged "window of time" could allow you to more properly study the matrix deposition that you substrate may provide. We also have experience in dorsal murine and porcine wounds, as well as in establishing polyvinyl sponges in the animal. The latter could also address the recruitment of cells critical to wound healing (stem cells, endothelial cells, fibroblasts, macrophages) and in measuring the deposition of collagen and other extracellular matrix components. Some of these studies are detailed in a recent publication by our group (J. Tissue Engineering and Regenerative Medicine).

Equally timely in considering your work, is our research with bone marrow-derived mesenchymal stem cells (MSCs) for the treatment of chronic wounds. This research is presently sponsored by the National Institutes of Health. I personally believe that applying stem cells alone is probably not optimal, due to problems with infection and the need for additional matrix materials. We are delivering the stem cells topically by using a modified fibrin spray. In reading your proposal, I am quite enthusiastic about the possibility that it could lead to additional MSCs approaches (or with other multipotent or pluripotent stem cells).

In summary, I am quite keen on the work of your team. It has the potential to fill a large void in the way we address wound healing problems of a variety of etiologies. I would be most pleased to advice you as you develop your smart material, provide you with suggestions about the clinical implications and, if so needed, also develop early in vivo pre-clinical preliminary data.

I wish you the best in your scholarly and promising work.

Sincerely Yours,

Vincent Falanga, MD, FACP
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Profile:
http://profiles.bu.edu/display/152152