University of Milano-Bicocca
PhD Course in Chemical, Geological and Environmental Sciences
Call for Interest 38th cycle - Curriculum Chemical Sciences

Nr 1		**Supervisor**	**Davide Ballabio**
Title	**Chemometrics strategies for the prediction of the molecular structure by LC-MS/MS spectra**		

Liquid chromatography with tandem mass spectrometry (LC-MS/MS) is one of the most effective analytical techniques to characterize environmental, food, forensic and biological samples. The identification of substances in the sample is usually based on a similarity match between the experimental MS/MS spectrum and the spectra included in specific libraries. This process may be dependent on the experimental settings used for the spectrum measurement; moreover, it is likely that a detected molecule is not present in the reference spectral library, in particular when omics untargeted experiments are carried out.

Recent studies have shown that chemometrics can support the identification of substances from LC-MS/MS spectra by developing novel deep learning tools to directly correlate the chemical information encoded in MS spectra with the molecular structures of compounds. In this way, it may be possible to directly predict molecular structures (encoded in molecular descriptors) from large databases of spectra measured under different experimental conditions. Then, the descriptors can be used to search for the target compound in huge chemical database, containing millions of substances.

Being a novel development, there are many improvements in the approach to be evaluated, such as different representations of both spectra (input) and molecular structure (output), as well as the deep

learning algorithms and their optimisation. The PhD student is expected to acquire knowledge on both the interpretation of the MS analytical information and on the development of proper chemometric approaches. The period abroad can be planned at the Eindhoven University of Technology (NL) to acquire knowledge on deep learning strategies.

Supervisor web page: https://www.unimib.it/davide-ballabio

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Nr 2		**Supervisor**	**Simona Binetti**
Title	**Wet chemistry process for new generation solar cells based on sustainable chalcogenide thin film**		

This research project is focused on the optimization of the wet low-cost deposition methods for the synthesis of inorganic chalcogenide thin films (employable as absorbers in new generation solar cells). The quaternary alloys involved in this research are structured as Cu2XY(S,Se)4 (with X = Zn, Mn and Y = Sn, Ge), already known and well-documented in the literature thanks to their good performances, high stability, high sustainability and possibility to modulate the energy gap, aiming to make them suitable for tandem applications with silicon or perovskites. The thin films deposition will be performed on rigid and flexible substrates, transparent or otherwise. The corresponding Cd-free n-type buffer layer that will be examined in this project are Zn(O,S), ZnS, ZnSnO e TiO2, and the most performing deposition techniques among chemical-bath deposition, film applicator deposition, spray pyrolysis, ink-jet printing and Atomic Layer Deposition (ALD) will be investigated. The optimization of the back contact with a proper transparent conductive oxide will make the devices suitable for bifacial or tandem application, allowing to overcome theoretical efficiency limitations. The collaborations with other European research centers such as Tallinn University of Technology, Technische Universiteit Delft and Institut Photovoltaique d'Ile-de-France will allow the candidate to spend a period abroad, expanding its knowledge by learning complementary characterisation skills and techniques for the above-mentioned materials.

Supervisor web page: https://www.unimib.it/simona-olga-binetti

University of Milano-Bicocca
PhD Course in Chemical, Geological and Environmental Sciences
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Nr 3		**Supervisor**	**Simona Binetti**
Title	**High efficiency solar cells based on metal halide perovskites**		
The research project is focused on the production of solar cells based on metal halide perovskites, stable and with performance comparable to the state of the art. The mixed cation and halogen composition will be considered, working on optimizing the stability of the device's performance. With this aim, not only the chemical-physical properties of the material and their relationship with the growth process will be studied, but also the performance of the photovoltaic devices that will be manufactured. Part of the work will be dedicated to the deposition of thin films for the realization of the back contact on rigid and flexible substrates. To this end, in addition to traditional deposition techniques, the Atomic Layer Deposition technique will also be used to complete the solar cell. Furthermore, original hole extractors will be implemented with the aim of obtaining high performances that are stable in real working conditions.			
Supervisor web page: https://www.unimib.it/simona-olga-binetti			

