

**Ammissione al corso di Dottorato di Ricerca in Scienze Farmaceutiche del XL ciclo, A.A. 2024/2025 – Tematiche di Ricerca.**

**Admission to the PhD program in Pharmaceutical Sciences XL cycle, A.A. 2024/2025 – Research Projects.**

**Thematic 1 (D.M. 630, Impresa Partner: Buona Spa)**

**Titolo:** Analisi di estratti di lipidi polari da scarti vegetali: studio degli effetti per preservare lo stato di salute.

**Title:** Analysis of polar lipid extracts from vegetable waste: investigation of health preservation effects.

**Project referent:** Prof.ssa Elisabetta Albi, [elisabetta.albi@unipg.it](mailto:elisabetta.albi@unipg.it)

Recent scientific research has focused on the role that polar lipids, phospholipids and sphingolipids, have in brain maturation from the embryonic stage to the neonatal period up to adolescence as well as in the prevention of cognitive decline. It is known that milk and eggs are rich in polar lipids but very little is known about their content in vegetables and, above all, in vegetable waste. Preliminary studies conducted in our laboratory have shown that the pods and peels of broad bean seeds (*Vicia Faba*) contain a high content of polar lipids. The aim of the project is to prepare extracts of polar lipids from numerous vegetable wastes in order to identify the best preparation that could be used for the creation of supplements useful for childhood and aging. Therefore, experimentation in the new product will be focused on neurodevelopment and neurodegeneration in monolayer cellular cultures and organoids models.

**Thematic 2 (D.M. 630, impresa partner Società Innovatune Srl)**

**Titolo:** Approcci computazionali all'avanguardia per individuare piccole molecole come potenziali agenti terapeutici contro il cancro.

**Title:** Cutting-edge Computational Approaches to Identify Small Molecules as Potential Anti-Cancer Agents.

**Project referent:** Prof.ssa Maria Letizia Barreca, [maria.barreca@unipg.it](mailto:maria.barreca@unipg.it)

The research activity will be carried out within the framework of a multidisciplinary project aimed at discovering small molecules as new therapeutic agents for human diseases currently considered incurable for many patients. Specifically, the candidate will be required to develop and apply computational approaches and ad hoc predictive models (e.g., to predict the toxicity of studied chemical compounds) to support the rational identification of small molecules capable of modulating the function of proteins crucial in the development and progression of cancer (e.g., AKT1, IL4i1 and Poltheta). The most promising candidates will subsequently undergo biological validation to assess their therapeutic efficacy.

**Thematic 3**

**Titolo:** Eterostrutture ibride a bassa dimensionalità per applicazioni biomediche.

**Title:** Low dimensional hybrid heterostructures for biomedical applications.

**Project referents:**

Prof.ssa Monica Pica, [monica.pica@unipg.it](mailto:monica.pica@unipg.it)

Prof. Riccardo Vivani, [riccardo.vivani@unipg.it](mailto:riccardo.vivani@unipg.it)

Low dimensional nanomaterials, including several classes of 2D compounds, are known to be suitable for surface interactions with biomolecules. Early fundamental medical studies suggested to explore their use for biomedical applications, including drug delivery, tissue

engineering, bioimaging and cancer therapy, biosensing and bioelectronics, wearable nanodevices. Many of them exhibited good biosafety and it was also demonstrated that functionalization of 2D nanomaterials plays an important role in decreasing their possible toxicity. Owing to these reasons, this project proposal aims to design and synthesize drug delivery and antibacterial systems, consisting of 2D heterostructures based on layered double hydroxides, metal phosphates and phosphonates, and bioactive species and biocompatible metallic nanoclusters. Suitable functional groups will be introduced by direct synthesis or by post synthesis treatments. A systematic characterization will be devoted to the study of their physico-chemical properties, including microstructure, surface and porosity properties, biological activity and biocompatibility features as well.

