IQAC-CSIC Hosting offer
MSCA-IF-2020

THE RESEARCH CENTER

The Institute for Advanced Chemistry of Catalonia (IQAC) belongs to the Spanish National Research Council (CSIC), the largest public research institution in Spain and the third among Europe's largest research organisations.

The IQAC is located in Barcelona and it was created with the mission to perform **multidisciplinary research of excellence in both basic and applied chemical sciences** with the main purpose of improving the quality of life.

The research carried out at IQAC is based on the application of chemical approaches to address and solve societal challenges, mainly those related to human health, the sustainability of chemical processes and products, and the needs for novel materials for different applications. In this regard, the **research programs** carried out in our institute are aimed at:

- the development of methods and strategies for the synthesis of molecules of high added value (**Methods & Strategies**)
- the discovery of chemical and molecular entities of therapeutic, biological and biomedical interest (**Tools & Hits**)
- the study of molecules with surfactant properties, including synthesis, biophysical studies and applications (**Surfactants**)
- the generation and use of nanobiotechnology knowledge for the prevention, diagnostic and treatment of diseases (**Nanomedicine**).

Administratively, the research groups at IQAC are organized in two **departments**: Biological Chemistry, and Surfactants and Nanobiotechnology. Moreover, research is complemented with a range of diverse **scientific and technical platforms** (including cell culture and animal facility), which offer their capabilities to both internal and external users.

OUR HOSTING OFFER

IQAC is delighted to host experienced researchers from any country in the world interested in applying for the MSCA-IF 2020 call (the research groups looking for applicants are found below).

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The candidate must hold a doctoral degree or have at least four years of full-time research experience by the call deadline (September 9 2020). Please, check the eligibility criteria for MSCA-IF in the Funding & Tenders Portal:

MSCA-IF-2020

If you are interested, please send a CV, a motivation letter explaining your research interest and contact details of two referees by 30th June 2020 to the corresponding supervisor.

Successful applicants will receive help and support from our International and European Programme Unit during proposal preparation.

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RESEARCH GROUPS

Biotransformation and Bioactive Molecules

Supervisor: Pere Clapés

Contact: pere.clapes@iqac.csic.es

Web pages:

- Biotransformation and bioactive molecules
- https://pereclapes.wordpress.com/

Keywords: Carbon-carbon bond formation, Carboligases, Biocatalysis, artificial metaloenzymes

Research lines:

Natural carboligases are often limited by the type of C-C forming reaction they can catalyze (e.g., aldol, benzoin). However, no enzyme or variant thereof can catalyze effectively such synthetically important reactions like enantioselective Morita-Baylis-Hillman, iminium activated Diels-Alder, [3+2]- and [4+3]-cycloadditions, or Friedel-Crafts alkylations among others. The aim of the project is to construct hybrid catalysts, consisting of a protein/enzyme scaffold with an appropriate pocket (cavity) in which a key amino acid residue or metal complex is implanted at a specific site, defined by structure guided approach. This key residue will be the anchor of small synthetic catalytic molecules, as organocatalyst or metal ligands. Thus, the active organic molecule or metal will be surrounded by amino acid residues of the protein site directing the orientation the substrates by means of hydrogen bonding interactions. We, thus, envisaged an improvement of the catalytic properties such as activity, by reducing the activation energy, and the stereochemical outcome of the reactions. The result will be an improvement of the performance of the hybrid biocatalyst as compared with the solely organocatalyst or metal catalyst molecule. We foresee modifications of the protein amino acids around the organocatalyst to adjust the environment to the new foreign active residue.

RESEARCH GROUPS

Unit of Synthesis and Biomedical Applications of Peptides

Supervisor: Isabel Haro

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Web page:

- Unit of Synthesis and Biomedical Applications of Peptides

Keywords: Synthetic peptides, Peptide Amphiphiles, Posttranslational modifications, Autoimmune Rheumatic diseases, Diagnosis, HIV-1, Pre-exposure prophylaxis, Nanosystems, Drug delivery

Research group

Our group has been working with peptides for over 25 years. The group's main objective is the chemical synthesis of peptides with biomedical applications. We have collaborated with other Spanish research groups and also with groups from abroad in different fields, including morphinomimetic peptides, novel alternative cancer treatments, the inhibition of proliferative vitreoretinopathy and peptide vaccines; as well as the use of peptides in the diagnosis of multiple sclerosis, rheumatoid arthritis and both hepatitis A and G.