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Nr 4		**Supervisor**	**Laura Bonati**
Title	**Molecular dynamics methods for the study of properties and interactions of biomolecules**		

Biology largely runs on the operation of complex biomolecular systems involving protein folding and dimerization, binding of small molecules, and allosteric communication. The study of these processes at atomistic level is of great relevance for the comprehension of mechanisms behind physiological processes, human diseases, pharmacological and toxicological activity of chemical compounds, as well as for the development of new drugs. The PhD project will be focused on the use of Molecular Dynamics (MD) simulations to study diverse biological processes. Such processes, however, involve large systems up to thousands or even millions of atoms and may happen on timescales of seconds, thus their study requires the use of methods based on the Molecular Mechanics approximation. When the timescale of the mechanism under study is beyond current computational limits, enhanced sampling methods (such as steered MD, Metadynamics, or accelerated MD) will be used to speed-up the calculation and obtain a deeper understanding of the underling free-energy landscape. Furthermore, in order to achieve a good level of accuracy and keep the computational cost affordable, hybrid QM/MM simulation approaches will be evaluated. During the PhD period the candidate will be part of a research group and collaborations with international groups will be carried out.

Supervisor web page: https://www.unimib.it/laura-bonati

University of Milano-Bicocca
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Nr 5		**Supervisor**	**Claudio Greco**
Title	**Theoretical studies of enzymatic and biomimetic catalysts for sustainable applications in prevention and abatement of air pollution**		
The PhD project will regard the study of enzymes and of bio-inspired molecular catalysts able to activate small gaseous molecules that are present in traces in Earth's atmosphere. In particular, focus will be on the elucidation of the catalytic mechanisms of the CO-oxidizing enzyme Cu/Mo CO-dehydrogenase, and of the methane-oxidizing particulate methane monooxygenase (pMMO) enzyme. Investigations will be performed by means of quantum chemical methods, quantum mechanics/molecular mechanics approaches and hybrid dynamic simulations. PhD candidates will have the possibility to spend a research period abroad (e.g., at the Dept. of Theoretical Chemistry of Lund University, Sweden).			
Supervisor web page: https://www.unimib.it/claudio-greco			

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Nr 6		**Supervisor**	**Dario Narducci**
Title	**Novel materials for thermoelectric heat harvesting and cooling**		

Thermoelectricity has been a cornerstone in irreversible thermodynamics. At the same time, it has been largely used as a tool to either convert heat into electric energy or to pump heat in refrigerating machines – in both cases with no need for moving parts. Still, efficiency of both classes of devices needs to be improved to fully exploit thermoelectricity as a viable strategy for heat harvesting and management. To this aim, this research activity explores different routes to enhance the efficiency of thermoelectric materials (and devices, thereof), all making use of nanotechnology. This includes bottom-up and top-down strategies to energy filter charge carriers, fabrication of dimensionally constrained inorganic nanostructures, and the chemical control of the oligomerization process of thiophenes. The project is carried out in collaboration with several European universities and research centres, including the University of Warwick (UK), Aix-Marseille University (France), and the Institute of Micro and Nanotechnology of the Spanish National Research Council of Madrid (Spain), where the Ph.D. candidate might spend research stages.

Supervisor web page: https://www.unimib.it/dario-narducci

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Nr 7		**Supervisor**	**Massimiliano D'Arienzo**
Title	**Design and characterization of $SrTiO_3$ materials with in-situ exsolved transition metal nanoparticles for catalytic applications**		