#### **Thematic 4**

**Titolo:** I biomateriali nella prevenzione e terapia delle patologie ossee e dentali.

**Title:** Biomaterials in the prevention and therapy of bone and dental pathologies.

**Project referents:**

Prof.ssa Valeria Ambrogi, [valeria.ambrogi@unipg.it](mailto:valeria.ambrogi@unipg.it)

Prof.ssa Milena Villarini, [milena.villarini@unipg.it](mailto:milena.villarini@unipg.it)

Restoring tooth structure and bone regeneration are important challenges of modern society mainly due to the increase in the average population's age. Trauma and disease of bone tissues result in severe pain and disability for a lot of people worldwide and their treatments have a high economic impact. Biomaterials for bone and dental application should have specific requirements such as osteoinduction, osteoconduction and osseointegration. Moreover, as infections are among the main causes of the failure of bone implant, also antimicrobial and antibiofilm activities should be required. Also, new long-term implantable devices are required to undergo genotoxicity tests for safety assessment. The project's aim is to obtain biomaterials functionalized or loaded with agents able to interact with bone cells and with agents with antimicrobial, antibiofilm activities. These biomaterials should be able to release these agents locally and in a prolonged way without inducing genotoxic effects.

#### **Thematic 5**

**Titolo:** Affrontare la strongiloidosi e altre malattie neglette: approcci integrati e innovativi per la scoperta di modulatori del recettore DAF-12.

**Title:** Tackling Strongyloidiasis and other neglected diseases: Integrated, innovative approaches for the discovery of DAF-12 receptor modulators.

**Project referents:**

Prof. Andrea Carotti, [andrea.carotti@unipg.it](mailto:andrea.carotti@unipg.it)

Prof. Antimo Gioiello, [antimo.gioiello@unipg.it](mailto:antimo.gioiello@unipg.it)

The nuclear receptor DAF-12 has been recognized as the key molecular player regulating the life cycle of nematodes including the *Strongyloides stercoralis*, a pathogenic parasitic roundworm causing Strongyloidiasis. This neglected tropical disease infects more than 200 million people worldwide with up to 2.5% of these infections progressing into a hyperinfection syndrome with a 90% mortality rate if untreated. To date, no reliable solutions exist to treat these severe forms. Recent findings have shown that the binding of ligands to DAF-12 allows the receptor to act as an on/off switch modulating infection, making it vulnerable to therapy. The goal of this project is to discover efficacious DAF-12 modulators as novel agents for the treatment of Strongyloidiasis. Different computational tools such as molecular dynamics simulations and deep learning methods will drive the design of molecules that will

be synthesized by merging sustainable enabling chemical technologies including flow technology, photochemistry and LSF approaches.

### **Thematic 6 (riservata ai dipendenti JANSSEN)**

**Titolo:** Digitalizzazione delle informazioni per i pazienti nel mondo farmaceutico

**Title:** Digitalization of patient information in the pharmaceutical world

**Project referents:**

Prof.ssa Luna Perioli [luana.perioli@unipg.it](mailto:luana.perioli@unipg.it)

Dott.ssa Nicoletta Scione

In the digital age we live in, technological innovation continues to transform our daily processes and customs. In line with this trend, the pharmaceutical field is committed to introduce a major change in the presentation of the information to patients: the digitalization of package leaflets.

The aim of the PhD is to examine the implications, opportunities and challenges related to the digitalization of package leaflets. This process is profoundly transforming the pharmaceutical industry, offering new possibilities for communication, interactivity, personalization and accessibility of content. Therefore, it is critical that we thoroughly examine this transition and understand its potential benefits for patients and implications for the industry.

During the three-years PhD course, emerging technologies and digital solutions used for the creation and distribution of digital leaflets will be examined. The technical and regulatory aspects related to this transition will also be assessed, as well as exploring best practices and challenges to be faced during the digitalization process.