We are currently researching peptide chemistry from three different perspectives: design (lipoderivatives; cyclic; multimeric peptides), synthesis (solid phase and solution) and research into their possible application, both in therapy (HIV entry inhibitors; peptide controlled-release nanosystems for ocular administration of drugs) and in the diagnosis of human diseases (rheumatoid arthritis; HIV/GBV-C co-infection).

The MSCA fellow will be involved in one of the projects described below.

Current projects

PEPTIDE HUMAN IMMUNODEFICIENCY VIRUS ENTRY INHIBITORS: The interest in inhibitors of viral entrance and fusion, as future anti-HIV-1 drugs, is growing exponentially. They can be applied in combined therapies or when resistance to other antiretroviral drugs is detected and they can have the same potential as the immunity induced by a vaccine: pre-exposure prophylaxis. The objective of this line of research is the design of new therapeutic agents based on peptide entry inhibitors to be used as microbicides.

PEPTIDES FOR THE DIAGNOSIS AND PROGNOSIS OF RHEUMATOID ARTHRITIS (RA): There is growing interest in improving the precision of the tests for the diagnosis of RA and also for its early differentiation from other rheumatic diseases that affect joints and connective tissue. In this line of research, we aim to identify new peptides, derived from proteins present in rheumatoid synovial fluid to identify patients who require more aggressive therapies right from the moment of diagnosis of

the disease. Through the simultaneous analysis of the target peptides, incorporated into a multiplex test, we aim to facilitate the biological fingerprinting of autoantibodies in serum to identify subgroups of patients with specific clinical characteristics; different prognoses; and who either respond well to, or suffer negative effects from, certain therapeutic interventions.

PEPTIDE NANOSYSTEMS FOR OCULAR ADMINISTRATION OF DRUGS: The administration of drugs via ocular tissues is problematic due to the low bioavailability of drugs in the current topical formulations. The aim of this line of research is the development of new systems of administration based on liposomes and nanoparticles targeted with peptides that can ensure sufficient bioavailability and compatibility with ocular tissues.

RESEARCH GROUPS

Theoretical and Computational Chemistry

Supervisor: Ramon Crehuet

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Web page:

- The computational and theoretical chemistry group

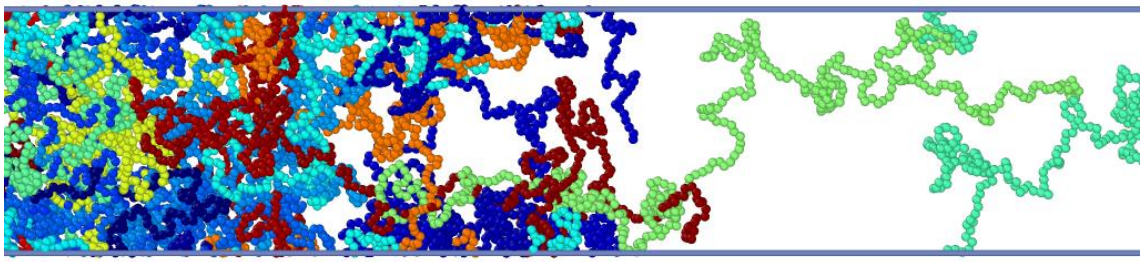
Keywords: Intrinsically Disordered Proteins, computational biophysics, molecular simulations, neurodegenerative diseases, liquid-liquid phase separation, membraneless organelles

Research

Liquid-liquid phase separation (LLPS) of intrinsically disordered proteins is the underlying mechanism in the formation of cellular membraneless organelles. The function and physiological roles of these organelles is still under study, but it is clear that understanding the biophysical processes of LLPS is crucial to determine when and how proteins will condensate and form membraneless organelles.