Supported nanoparticle systems have received increased attention over the last decades because of their potential for high activity levels in catalytic conversions though, due to their nanoscale nature, they tend to exhibit problems with long-term durability. Mostly in the frame of perovskite-type materials, the discovery of the so-called *exsolution* concept has addressed many of these challenges, providing a relatively simple, single-step, synthetic pathway to produce supported metal nanoparticles which combine high stability against agglomeration and poisoning and superior catalytic properties.
In this context, the project aims at the preparation of transition metal doped $SrTiO_3$ systems exploiting, in particular, the exsolution process needed to segregate the metal active sites on the surface of the nanoparticles. Besides intense efforts in the synthesis and materials processing, a comprehensive structural and morphological characterization will be pursued, with a special attention to the possibility of monitoring the perovskite defectivity during the exsolution process by Electron Spin Resonance (ESR). Finally, the catalytic activity of the novel catalysts will be evaluated in the production of H_2 from natural gas as CH_4 and in the reduction of CO_2. The project will be developed in collaboration with other University groups in Italy and abroad (i.e. Universities of Trento and Hamburg) offering educational and professional tools which will encourage career perspectives.

Supervisor web page: https://www.unimib.it/massimiliano-darienzo

University of Milano-Bicocca
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Nr 8		**Supervisor**	**Heiko Lange**
Title	**Advanced isolation of natural polyphenols for SAR-driven value-added applications**		

In a first aspect of the PhD project, structural features of lignins and fractions of lignins generated by different fractionation techniques will be independently delineated in detail using state-of-the art techniques. Identified structural features will then be correlated to key physical-chemical properties and chemical behaviours, both reported or independently established, in a complexity that has not yet been achieved. Lignins used for this initial mapping will comprise current standard technical lignins as well as new lignins, produced in collaboration with ENEA on the basis of both novel, less explored abundant feedstocks and novel combinations of standard biorefinery and fractionation approaches. Fractionation-based tuning of lignin characteristics will be experimentally verified, and data will be used to generate a quantitative structure-activity relationship (SAR) for molecular features of lignins for the first time, making use of a newly developed in-silico description of lignin.
Exploiting the SAR insights, the first part will ideally conclude with the generation of the most suitable polyphenol for the second aspect of the PhD project, which will see the development of a novel valorisation protocol in the area of biomass-based catalysts.
The work is primarily done at the DISAT, with regular visits to ENEA research sites; a collaboration agreement facilitating such visits is currently being implemented.

Supervisor web page: https://www.unimib.it/heiko-lange

University of Milano-Bicocca
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Nr 9		**Supervisor**	**Cristina Airoldi**
Title	**Advanced bioorganic and bioanalytical techniques for drug discovery, drug delivery and diagnostics**		
The research project involves the use and the implementation of advanced techniques, mainly NMR spectroscopy, for the study of molecular recognition processes of biological relevance. These studies allow the identification of the structural determinants of ligand-receptor interactions involving biomolecules. The experimental work also requires the organic synthesis of bioconjugates as potential multifunctional ligands to be used as molecular tools in the in the fields of drug discovery, drug delivery and diagnostics. Collaboration with research groups form other European Universities and Research Centers, as well as participation in international congresses, seminars and workshops is expected.			
Supervisor web page: https://www.unimib.it/cristina-airoldi			

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Nr 10		**Supervisor**	**Luca Beverina**
Title	**The role of micellar catalysis in the green synthesis of organic semiconductors for plastic electronics**		
Plastic electronics uses semiconducting polymers and molecules instead of traditional inorganic semiconductors for the manufacturing of low cost, flexible electronic components. The research in the field developed very efficient materials and sound structure property relationships, thus making a case for a transition from laboratory to industrial environment. At this critical juncture, sustainability and ease of scaling up are at least as important as performances, to the point that efficient materials on a lab scale could become unpractical for the industry. The development of more efficient synthetic protocols and the complete removal of all organic solvents from both the synthesis and the processing of semiconducting polymers can help tremendously to improve sustainability and reduce costs. In the last 5 years we have demonstrated that the use of an aqueous dispersion of surfactants (including food grade lecithin), enables the synthesis and processing of representative semiconducting polymers. In this project we aim at producing more complex materials according to the same techniques. We also aim at developing techniques for the direct production of aqueous inks not requiring the purification of the polymer. Results will have a transformative impact on the growing printed electronics industry. The development of micellar chemistry will also impact in more traditional synthetic chemistry fields like pharmaceutical and specialty chemicals.			
Supervisor web page: https://www.unimib.it/luca-beverina			

