Ammissione al corso di Dottorato di Ricerca in Scienze Farmaceutiche del XXXIX ciclo, a.a. 2023/2024 – Progetti di Ricerca

Admission to the PhD program in Pharmaceutical Sciences XXXIX cycle, a.a. 2023/2024 – Research Projects.

<u> Tematica 1 (D.M. 117, Impresa Partner: Vivatis Pharma Italia Srl)</u>

Titolo in Italiano: Sviluppo di protocolli d'indagine nutrigenomica e farmacogenomica innovativi per verifiche di efficacia e sicurezza di nutraceutici e alimenti funzionali.

Titolo in Inglese: Innovative nutrigenomics and pharmacogenomics methods to assess efficacy and safety of nutraceuticals and functional food products.

Referente del progetto: Prof. Francesco Galli, francesco.galli@unipg.it

The project will develop innovative nutrigenomics and pharmacogenomics methods and research protocols for the study of nutraceuticals and functional food products supported by the industrial partner. The research and the pre-training course will primarily take place in the laboratories of the tutor and at the Delphi Star-lab departmental platform which harbors high-throughput technology and equipment necessary for the project. The industrial partner and the network of research partners of the tutor will host the student to complete his/her training and research program. These partners include the networks of the PNRR project Vitality, MOOD project (funded by the IT Ministry of Health) and of the European projects Choko-agE, ERA-HDHL program, and the EpiLipidNet COST Action.

Tematica 2 (D.M. 117, impresa partner Sterling S.p.a)

Titolo in Italiano: Sviluppo di strategie di veicolazione orale, polmonare ed intranasale per principi attivi steroidei ad azione centrale

Titolo in Inglese: Development of oral, pulmonary and intranasal delivery strategies for centrally acting steroidal active ingredients

Referente del progetto: Prof.ssa Aurélie Schoubben, aurelie.schoubben@unipg.it

Steroidal active pharmaceutical ingredients have therapeutic potential in the treatment of neurodegenerative pathologies and disorders of the central nervous system (CNS). Many of the existing pharmaceutical forms based on these drugs are inadequate to hypothesize their use for the treatment of CNS pathologies due to pharmacokinetic, toxicological and compliance problems. Furthermore, to date strategies aimed at selectively distributing the active pharmaceutical ingredients to the CNS are lacking and there is little evidence of delivery systems to the CNS. The aim of the project is therefore to develop delivery systems for these drugs to target the CNS by exploiting different routes of administration. Formulations for the oral route, characterized by better compliance and reduced costs, formulations for the pulmonary route to take advantage of the direct access to the systemic circulation and intranasal formulations to favor rapid uptake at the CNS level.

Tematica 3 (D.M. 118)

Titolo in Italiano: Sviluppo di formulazioni dermocosmetiche eco-sostenibili a base di sottoprodotti di origine animale e vegetale per il trattamento di patologie cutanee

Titolo in Inglese: Development of eco-sustainable dermo-cosmetic formulations based on animal and vegetal by-products for the treatment of skin diseases

Referenti del progetto:

Prof.ssa Luana Perioli, <u>luana.perioli@unipg.it</u>

Prof. Roccaldo Sardella, roccaldo.sardella@unipg.it

In the project, by-products and waste of animal origin (e.g. snail slime) and vegetable origin will be used, as sources of active ingredients for the production of dermo-cosmetic formulations. These materials will be selected in relation to their antioxidant, anti-inflammatory, antimicrobial and healing activity. For animal matrices, the effect of feeding and environmental conditions of growth on the

above activities will be evaluated. For vegetable matrices, the most widespread ones on the national territory will be considered. The choice will be suggested by the business partner. The selected materials will be studied in vitro from an analytical, biological, pharmacological and antimicrobial point of view. The most interesting ones will be used for the development of formulations and these will be characterized in vitro from a rheological, microbiological point of view, along with their stability (physical and microbiological) over time.

Tematica 4 (D.M. 118)

Titolo in Italiano: Sviluppo di protocolli metabolomici e lipidomici innovativi della piattaforma dipartimentale Delphi Star-lab per lo studio di micronutrienti e vitamine d'interesse nutraceutico. **Titolo in Inglese**: Innovative metabolomics and lipidomics protocols of the Delphi Star-lab platform for the study of micronutrient vitamins of nutraceutical interest.

Referente del progetto: Prof. Francesco Galli, <u>francesco.galli@unipg.it</u>

The project will develop innovative metabolomics and lipidomics methods and research protocols for the study of micronutrients and vitamins (nutraceuticals and functional food area of application). The research and the pre-training course will primarily take place in the laboratories of the tutor and at the Delphi Star-lab departmental platform which harbors high-throughput technology and equipment necessary for the project. The Elle Elle Srl company, active in the nutraceutical sector, and the network of research partners of the tutor that will be available to host the student to complete training and research tasks. These partners include the networks of the PNRR project Vitality, MOOD project (funded by the IT Ministry of Health) and the European projects Choko-agE, ERA-HDHL program, and EpiLipidNet COST Action.

