Project 6

Name/title of the PhD course	**Chemical Sciences**
Name of the PhD coordinator	Prof. Angelina Lombardi
Name/Title of the PhD project	***Gut microbiota-metabolized agri-food wastes: new perspectives for the recovery of bioactive compounds and development of novel prebiotics***
Department of reference	Department of Chemical Sciences of University of Naples Federico II (http://www.scienzechimiche.unina.it/)
Working conditions, research team, infrastructures, equipment	The Department hosts about 100 researchers/professors and 20 units of technicians and administrative personnel. The department hosts several large instrumentations used in different research areas by researchers and students of degree and PhD courses, including several 400-600 MHz NMR spectrometers, a LC-MS ESI-TOF and a MALDI TOF-TOF spectrometer, several small/wide angle X-rays diffraction instruments, UV/VIS spectrophotometers, a spectropolarimeter, FT-IR and ATR-FTIR instruments, a spectrofluorimeter, an EPR spectrometer, a DLS instrument, and SEM and TEM instruments. The research activities carried out in the department cover several areas of chemistry, and in particular the working groups where the recruited PhD will work with are involved in research projects on 1) structure and property characterization of natural and bioinspired polyphenols for health and food applications, surface functionalization with catechol compounds, melanin pigments as innovative functional materials for dermocosmetic and technological applications, and 2) carbohydrate chemistry and biochemistry, structural and chemical biology of microbial glycans and glycoconjugates aimed at assessing their structure, conformation, function and immune recognition, study of molecular recognition events in glycans-protein interaction by spectroscopic, biophysical, computational techniques, and characterization of 3D complexes. These working groups are overall composed of 4 full professors, 6 associate professors, 1 post-docs, 1 RTD-A and 9 PhD students.
Scientific context	Largely produced waste materials and by-products from the agri-food industry represent a sustainable and easily available source of bioactive compounds such as polysaccharides and phenolic compounds The prebiotic activity of some of these materials, such as spent coffee grounds, grape pomace, hazelnut shell, mango, apple, lemon and banana peels, and soybean by-products has been also recently reported, paving the way toward the recovery of agri-food wastes as food supplements. On the other hand, biotechnological approaches aimed at the recovery of bioactives from agri-food by-products are actively pursued and represent an environmentally clean technology for the production of high activity compounds and extracts for application e.g. as food additives or cosmetic ingredients. As a remarkable example, solid state fermentation of pomegranate peels and husks could afford the recovery in very high yields of ellagic acid, a phenolic compound which is endowed with anti-mutagenic and anti-carcinogenic activity and is able to prevent the onset of cardiovascular diseases, atherosclerosis, and dyslipidemic disorders as well as to stimulate wound healing and skin elasticity. Solid state fermentation has also been found to effectively enhance the bioaccessible and bioavailable phenolic contents in cereal by-products, whereas enzymatic biotransformation has been reported to increase the antioxidant activity of polyphenols form grape pomace. Solid state fermentation by *Aspergillus niger* of mixtures of wastes from wineries, olive mill and breweries to produce antioxidant compound has been also reported. Polysaccharides from agri-food by-products are also extensively modified by microbial fermentation; for example, sustainable and clean processes for the production of xylooligosaccharides from lignocellulosic biomasses based on enzymatic hydrolysis or microbial fermentations have been recently reviewed. Production of a wide variety of functional carbohydrates through fermentation of vegetable food waste and by-products by *Aspergillus*, *Yarrowia*, *Trichoderma*, *Amycolatopsis*, and *Xanthomonas* species has been reported as well. The immune-enhancing effects of polysaccharide extracted from by-products of Korean liquor fermented by *Saccharomyces cerevisiae* have been very recently reported. Therefore, bacterial modification of polysaccharides from agri-food by-products represents an important research field in biotechnology. The potential production/conversion to value-added products has increasing applications in pharmacological, nutraceutical, functional food, cosmeceutical, and agricultural fields, and future prospects for the development of immunomodulators, anti-inflammatories and bioflocculants.
Project Research plan	The general objective of the project is a systematic investigation of the structural modifications induced by gut microbiota on the main polysaccharidic and phenolic components of a series of agri-food wastes. These latter will be selected among those easily available in high amounts and well-characterized in terms of the chemical structure of the main polysaccharidic and phenolic components, in order to define the metabolic transformation pathways. Based on the information collected, ad hoc fermentation conditions will be developed for the recovery of bioactive compounds for food and cosmetic applications. The project will be divided into 5 main work packages (WPs): *WP1: Characterization of the structural modifications induced on the phenolic and sugar components of the agri-food wastes by an in vitro simulated gastrointestinal digestion followed by gut microbiota fermentation.* *WP2: Determination of the prebiotic activity of the agri-food wastes.* *WP3: Determination of the antioxidant properties of the agri-food by-products before and after simulated gastrointestinal digestion and gut microbiota fermentation.* *WP4:Optimization of the fermentation conditions on the more promising agri-food wastes to improve the recovery yields of the bioactive compounds and implementation of green and sustainable methodologies for their extraction (in collaboration with University of Coahuila, Mexico).*

	WP5: Preliminary evaluation of the obtained bioactives as functional ingredients in the food and cosmetic sector (in collaboration with Beiersdorf AG, Germany).