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Nr 11		**Supervisor**	**Laura Cipolla**
Title	**Design, preparation, and characterization of bio-based hydrogels**		

Hydrogels have become popular as three-15 dimensional (3D) scaffolds for cell culture providing robust platforms for different applications, such as investigation of cell physiology, pathology, tissue regeneration, drug discovery, and delivery. Depending on the desired application, hydrogel chemico-physical features should be tuned by cross-linking strategies. In this framework, the search for new hydrogels and cross-linking strategies is still ongoing, in order to ameliorate their performances toward the desired application. The increasing need for advancements in hydrogels as robust platforms as 3D cell culture scaffolds (i.e., for cell therapies, tumor models, drug delivery systems, and tissue engineering) is prompting the research in the field, that is expected to boost the market growth in the next years (CAGR of 10.7% from 2021 to 2028, https://www.grandviewresearch.com/industry-analysis/3d-cell-culture-market).

The project will focus on the study of innovative chemical cross-linking strategies for hydrogel preparation, starting from natural polymers including proteins (i.e. gelatin), and polysaccharides (i.e. chitosan, starch).

The effectiveness of chemical cross-linking will be assessed by analytical spectroscopic techniques such as NMR and FT-IR, while morphology will be assessed by SEM. Biological behavior and drug release studies will also be performed in collaboration with research groups at UNIMIB.

Supervisor web page: https://www.unimib.it/laura-francesca-cipolla

University of Milano-Bicocca
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Nr 12		**Supervisor**	**Barbara La Ferla**
Title	**Development, Synthesis and Characterization of nanodevices to address Alzheimer disease with a multitarget approach**		

Alzheimer's disease (AD) is the most common cause of dementia among neurodegenerative diseases in the elderly population. A central pathological feature of AD is the accumulation of misfolded amyloid-β (Aβ) peptides. In our laboratory we have identified and developed a new class of compounds able to interact with toxic amyloid-β peptides and to contrast their pathological effect in vitro.
Recent developments in biological systems and overall clinical experience have revealed that the single-target drugs may not always induce the desired effect to the entire biological system due to compensatory strategies and other effects. Thus, scientists have recently proposed the multi-target drug design concept. In this regard, and looking at the context of Alzheimer disease, the present PhD project has the aim of addressing the pathology in a multifunction-multitarget approach, combining the aβ peptides ligands with other "active ingredients" such as antioxidants in a synergistic fashion exploiting a multifunctional platform. The Aβ peptides ligands have the role of inhibiting the formation of Aβ aggregates/plaques, while the antioxidant compound contrasts the oxidative stress produced by the same aggregates. thus "hitting the enemy from two fronts" to use a military term in the war against this pathology. As platforms both small multifunctional dendrimers and polymeric nanoparticles will be considered.
Possible destinations abroad: Bilbao, Patras.

Supervisor web page: https://www.unimib.it/barbara-ferla

University of Milano-Bicocca
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Nr 13		**Supervisor**	**Norberto Manfredi**
Title	**Conductive molecular materials for biomedical application**		
The aim of this research project is to design and synthesize conductive organic materials, both p-type and n-type, to be integrated into biopolymer-based devices for applications in the biomedical field. The new materials will be developed to be easily functionalized to be chemically bonded to the biopolymers chosen to create a device that has good stability in a biological environment. The synthesized materials will be characterized in their chemical-physical properties and subsequently integrated into biopolymers of interest. The properties of the composite materials thus made will be studied from the point of view of stability in the biological environment and their electrical properties. The cytotoxicity of the most promising materials will be studied to evaluate their applicability in biomedical applications.			
Supervisor web page: https://www.unimib.it/norberto-manfredi			

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Nr 14		**Supervisor**	**Alessandro Palmioli**
Title	**Discovery of bioactive compounds from natural sources**		

