Research topics

Exploring neuroinflammation in lysosomal storage diseases

Laboratory: Advanced Cell Models

Contact person: Catarina Brito (anabrito@itqb.unl.pt)

Project description: Neuroinflammation is a critical yet poorly understood contributor to the neuropathology of lysosomal storage diseases (LSDs). This project aims to elucidate the mechanisms driving neuroinflammatory responses in LSDs, focusing on mucopolysaccharidosis type VII (MPSVII). Leveraging our advanced 3D human induced pluripotent stem cell (hiPSC)-derived brain models of MPSVII, we will integrate a newly developed microglia-containing system to capture neuron–glia interactions in a physiologically relevant context. These models enable precise investigation of lysosomal dysfunction, cytokine signaling, and microglial activation within a human cellular environment. By combining transcriptomic profiling, imaging, and functional assays, we seek to identify key inflammatory pathways and potential therapeutic targets. This research will provide novel insights into the interplay between lysosomal impairment and neuroimmune responses, paving the way for innovative strategies to mitigate neurodegeneration in LSDs.

Structure and dynamics of the Xport-A/Rhodopsin1 interaction in *Drosophila*

Laboratory: Cell Signalling in *Drosophila*

Contact person: Pedro Domingos (domingp@itqb.unl.pt)

Project description: Rhodopsin-1 (Rh1) is a seven-transmembrane domain protein inserted co-translationally in the endoplasmic reticulum (ER) membrane. Maturation of Rh1 occurs in the ER, where various chaperones interact with Rh1 to aid in its folding and subsequent transport in the secretory pathway. Xport-A has been shown to be a chaperone/ transport factor for Rh1, but the exact molecular mechanism for Xport-A activity upon Rh1 has yet to be discovered. Based on our previous results and computational predictions, we proposed a model where Xport-A functions as a chaperone in the biosynthesis of Rh1 by binding to and stabilizing the first 5 transmembrane domains of Rh1. In this project, we aim to test our hypothesis using biophysical approaches (SAXS, NMR) to determine the structure of the Rh1/Xport-A complex. In parallel, we will do in vivo assays in *Drosophila*.

This proposal intends to go beyond the state-of-the-art by gaining access to dynamic structural information on chaperone-client protein interactions in membranes by monitoring dynamic intra- and intermolecular interactions of Xport-A (chaperone) with Rh1 (client). These two proteins are essential for vision, and rhodopsins (such as Rh1) belong to the family of G-protein coupled receptors, which play many roles in biology. Hence, our approach should be transferable to other membrane proteins amenable to reconstitution in nanodiscs, including G-protein coupled receptors and other membrane proteins.

Recent publications from the lab: PMIDs: 40804044, 38025784, 35332141 and 34918864.

From Drought to Ice: Evolutionary and functional convergence of plant-associated microbiomes under osmotic stress

Laboratory: iPlantMicro

Contact person: Juan Ignacio Vilchez (nacho.vilchez@itqb.unl.pt)

Project description: This project investigates how plant-associated microbiomes adapt to extreme water limitation across highly contrasting environments. The research focuses on semi-arid and salt-affected ecosystems in southern Portugal and southeastern Spain, together with Arctic tundra sites in Svalbard and northern Norway. Although these regions differ climatically, all impose strong osmotic stress on plants and their microbial partners, whether through drought, salinity or freezing. This natural contrast offers an opportunity to identify universal, uncommon/unconventional and convergent mechanisms that support microbial and plant resilience under climate extremes.

The project will combine metagenomic, metatranscriptomic and comparative genomic analyses to uncover conserved genes, pathways and regulatory systems involved in osmotic balance, oxidative stress protection and membrane stabilization. By analysing microbiomes from dry Mediterranean soils and cold Arctic soils within a shared framework, the study aims to detect functional and evolutionary convergence, revealing strategies that unrelated microbial communities have independently developed to cope with water scarcity. To link genetic patterns with ecological function, selected microbial isolates will be tested under controlled drought, salinity and freeze–thaw conditions. Biochemical assays will quantify osmolytes, antioxidant activity and biofilm formation, validating predicted stress-response mechanisms. The final outcome will be an integrated model explaining how microbiomes contribute to plant performance and soil health under severe osmotic stress. The findings are expected to advance fundamental understanding of microbial adaptation, improve predictions of ecosystem responses to climate change, and identify microbial traits and biotechnological mechanism with potential relevance for sustainable agriculture and water deficit management.