Research and Training Innovative aspects	Although it is well-known that waste products of the agricultural and food industry can be metabolized by the gut microbiota, thus resulting in the production of bioactive compounds as well as in prebiotic effects, a systematic investigation of the modifications induced on structure and properties of the main bioactive constituents is still lacking in the literature. The understanding of the chemical and metabolic processes underlying the gut microbiota-induced transformation of agri-food by-products will allow not only to further exploit the potential of these easily available materials as prebiotics, to be eventually used as food supplements, but also to open new technological perspectives for the recovery of compounds to be used as functional additives in a wide range of materials by a more efficient control and modulation of the bioprocessing conditions. The social and economic impact of the project is also well-apparent considering that it is aimed to strengthen the importance of agri-food by-products as an easily accessible and sustainable alternative for the production of value-added functional compounds, therefore ultimately leading to a reduction of the disposal costs and of the environmental hazard as well as to an enhancement of the sustainability of the agri-food industrial sector, also in a circular economy perspective. In addition, fermentation and related biotransformation for production of bioactive compounds represent environmentally clean technologies, providing high quality and high activity extracts for application as biocompatible food additives or cosmetic ingredients.
Inter-Multidisciplinary aspects	The present project will allow the PhD student to acquire expertise in several disciplines of chemistry such as organic chemistry (methodologies and biophysical/spectroscopic and spectrometric approaches for the structure and property characterization of heterogeneous and complex compounds of natural origin), analytical chemistry (development of extraction and analytical methods for identification and quantitation of natural compounds in complex mixtures), green chemistry (development of green and sustainable methodologies for the recovery of functional compounds), and fermentation chemistry (characterization of the main metabolic transformations induced by the gut microbiota and optimization of bioprocessing conditions for the recovery of functional compounds). The collaboration with food chemists, biologists and microbiologists will further reinforce the intersectoral and multidisciplinary aspects of the project. Finally, the collaboration with a industrial partner will further contribute to the professional growth of the PhD student by providing the opportunity to transfer the basic knowledge acquired from the studies conducted on a laboratory scale at the university to the practical implementation of a functional additive on an industrial scale.
Secondment opportunities	The **Universidad Autonoma de Coahuila (Mexico, http://www.uadec.mx),** a public higher education with research activity of the Bioprocesses & Bioproducts Research Group of the Food Research Department is focused on engineering of bio-products from renewable bioresources. The co-supervisor of this research project, **Dr. Juan A. Ascacio-Valdes**, He will contribute to this project by hosting the PhD student for a secondment of two/three months during which he/she will come in contact with his research and production activities oriented to define the fermentation conditions on the more promising agri-food wastes in order to improve the recovery yields of the bioactive compounds and to implement green and sustainable methodologies for their extraction. **Beiersdorf AG, Hamburg, Germany (https://www.beiersdorf.com/),** a German multinational company that manufactures and retails skin-care products. The co-supervisor of this research project, **Dr. Jörn Hendrik Reuter**, the Head of the Microbiome Research Team of Beiersdorf AG with expertise on research in all aspects of the microbiome with regards to skin and consumer products, with particular reference to atopic dermatitis and acne. He will contribute to the project by hosting the PhD student for a secondment of six months during which he/she will come in contact with Beiersdorf research and/or training activities, which will further contribute to the development of knowledge and skills of the doctoral researcher. In particular he/she will be hosted in the Global Skin Research Center in Hamburg with laboratories for skin research and disease as well as microbiology research, where he will acquire expertise on cosmetic formulations, by testing the more promising agri-food by-products derived extracts and products in the dermo cosmetic sector (e.g. as photoprotectors or anti-aging agents).