Recently, the research of bioactive natural compounds is gaining renewed interest. Natural extracts obtained from medicinal plants, foods, and algae, but also fungi and bacteria, are considered fundamental sources for exploring a large chemical diversity of healthy ingredients with pharmacological and nutraceutical applications. Our group combines expertise in bioorganic and medicinal chemistry as well as in advanced analytical techniques (including NMR and LC-HR-MS) for the preparation and characterization of bioactive-enriched extracts and for the identification and isolation of bioactive compounds from natural complex mixtures.
In this context, the PhD student involved in this research project will have the chance to develop different and complementary skills concerning:
- extraction and purification of bioactive compounds from natural sources;
- NMR spectroscopy for extract component identification and molecular recognition studies (with the target(s) of interest);
- mass spectrometry coupled with chromatographic techniques for extract component identification and isolation;
- biophysical, biochemical, and biological assays to assess extract biological activities (as amyloid inhibitors, antioxidants and modulators of autophagy, antitumoral, antibacterial agents).

Supervisor web page: https://www.unimib.it/alessandro-palmioli

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Nr 15		**Supervisor**	**Francesco Peri** **Barbara Costa (CP2 Biotech)**
Title	**Synthesis, optimization and formulation studies of novel TLR4 receptor agonists**		

CP2 Biotech is a spinoff of the University of Milano-Bicocca, founded in 2020 and operating in the drug discovery field with the mission to bring to clinical phase of experimentation new bioactive synthetic and natural molecules. CP2 operates in the preclinical stage of drug discovery and development and in the field of natural compounds.
Very recently Croda, one of the main global players in the field of vaccine adjuvants, funded a big research program involving CP2 with the aim to develop new vaccine adjuvants based on small molecules discovered by Peri's group active in stimulating human innate immunity through activation of the Toll-Like Receptor 4 (TLR4). There is an important global need for new, safe and effective vaccine adjuvants to include into vaccines for use in humans and animals.
The PhD student will be hired by CP2 biotech and will be directly involved in the rational design, synthesis and characterization of TLR4 agonists.
The PhD student will be trained to the dissemination of scientific results through the writing of scientific paper to be submitted to peer-reviewed international journals, oral and poster presentation to international congresses and participation to congresses, participation to departmental seminars and to the international networks of researchers for granted projects of F. Peri.
The ideal candidate should fluently speak English, have excellent practical and theoretical knowledge of organic synthesis techniques and should have relational skills and attitude to teamwork.

Notes: *Advanced Apprenticeship PhD at CP2 BIOTECH S.R.L. (This type of contract is reserved for those who have not yet reached the age of 30 at the time of recruitment)*

Supervisor web page: https://www.unimib.it/francesco-peri

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Nr 16		**Supervisor**	**Francesco Peri**
Title	**Computer-assisted rational design and synthesis of new drug leads optimization by semisynthesis of bioactive natural compounds**		
The ongoing projects in the F. Peri lab (https://theperilaboratory.btbs.unimib.it) are in the fields of organic and medicinal chemistry, and are focused on the drug development process and on the understanding of ligand/target interactions and study of biological pathways relevant for pathologies. The PhD student will be directly involved in molecular modelling and dynamics applied to rational drug design, chemical synthesis of new drug hits, extraction of purification of natural compounds and their chemical modification (semisynthetic drugs). The binding and interaction with target will be characterized by biophysical methods (NMR, fluorescence, SPR, calorimetry) and the first screening for biological activity will be done by the biology lab of the same research group. The PhD student will be trained to the dissemination of scientific results through the writing of scientific paper to be submitted to peer-reviewed international journals, oral and poster presentation to international congresses and participation to congresses, participation to departmental seminars and to the international networks of researchers for granted projects of F. Peri (for instance, the BactiVax project).			
Supervisor web page: https://www.unimib.it/francesco-peri			