In our group, we use simulation to describe the process of LLPS. Simulations arise as a useful complement to biophysical methods. However, because LLPS is inherently a collective process, a large number of protein molecules need to be simulated, which prevents the use of explicit solvent all-atom molecular dynamics. Instead, coarse grain methods provide an intermediate resolution solution with an affordable cost --at the expense of a reduced accuracy. Because of that, coarse-grained methods need to be adapted and parameterized for the specific systems under study.

We use experimental data from our collaborators to construct models that describe the physical behaviour of intrinsically disordered proteins in condensates and determine the driving interactions of these processes.



RESEARCH GROUPS

Research Unit on Bioactive Molecules (RUBAM)

Supervisors: Antonio Delgado (UB, RUBAM-IQAC) and Bernat Crosas (IBMB)

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Web pages:

- RUBAM
- IBMB group

Keywords: Protacs, Ubiquitin-Proteasome system, Protein degradation, Molecular and cellular biology, Organic synthesis, Chemical biology, In silico analysis

Brief description of the Centers / Research Groups

The host groups are based at two different Institutes of the Spanish National Research Council (CSIC), an autonomous, multisectoral, and multidisciplinary research state agency with more than 100 Institutes throughout Spain, most of them devoted to scientific and technical research in all branches of knowledge. The "Regulation of the proteasome" (RP) group is based at the Molecular Biology Institute of Barcelona (IBMB-CSIC), located in the Barcelona Science Park (PCB) inside the "Diagonal Portal of Knowledge Campus" of the University of Barcelona (PKC), the main reference cluster in southern Europe in the field of University teaching, research and knowledge transfer. The goal of the group is to examine novel levels of regulation of the proteasome pathway focusing on the mechanisms that control proteasome function and its interaction with protein substrates.

RUBAM is a multidisciplinary group based at the Institute for Advanced Chemistry of Catalonia (IQAC), also in the UB Campus area. The group is composed of staff members of CSIC and UB and focuses its research on the design, synthesis and evaluation of chemical probes and biochemical tools to monitor and modulate sphingolipid localization and activity. In a recently started collaboration, both RP and RUBAM groups have undertaken the development of a new concept of proteolysis targeting chimeras ("protacs") addressed at cellular targets of biomedical relevance and high therapeutic potential.

In terms of facilities and equipment the host groups fully meet the requirements necessary for the successful execution of a research project in chemical biology. In addition to the own services, access to the facilities at the PCB, the PKB and the UB will be available.

The Marie Curie fellow will be integrated into the RP-RUBAM consortium, taking active part in the development and execution of the current project (see next section). Candidates with a solid background in molecular biology and/or chemical biology are sought, given the interdisciplinary nature of our research. The candidate will join an enthusiastic team, offering a stimulating and creative working atmosphere in one of the most scientifically active poles of research of the country.

RESEARCH GROUPS

Project description

Our research is aimed at the design and development of a novel class of proteolysis targeting chimeras ("protacs"). The concept of protacs has recently emerged as a new approach in drug discovery. The classical protacs are heterobifunctional molecules containing two ligands, one directed to the protein to be degraded (the protein of interest, POI) and another to the E3-ubiquitin-ligase (E3UbL) that is required for the POI ubiquitination and its subsequent targeting to the proteasome. In connection with this idea, we are currently developing a novel class of protacs capable of directly targeting the POI to the proteasome, thus bypassing the ubiquitination step. This approach is under development in our team with promising results. This strategy is intended to be applied to the degradation of essential POIs, whose degradation is expected to be of therapeutic relevance in a variety of fields, ranging from antiviral to metabolic regulators and anticancer agents. The methodologies applied in our projects comprise in silico techniques (docking, molecular dynamics, etc), synthesis and characterization of small molecules, general drug design principles, recombinant expression and isolation of protein complexes, protein turnover assays, determination of enzymatic and affinity constants, compound screening in cellular platforms, ubiquitin-proteasome pathway methods.

Post-doctoral fellows with a solid background in some of the above disciplines are suitable candidates for this application.