Infection Biology, Super-Resolution Microscopy, Organ-on-Chip, *Staphylococcus aureus*, Antimicrobial Resistance, Intracellular Infection

Laboratory: Intracellular Microbial Infection Biology

Contact person: Pedro Matos Pereira (pmatos@itqb.unl.pt)

Project description: Reoccurring multidrug-resistant *Staphylococcus aureus (S. aureus)* infections reached global epidemic proportions. A chief factor suggested to contribute for this is the capacity of *S. aureus* to divide (and persist) inside host cells, effectively "hiding" from antibiotic challenges and immune system recognition. Classically viewed as an extracellular pathogen, we now know that *S. aureus* is in fact a facultative intracellular pathogen, which is thought to be a major factor in continuance of carriage, chronicity of infection and dissemination within the host. However, the mechanisms employed by *S. aureus* to divide intracellularly, and escape host cell autonomous immunity (intracellular recognition and clearing of pathogens) are largely unexplored. To explore these questions, we need to: 1) understand the intracellular infection dynamics of *S. aureus*; 2) develop cellular models that resemble the context of infection in human patients, such as organ-on-chip based models; 3) characterize of the effect of antimicrobial molecules on *S. aureus* evasion from autonomous immunity; 4) understand bacterial ultrastructure in different environments. To address these tasks the selected candidate will use a combination of advanced bacterial/mammalian cell biology and fluorescence (super-resolution) microscopy approaches. The selected candidate will have the opportunity to: 1) become proficient in *S. aureus* cell biology, super-resolution imaging, mammalian cell biology, infection assays in the context of *S. aureus* intracellular infection and advanced 3D cell models; 2) help tackle the challenge of *S. aureus* infections that cause over 1 million deaths annually and are the leading antimicrobial resistance-associated infections in Portugal; 3) be part of a young and dynamic research team.

Microfluidic Integrated Enzyme-Mediated Nucleoside Synthesis

Laboratory: Bioorganic Chemistry

Contact person: Rita Ventura (rventura@itqb.unl.pt)

Project description: Modified nucleosides have important applications as antiviral and antitumor agents. Notably, nucleosides substituted at the sugar C-2' position have emerged as particularly relevant. Important examples include the anticancer drugs clofarabine and gemcitabine, as well as the hepatitis C medication sofosbuvir. A major challenge in preparing such molecules is differentiating the secondary hydroxyl groups of D-ribose, which show nearly identical reactivity. Classical carbohydrate synthesis relies on lengthy protection and deprotection steps, requiring many reagents and complex purifications to target a single hydroxyl group.

Although enzymes have long been recognised as powerful tools for organic synthesis, their potential in carbohydrate chemistry remains underused. Reaction optimisation in traditional batch systems is slow, material-intensive and difficult to perform in parallel, as it often requires multi-millilitre volumes and several labour-intensive operations.

This project aims to overcome these limitations by integrating two complementary and underexploited strategies: biocatalysis and microfluidics. Their combination is intended to streamline carbohydrate synthesis for drug discovery, enabling faster optimisation, reduced reagent consumption and more sustainable workflows.

The main objectives are:
1. apply biocatalysis for regioselective modification of specific positions in D-ribose and D-deoxyribose nucleosides, precursors of antiviral and anticancer agents;
2. design a microfluidic platform for rapid, efficient screening of enzymes and reaction conditions;
3. develop fast, high-yielding chemoenzymatic routes to new nucleoside analogues with potential anticancer properties;
4. assess cytotoxicity and preliminary biological activity of the newly synthesised derivatives.

Exploring heme enzymes for biotechnological applications

Laboratory: Laboratory for Raman BioSpectroscopy

Contact person: Smilja Todorovic (smilja@itqb.unl.pt)

Project description: Heme enzymes offer unmatched potential for biosynthesis of valuable molecules for which synthetic catalysts show poor performance. Understanding how the protein environment governs the chemistry of the heme, and how to translate these intrinsic traits into efficient bioelectronic devices, paves the way to exploiting these exceptionally diverse biocatalysts for biotechnological applications.

In this work, we will study unspecific peroxygenases (UPOs) that catalyze the monooxygenation of versatile substrates, which is among the most essential reactions in organic synthesis. For these reasons UPOs have been attracting significant interest for applications in pharmaceutical and fine chemical synthesis, however their actual implementations have been lagging behind. The work covers the state-of-the-art molecular biology, biochemistry and biophysical approaches for production and characterization of UPOs, and will be performed in collaboration with TU Delft in the Netherlands.

Biochemical and Structural Characterization of a Redox Enzyme as a Therapeutic Target in Antibiotic-Resistant Anaerobic Pathogens

Laboratory: Bacterial Energy Metabolism

Contact person: Inês Cardoso Pereira (ipereira@itqb.unl.pt)

Project description: Anaerobic bacterial pathogens contribute substantially to chronic and refractory infections in humans. The increasing prevalence of antibiotic resistance among these organisms represents a major clinical challenge, particularly because many current antimicrobial agents show limited efficacy under oxygen-depleted conditions. There is thus an urgent need to identify novel molecular targets and develop alternative therapeutic strategies that can overcome these limitations.