Tematica 5:

Titolo in Italiano: Sviluppo di piccole molecole quali inibitori della Polimerasi Theta per implementare la letalità sintetica nell'oncologia di precisione.

Titolo in Inglese: Deploying Synthetic Lethality in Precision Oncology by Developing Polymerase Theta Small Molecule Inhibitors.

Referenti del progetto:

Prof.ssa Serena Massari, <u>serena.massari@unipg.it</u> Prof.ssa Violetta Cecchetti, <u>violetta.cecchetti@unipg.it</u>

Tumor cells defective in DNA repair pathways have a selective growth advantage but often become reliant on backup pathways that can be targeted to kill the cells. This concept is the basis of synthetic lethality. In this context, the DNA polymerase Theta (Pol Θ) is emerging as a promising target for the treatment of DNA repairdeficient cancers. It is essential for the survival of homologous recombination-defective cells, and it is overexpressed in many cancers but is largely absent in normal cells. The doctoral project we propose will concern the identification of novel, validated inhibitors of Pol Θ that can be progressed along the drug discovery process. It will consist of: i) identification of hit compounds able to inhibit the Pol Θ polymerase domain in a biochemical assay; ii) optimization of the hit compounds, aiming at improving their activity; iii) validation of the best compounds in cell-based assays.

Tematica 6 (borsa PRO3)

Titolo in Italiano: Sintesi e valutazione bioorganica di composti organici del selenio con proprietà regolatorie di processi redox.

Titolo in Inglese: Synthesis and bioorganic evaluation of redox regulating organoselenium derivatives.

Referenti del progetto:

Prof. ssa Francesca Marini; <u>francesca.marini@unipg.it</u> Prof.ssa Luana Bagnoli, <u>luana.bagnoli@unipg.it</u> Sulfonyl containing compounds exhibit therapeutic effect against bacterial affections, tumors, Parkinson and other oxidative stress-related diseases. These compounds have been found to activate the Nrf2 pathway alleviating oxidative stress and inflammatory conditions. The ability to react with the thiol group of free cysteine residues of Keap1, which is a negative modulator of Nrf2, is a common property of many Nrf2 inducers. Starting from the synthetic know-how of the promoters, strategies for the synthesis of new libraries of selenium derivatives and their bioorganic evaluation through modern NMR technologies will be investigated. New compounds will be designed in order to modulate the electrophilicity. The molecule-protein(s) interactions could be investigated using waterLOGSY experiments combined also with other biophysical analysis. Biological and computational evaluations will be carried out using existing collaborations within the Department as well as the international scientific network SeSReCat.

Tematica 7 (riservata dipendenti JANSSEN-CILAG SpA)

Titolo in Italiano: Sviluppo di un modello MVA per l'ottimizzazione di processo, risoluzione di problematiche e monitoraggio "Real Time" dei processi produttivi

Titolo in Inglese: Development of MVA model for process optimization, troubleshooting and process Real Time Monitoring

Referenti del progetto:

Prof Luana Perioli <u>luana.perioli@unipg.it</u> Dott.ssa Sarah Nielsen

The MVDA techniques are proving to be a very effective tool for process analysis and optimization. The MVA model will be designed to analyze multivariate data from production systems and provide valuable insights to enhance process efficiency and quality, being applicable both to batch-mode and Continuous Manufacturing line. By utilizing advanced data analysis techniques, the model will identify critical variables, detect anomalies, and offer suggestions for optimizing operational parameters. Additionally, the MVA model will be integrated with a real-time monitoring system to enable immediate visualization of process performance and timely alarms in case of deviations. The implementation of this model will provide a valuable resource to enhance process productivity and quality, while reducing downtime and waste.

Tematica 8 (riservata dipendenti ITEL Telecomunicazioni Srl)

Titolo in Italiano: Perfezionameno della produzione, in accordo con le GMP, e sviluppo di metodi analitici, secondo la Farmacopea Europea, della soluzione iniettabile di 6-[¹⁸F]fluoro-L-DOPA, con autorizzazione all'imissione in commercio di proprietà

Titolo in Inglese: Improvement of GMP-compliant production and development of analytical methods, according Eu. Ph. c.e., of 6-[¹⁸F]fluoro-L-DOPA injectable solution with proprietary marketing authorization.

Referenti del progetto:

Prof Luana Perioli <u>luana.perioli@unipg.it</u> Dott.ssa Anna Tolomeo

The neurotracer 6-[¹⁸F]fluoro-L-DOPA is a powerful tool in PET imaging of neuropsychiatric diseases, movement disorders and brain malignancies.

More recently, it also demonstrated good results in the diagnosis of other malignancies such as neuroendocrine tumours, pheochromocytoma or pancreatic

adenocarcinoma. The multiple clinical applications of this tracer fostered a very strong interest for this radiotracer. The aim of the work is to improve the radiopharmaceutical production and to develop the analytical methods, in accordance with Eu. Ph. C.e., of 6-[¹⁸F]fluoro-L-DOPA, with ITEL's marketing authorization.