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RESEARCH GROUPS

Surface Chemistry

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Web page:

- Colloid and Interface Chemistry

Keywords: Biocompatible Colloids, Water-in-Water Emulsions, Biomedical Applications and Drug Delivery

Research project

The present proposal wishes to study the formation and properties of water-in-water emulsions and their derived systems. Water-in-water (W/W) emulsions can be formed in aqueous mixtures that contain two immiscible hydrophilic polymers, without oil and without surfactant [1,2]. These systems can separate in two equilibrium aqueous solutions, and are usually known as Aqueous Two-Phase Systems (ATPS), since the two solutions are in thermodynamic equilibrium, with water as the only solvent. One phase is enriched in one polymer, whereas the other phase contains most of the other polymer. ATPSs are often observed in aqueous mixtures of biocompatible mixtures of soluble proteins and polysaccharides. In recent years, a great interest has been focused on the formation of W/W emulsions in these mixtures, because of many potential applications in the food industry, in cosmetics and drug delivery. Moreover, recent works have shown that W/W emulsions can be stabilized by adsorption of particles on the W/W interface, like conventional O/W Pickering emulsions. Moreover, recent works have shown that ATPS can be used to obtain multiple water-in-water-in-water (W/W/W) multiple emulsions [2]. Some examples are shown in Fig. 1.

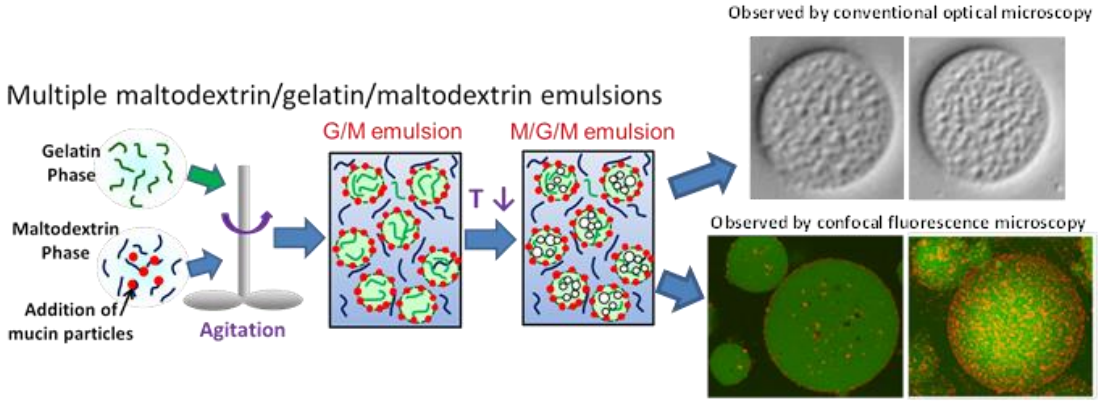

Fig. 1. Examples of Maltodextrin-in-Gelatin-in-Maltodextrin (M/G/M) emulsions and illustrative examples observed by microscopy techniques. Gelatin was labelled with FITC (seen as green) and mucin particles with RBITC (seen as red). (described in Reference [2]).

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RESEARCH GROUPS

The Marie Curie fellow would join a research project to discover and study new W/W emulsions and finding novel applications in the biomedical and drug delivery fields. The fellow would be part of the Surface Chemistry Group, headed by Dr. Jordi Esquena in IQAC-CSIC, and will be integrated in a wider research team, interacting with coworkers, other research groups and international collaborators. A wide range of updated instrumental equipment will be used, mainly in the IQAC-CSIC and the Faculties of Pharmacy and Medicine of the University of Barcelona.

References

[1] J. Esquena, Water-in-Water (W/W) Emulsions, Current Opinion in Colloid and Interface Science, 25 (2016), 109-119.

[2] Y. Beldengrün et al., Formation and Stabilization of multiple Water-in-Water-in-Water emulsions. Food Hydrocolloids 102 (2020) 105588.

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RESEARCH GROUPS

Chemical Biology

Supervisors: Gemma Triola, Juan Bautista Blanco

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Web page:

- Chemical Biology

Keywords: Sonic Hedgehog, D-protein synthesis, phage display, heterogeneous S-acylation, Ras, lipidomics

Research group

In the last two decades there has been remarkable achievements in the field of Biology specially due to the application of chemical approaches. Relevant examples include the synthesis of molecules able to tune enzymatic activity or disrupt protein-protein interactions, design of new fluorescent probes, novel proteomic methods that allow the identification of new cellular targets and the development of techniques for the synthesis and modification of proteins.