### **Thematic 7 (riservata ai dipendenti ITEL Telecomunicazioni Srl)**

**Titolo:** Progettazione e produzione GMP in asettico di un radiofarmaco a base di 18F-Colina

**Title:** Design and GMP manufacturing in aseptic way of a radiopharmaceutical based on 18F-Choline

**Project referents:**

Prof Luana Perioli [luana.perioli@unipg.it](mailto:luana.perioli@unipg.it)

Dott.ssa Anna Tolomeo [anna.tolomeo@unipg.it](mailto:anna.tolomeo@unipg.it)

The PET (acronym for Positron Emission Tomography) investigation is an advanced diagnostic technique that allows obtaining images of functional interest (unlike other techniques such as CT and Magnetic Resonance Imaging which generate images of morphological interest) widely used in various areas, including the diagnosis of neoplastic pathologies, neurodegenerative pathologies and functional neuroimaging. The procedure begins with the injection of a radiopharmaceutical: a molecule that can be described in two components:

- Ligand, which represents the portion that interacts in cellular physiological processes;
- Radioisotope, which represents the portion of the molecule capable of being detected by the detection apparatus.

The ligand is generally a metabolite that is particularly active in the cellular processes of the tissue for which the investigation is active; in fact, among the most used there is Glucose, the main metabolite used for energy purposes in all the cells. The used radioisotope is selected according to some characteristics, including the half-life, the production process for its creation, the diagnostic accuracy and its chemical-physical stability.

The main aim of the project is to implement the synthesis of an 18F-Fluorocholine-based radiotracer owned by the ITEL Telecommunications company. The synthesis of the product and dispensing of the new radiotracer will be carried out in GMP-classified environments which allow the creation of sterile products in accordance with international standards and regulations.

### **Thematic 8 (riservata ai dipendenti TES PHARMA)**

**Titolo:** Studio di nuovi ligandi del recettore PXR e del loro effetto su meccanismi di transregolazione e coregolazione del recettore.

**Title:** Study of new ligands of the PXR receptor and their effect on receptor transregulation and coregulation mechanisms.

**Project referents:**

Prof. Francesco Galli [francesco.galli@unipg.it](mailto:francesco.galli@unipg.it)

Dott.ssa Francesca De Franco

Activity n.1: Study of nuclear receptors as new therapeutic targets for the treatment of metabolic and oncological diseases. This activity involves the development of techniques and methods useful for understanding the pathophysiological and molecular biology mechanisms essential for discovery and development of new drugs.

Activity n.2: Validation from a biological, biochemical and pharmacological point of view of druggable nuclear receptors entailing the synthesis of proteins in the lab with subsequent set-up of biological binding and in vitro pharmacological assays. This activity will be conducted to support the research carried out in Tes and in collaboration with universities and research institutes.

Activity n.3: In vitro profiling of synthetic compounds for structure-activity relationship studies and for the evaluation of the in-vitro pharmacological profile in cellular assays mimicking the pathologies of interest.

Industrial Doctorate - Employee Commitment:

The employee, already part of the Tes Research and Development team, undertakes to carry out the previously mentioned activities and to conduct bibliographic research to support the project activities concerning the study and characterization of new chemical compounds for nuclear receptors as targets therapeutic.

### **Thematic 9 (riservata ai dipendenti ABOCA)**

**Titolo:** "Sviluppo di matrici naturali complesse, attraverso l'applicazione di tool statistici"

**Title:**

**Referenti del progetto:**

Prof. Stefano Giovagnoli [stefano.giovagnoli@unipg.it](mailto:stefano.giovagnoli@unipg.it)

Dott.ssa Daniela Quattrone

The training objective is to acquire know-how relating to the study of pharmaceutical processes and natural formulations, through the identification of:

- predictive chemical-physical and verification tests regarding the process progression;
- The critical process parameters;
- DoE study: to understand when it is applicable and how to develop lean models applicable to a wide range of products.