This project aims to investigate a redox-active enzyme central to the metabolic network of a clinically relevant anaerobic pathogen. The selected enzyme plays a pivotal role in maintaining redox balance and energy generation in the absence of oxygen, making it an attractive target for therapeutic intervention. The proposed work will encompass recombinant expression and purification of the enzyme, followed by comprehensive biochemical and kinetic characterization. Structural studies, including crystallography, will be undertaken to define the active site architecture and elucidate the mechanistic basis of catalysis.

Subsequent efforts will focus on the identification and evaluation of small-molecule inhibitors targeting this enzyme. Inhibitor screening and structure–activity relationship analyses will guide the design of compounds capable of disrupting the enzyme's function. By integrating structural and biochemical data, this study seeks to establish a foundation for rational drug design aimed at counteracting antibiotic resistance in anaerobic bacteria through selective inhibition of this essential redox enzyme.

Uncovering how metals shape antifungal drug activity

Laboratory: Yeast Molecular Biology

Contact person: Catarina Pimentel (pimentel@itqb.unl.pt)

Project description: Invasive fungal infections (IFIs) represent an increasingly serious global health concern, as recently emphasized by the World Health Organization. The rise of fungal resistance driven by widespread antifungal use is considered a major contributor to this growing threat. However, resistance do not always arise from known genetic mutations and many additional contributing factors remain unexplored. Growing evidence from our group suggests that metals can strongly influence the efficacy of antifungal drugs. This is particularly concerning because metals are central players in the host–fungus axis, and some of these natural interactions may blunt antifungal activity, further narrowing the already limited therapeutic options available to clinicians.

During this fellowship, the candidate will investigate molecular crosstalks between clinically used antifungals and biologically relevant metals, and determine how these interactions could shape infection outcomes in vivo.

Unravelling Staphylococcus aureus–Host Interactions in Chronic Immune-Mediated Skin Disorders: Towards Targeted Therapeutic Strategies

Laboratory: Laboratory of Bacterial Evolution and Molecular Epidemiology

Contact person: Maria Miragaia (miragaia@itqb.unl.pt)

Project description: Atopic dermatitis (AD) is a chronic inflammatory skin disease marked by a defective skin barrier, cutaneous microbiome dysbiosis, and type 2 immunity–driven inflammation in genetically predisposed individuals. Staphylococcus aureus colonizes over 90% of AD patients and dominates during severe disease and flares, driving cutaneous inflammation. Chronic AD is linked to an increased risk of cutaneous T-cell lymphoma (CTCL), suggesting that persistent inflammation and microbial imbalance may contribute to malignant transformation.

Despite its central role, the molecular mechanisms connecting chronic *S.aureus*–driven inflammation in AD to CTCL remain understudied. Current therapies mainly address symptoms, are variably effective, costly, and fail to act directly on *S.aureus*. Our preliminary data showed that specific *S. aureus* clonal lineages are enriched in AD lesions, and that certain bacterial factors are associated to persistence in the skin microenvironment, potentially serving as therapeutic targets. In contrast, Staphylococcus epidermidis, the dominant skin commensal, can inhibit *S.aureus* and modulate immunity. Notably, we identified a potent *S.epidermidis* strain antagonizing prevalent AD *S.aureus* lineages. The mechanisms behind this activity and its potential in AD and CTCL prevention remain unexplored.

This project aims to:

- Elucidate the mechanisms of *S.aureus* factors driving chronic inflammation in AD and their role in CTCL development.
- Characterize the antagonistic activity of *S.epidermidis* against *S. aureus* in the AD skin microenvironment.
- Develop *S. epidermidis*-based and *S.aureus*-targeted therapeutic strategies to prevent flares and reduce progression toward CTCL.

By integrating host–microbe interactions, microbial genomics, and functional studies in physiologically relevant skin models, this project will clarify the mechanisms linking chronic inflammatory skin disease to malignancy and lay the groundwork for innovative, microbiome-informed therapies.

Unveiling bacterial determinants of infection: targeting the transition of *Staphylococcus aureus* and *Enterococcus faecium* from carriage to disease

Laboratory: Laboratory of Molecular Genetics

Contact person: Teresa Conceição (teresagc@itqb.unl.pt)

Project description: Antimicrobial-resistant infections are a major global public health threat, contributing to 4.95 million deaths in 2019. These infections are predominantly caused by multidrug-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE), both designated by the WHO as high-priority targets for new antibiotics.

MRSA and VRE are opportunistic pathogens with a remarkable ability to acquire antimicrobial resistance, virulence factors, and adapt to adverse environments, enabling their persistence and spread in hospitals and communities. While primarily commensals of humans and animals, S. aureus and E. faecium asymptomatically colonize healthy individuals, posing a major risk for their spread and for subsequent infection.