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Nr 17		**Supervisor**	**Laura Russo** **Sabrina Bertini (Istituto Ronzoni)**
Title	**Derivatization and characterization of polysaccharides to be used for the functionalization of biomaterials**		
The aim of the project will be the production of biomaterials functionalized with polysaccharides. Polysaccharides are a heterogeneous class of biopolymers extracted by plants, algae, animals, and bacteria sources and a study of their properties, such as molecular distribution, viscosity, size, and surface charge, is of essential to determine and predict their biological functions or applications. Natural polysaccharides have a high degree of biodegradability, biocompatibility, bio-adhesive capacity and able to mimic the natural extracellular matrix (ECM) microenvironment. Furthermore, they present a low toxicity and are availability on a large scale in a relative low cost. Natural or chemically modified polysaccharides can be used in pharmaceuticals, food and cosmetical field, due to their interaction with several proteins. In this contest the PhD project will be focused on the research and development of new class of functionalized biomaterials. This project is funded and held in collaboration with Istituto Ronzoni (Milano).			
Notes: *Scholarship funded by Istituto di Ricerche Chimiche e Biochimiche G. Ronzoni*			
Supervisor web page: https://www.unimib.it/laura-russo			

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Nr 18		**Supervisor**	**Laura Russo**
Title	**Development of biomaterials for artificial 3D-printed tissues/organs**		

The development of artificial tissues mimicking specific organs in healthy and pathological states is the new frontier for regenerative medicine and personalized personalised therapeutic approaches.
The proposed project will develop biomaterials suitable for the production of different human tissues, in particular brain, pancreas and gum, exploiting also a 3D-bioprinting approach. Biopolymers such as collagen, elastin, gelatine, hyaluronic acids or chitosan, will be properly functionalized and crosslinked exploiting chemoselective approaches to generate "bioinks" suitable for 3D bioprinting in presence of specific cells. For regenerative medicine purposes particular attention will be devoted to the generation of biomaterials with antibacterial activity and coating properties. New or improved click chemistry approaches will be studied to make more efficient the conjugation and crosslinking protocols, requiring fast kinetics and experimental conditions compatible with cell survival. The project includes accurate chemical and morphological characterization of the obtained constructs, and the biomedical applications in collaboration with the clinical partners. Furthermore, microfluidic apparatus containing the synthesized artificial organs (organ on chip) will be generated to study the "ex vivo" performance. A potential stage abroad at the University of Maastricht (NL) can be considered to optimize the organ on chip providing angiogenetic properties.

Supervisor web page: https://www.unimib.it/laura-russo

University of Milano-Bicocca
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Nr 19		**Supervisor**	**Luca De Gioia**
Title	**Multiscale computational approaches to the modeling of lytic polysaccharide monooxygenases (LPMOs) and bacterial cytochromes P450 (CYP) variants**		

This PhD research project is part of a multi-disciplinary ongoing effort aimed at the development of a platform based on metal-dependent oxidative enzymes for the conversion of recalcitrant substrates from abundant marine waste biomass into low-carbon second generation biofuels. Achieving such goal would provide a long-lasting energy supply from a waste biomass thereby contributing to the transition to a smart and sustainable economic growth. In fact, second generation biofuels are made from non-edible biomasses, at variance with first generation biofuels that rely on starch and sugar, which are both food sources. The biomass made up of seafood waste materials, such as crustacean shells, fish bones and scales, is rich in the polysaccharide chitin, which can be depolymerized by bacterial lytic polysaccharide monooxygenases (LPMOs) to simple sugars, to be eventually fermented to alcohols. In parallel, the fatty acid component of this biomass can be converted into alkanes/alkenes through decarboxylation that is performed by a class of bacterial cytochromes P450 (CYP152).
Some of the key steps of this project will be the characterization, at a molecular level, of the substrate binding to the protein active site, the detailed kinetic studies and evaluation of the catalytic mechanism of the enzymes involved in the process, and the optimization of engineered and artificial enzymes in terms of stability and functionality under different working conditions. To reach these goals and complement the ongoing experimental investigations, several computational techniques and approaches will be used, including classical Molecular Dynamics simulations, docking simulations, quantum chemical calculations and QM/MM methods. Such an integrated approach, involving different levels of theory, will allow elucidating the molecular determinants responsible of the enzymatic activity of LPMOs, and for rationally tuning the catalytic properties, stability and substrate scope of CYPs.

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Supervisor web page: https://www.unimib.it/luca-de-gioia