Our main goal is the use of chemical tools to study and characterize diseases, and improve our knowledge of important biological phenomena, principally signaling pathways such as Sonic Hedgehog and lipid-protein interactions. As a result, our scientific interests span organic chemistry, biochemistry, biophysics and medicinal chemistry.

Projects

Chemical biology study of the Hedgehog (Hh) signalling pathway. The Hh cascade regulates embryo development, organogenesis and tissue patterning. Missregulation during embryogenesis leads to neonatal malformations. In adult organisms, upregulation of the Hh pathway is involved in the initiation and proliferation of several types of tumors including medulloblastoma, basal cell carcinoma and lung cancer. Our goal is to develop a mirror image phage display programme to identify D-peptide antagonists of the main components of the Hh signalling: the Sonic Hedgehog morphogen protein that activates the cascade, and the GPCR type protein Smoothened that transduces the signal intracellularly. We will study the potential of these D-peptides as inhibitors in cancer therapy.

Heterogeneous lipidation or proteins: The S-acylation of cysteinyl residues with fatty acids is one of the most common posttranslational modifications. Importantly, due to its reversibility the acyl group half-life is shorter than the protein half-life, resulting in a acylation/deacylation cycle that dynamically controls the localization and function of proteins. Although the pool of free fatty acids comprise more than 40 distinct molecular species, S-acylation has been thought to be restricted to palmitic acid. However, there is now accumulating evidence that heterogeneous acylation (shorter, longer,

unsaturated fatty acids) may have an additional role in the regulation of protein localization and function. Our goal is to uncover methods which allow the appropriate identification and quantification of S-linked fatty acids, to apply these methods to profile relevant proteins such as the oncogens Ras, to explore the implications of this lipid diversity on health and disease and to characterize the enzymes responsible of these modifications.

What we are looking for is a candidate/s that should have expertise in some of these fields:

- Organic synthesis, mass spectrometry analysis.
- Solid phase peptide synthesis, RP-HPLC purification.
- Peptide ligations in solution.

Or:

- Cell and molecular biology. Desirable: protein cloning and expression in bacteria
- Training in phage display.

Fellows will be also involved in the supervision of students, attending seminars and conferences and will be encourage to apply for research grants to move forward to his/her independent career.

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RESEARCH GROUPS

Medicinal Chemistry and Synthesis (MCS)

Supervisor: Amadeu Llebaria

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Web pages:

- Medicinal Chemistry and Synthesis

Keywords: photopharmacology, medicinal chemistry, organic chemistry

Research lines:

The MCS group is focused on basic and applied research aimed to obtain biologically active compounds and their application in therapy through the development of drugs, working in all areas of Medicinal Chemistry. Current main research include Photopharmacology, Immunotherapy and Protein labelling

The project will be oriented to find molecules therapeutically useful for the precise control of protein activity in vivo using photoactive molecules that bind to drug receptors. The candidate will work in the design, synthesis and characterisation of new molecules and will conduct compound testing to measure its activity in biological and cell assays and its photophysical characterisation. This program will cover most of the aspects of the preclinical drug discovery development of a candidate molecule and light biophysical control of proteins providing a valuable formation to the candidate.

The candidate will gain invaluable experience in photopharmacology, an exciting and rapidly-developing area of medicinal and biological chemistry, receiving extensive training in the synthesis and characterisation of organic molecules and in the use of key characterisation and purification techniques (including NMR spectroscopy, HPLC, HPLC-MS, chromatography, etc.) and in pharmacology. Patent filing is normally performed in the group to protect the results and the candidate will participate in this task as well. Transferable skills will also be developed by presenting results at group meetings and at national/international research conferences.

This project has strong potential for neurodegeneration, neuropathic pain and other brain diseases, cardiovascular diseases, cancer, etc., using radically new concepts in drug therapy.

Candidates are chemists, pharmacists or biochemists with knowledge of organic chemistry, synthesis, drug design, molecular pharmacology, computational drug/receptor modelling and/or biochemistry.