Main Supervisor: Prof. Lucia Panzella (https://www.docenti.unina.it/lucia.panzella); **Co-supervisor**: Prof. Alba Silipo (https://www.docenti.unina.it/alba.silipo)	
Brief CV	**Lucia Panzella** is Associate Professor of Organic Chemistry at the Department of Chemical Sciences of University of Naples "Federico II". In 2007 she received the prize "L'Oreal Italia Per le Donne e la Scienza" promoted by L'Oréal Italia in collaboration with the Italian National Commission for Unesco (2007). In November 2020 she received the National Scientific Qualification ("Abilitazione Scientifica Nazionale") as Full Professor in Organic Chemistry (03/C1) (2018/2020 session). Her teaching activities at University of Naples Federico II include "Organic Chemistry in Food Science" course for the Bachelor's degree in Chemistry, "Organic Chemistry and Laboratory" course for the Bachelor's degree in Biology, and "Natural phenolic compounds: structure, reactivity and applications" PhD course for the PhD course in Chemical Sciences. She has been/is supervisor of 2 PhD students in Chemical Sciences and 7 students in Biological Sciences, and co-supervisor of more than 50 students in Chemistry, Chemical Sciences, and Biology. Her research interests focus on the reactivity and functional properties of phenolic compounds, with particular reference to those deriving from agri-food by-products, for the development of functional materials to be used in cosmetics, food packaging and biomedicine; reactivity of dietary polyphenols with reactive oxygen and nitrogen species and their coupling reactions with sulfhydryl compounds of biological relevance; chemistry of melanin pigments. She is member of the Board of Directors and of the Travel Award Committee of the European Society for Pigment Cell Research since 2017. She is member of the Italian Chemical Society (Division of Organic Chemistry, Biotechnology Interdivisional Group, Green Chemistry Interdivisional Group) and of Groupe Polyphenols. She was member of the scientific and organizing committee of the '1st Virtual

	Symposium for Young Organic Chemists' (ViSYOChem) promoted by the Organic Division of Italian Chemical Society. Experience in supervising PhD students: Currently supervising 2 PhD students in Chemical Sciences. **Alba Silipo, co-supervisor,** is Full Professor of Organic Chemistry at the Department of Chemical Sciences of University of Naples Federico II. She is author/coauthor of 165 publications on international peer-reviewed journals (h-index 33, number of citations 3800 (Scopus, January 2022).
Publications	She is author/coauthor of 127 publications on international peer-reviewed journals (h-index: 36, number of citations: 3095, from Scopus on January 12, 2022). Most significant 5 publications: -Rajha, H. N.; Paule, A.; Aragonès, G.; Barbosa, M.; Caddeo, C.; Debs, E.; Dinkova, R.; Eckert, G. P.; Fontana, A.; Gebrayel, P.; Maroun, R.G.; Napolitano, A.; **Panzella, L.;** Pasinetti, G. M.; Stevens, J. F.; Schieber, A.; Edeas, M. Recent advances in research on polyphenols: effects on microbiota, metabolism, and health. Mol. Nutr. Food Res., 2022, 66, 2100670. -Ortenzi, M.A.; Antenucci, S.; Marzorati, S.; **Panzella, L**.; Molino, S.; Rufián-Henares, J.Á.; Napolitano, A.; Verotta, L. Pectin-based formulations for controlled release of an ellagic acid salt with high solubility profile in physiological media. Molecules, 2021, 26, 433 -Moccia, F.; Flores-Gallegos, A. C.; Chávez-González, M. L.; Sepúlveda, L.; Marzorati, S.; Verotta, L.; **Panzella, L.**;, Ascacio-Valdes, J.A.; Aguilar, C.N.; Napolitano A. Ellagic acid recovery by solid state fermentation of pomegranate wastes by Aspergillus niger and Saccharomyces cerevisiae: a comparison. Molecules, 2019, 24, 3689 -Verotta, L.; **Panzella, L.**; Antenucci, S.; Calvenzani, V.; Tomay, F.; Petroni, K.; Caneva, E.; Napolitano, A. Fermented pomegranate wastes as sustainable source of ellagic acid: antioxidant properties, anti-inflammatory action, and controlled release under simulated digestion conditions. Food Chem., 2018, 246, 129-136 **-Panzella, L.**,* Pérez-Burillo, S., Pastoriza, S., Martín, M. A., Cerruti, P., Goya, L., Ramos, S., Rufián-Henares, J. A., Napolitano, A., d'Ischia, M. (2017) High antioxidant action and prebiotic activity of hydrolyzed spent coffee grounds (HSCG) in a simulated digestion-fermentation model: toward the development of a novel food supplement. J. Agric. Food Chem., 65, 6452-6459
Projects participation	Main Funding: • H2020-MSCA-ITN-2020, "A multidisciplinary training network for the bioinspired development of glycomimetics tuning the Siglec-Sialoglycan axis", Proposal number 956758 (GLYTUNES, www.glytunes.eu), Coordinator • PRIN 2017, "Bioinspired development of glycomimetics tuning the Siglec-Sialylated glycan axis." (2017XZ2ZBK), Coordinator • COST Action (CA18103) INNOGLY, 2019-2023, Role: MC Substitute • European Union (FSE, PON Ricerca e Innovazione 2014-2020, Azione I.1 "Dottorati Innovativi con caratterizzazione Industriale"), Coordinator; partner Giotto Biotech (Prof. M. Fragai) and Prof. S. Martin Santamaria (CSIC, Madrid), (XXXIII cycle). • European Union (FSE, PON Ricerca e Innovazione 2014-2020, Azione I.1 "Dottorati Innovativi con caratterizzazione Industriale"), Coordinator; partner GSK (Dott. F. Berti) and Prof. S. Martin Santamaria (CSIC, Madrid), (XXXVII cycle). • H2020-MSCA-ITN-2014, "Toll-Like Receptor 4 activation and function in diseases: an integrated chemical-biology approach", Proposal number: 642157 (TOLLerant), Beneficiary partner (as PI) • H2020-MSCA-ITN-2019"SweetCrossTalk", Beneficiary partner (team member, tutor of a PhD student)