Preliminary data from intensive care unit and hospital surveillance studies in our lab showed that colonization and infection strains shared the same genetic background. However, the factors triggering infection development remain poorly understood. Addressing this gap is critical, as managing colonization could significantly impact infection prevention.

To investigate the bacterial determinants driving the transition from colonization to infection, two unique collections of *S. aureus* and *E. faecium* from colonization and infection stages will be studied. The study will follow two approaches: (1) characterization of bacterial phenotypic behavior under conditions mimicking colonization (e.g., nares, gut) and infection (e.g., bloodstream), and (2) an omics approach, including whole-genome analysis, proteomics, and metabolomics, to compare isolates that progress to infection with those remaining in carriage.

This project will provide a comprehensive understanding of the bacterial determinants driving the transition from colonization to infection, unveiling potential therapeutic targets to reduce multidrug-resistant infections and mitigate the global burden of antimicrobial resistance.

Metabolic Adaptation Mechanisms of *Streptococcus pneumoniae* to Host Immune Defenses

Laboratory: Molecular Mechanisms of Pathogen Resistance

Contact person: Sandra Carvalho (smcc@itqb.unl.pt)

Project description: *Streptococcus pneumoniae* is an opportunistic pathogen that causes severe diseases such as otitis media, meningitis, pneumonia, and sepsis, particularly in young children and the elderly. The high mortality rate caused by pneumococcal infections is exacerbated by the bacterium's ability to mutate its genome through natural incorporation of DNA from neighboring bacteria, leading to resistance against traditional antibiotics. Antibiotics against *S. pneumoniae* target mostly highly conserved cellular processes such as DNA replication, transcription, protein translation and cell wall synthesis. The excessive exploitation of these traditional targets has hindered the discovery of new treatments. Metabolic stress adaptation mechanisms of bacteria during infection offers promising opportunities for identifying alternative antimicrobial targets and uncover new inhibitors.

S. pneumoniae is a strictly fermentative bacterium that depends on carbon sources to grow. The survival of bacteria in host cells depends not only on the expression of virulence factors but also on the acquisition and biosynthesis of nutrients that are critical to bacterial pathogenesis. The bacteria exploit the host metabolism to survive by rewiring metabolic interactions. Therefore, several metabolic changes are induced in both pathogen and host cells in the course of infection. Despite this importance, the understanding of the pneumococcal pathogenesis of infection, considering the holistic view of the host-pathogen interaction, alongside the metabolic adaptation strategies of both entities and their mutual influence, remains considerably elusive. To address this gap, we will integrate cutting-edge experimental approaches including metabolomics, biophysics, molecular genetics, biochemistry, microbiology, and mammalian cell culture. The results will increase our understanding of the complex interactions between the pathogen and the host and provide solutions for antimicrobial resistance.

Microbiology; Fungal Biology; Host-microbiota interactions

Laboratory: Applied and Environmental Mycology

Contact person: Cristina Silva Pereira (spereira@itqb.unl.pt)

Project description: The filamentous fungal genus Aspergillus represents one of the most ecologically and biologically diverse fungal lineages, spanning environmental generalists, industrial workhorses, and major human pathogens. Despite the availability of extensive genomic resources and ecological data, the hidden microbial interactions that may underpin this ecological success remain underexplored. Recent work in Aspergillus fumigatus has revealed the presence of putative endohyphal bacterial symbionts, microbial partners stably residing within the fungal hyphae, that could play roles in, inter alia, stress tolerance, thermotolerance, and secondary metabolism. These findings raise fundamental questions about whether such endobacteria are evolutionary relics, recent acquisitions, or active drivers of innovation within the genus.

This project aims to test the central hypothesis that bacterial endosymbionts have contributed significantly to the ecological adaptation and diversification of Aspergillus, functioning as unseen architects of innovation across the marine-to-terrestrial transition. By mapping the distribution, identity, and functional integration of endobacteria across a representative evolutionary gradient, from ancient marine-associated lineages to terrestrial and opportunistic species, the project seeks to uncover a “core endobacteriome” that may have shaped key fungal traits. These bacterial partners, whether retained or lost, may hold the key to understanding how Aspergillus species adapted to extreme environments and emerged as ecologically dominant fungi.

Decoding the morphological language of infection using AI

Laboratory: AI-driven Optical Biology

Contact person: Ricardo Henriques (r.henriques@itqb.unl.pt)

Project description: Pathogens are master architects of structural remodeling. Whether it is a virus hijacking the cytoskeleton to reach the nucleus or a bacterium reorganising its internal protein architecture to survive antibiotic pressure, infection is defined by nanoscale dynamics. In the AI-driven Optical Biology Lab, we have pioneered quantitative imaging with VirusMapper and SReD to decode these events. We successfully applied these principles to discover the ""metastability"" of Vaccinia virus, revealing that fusion receptor polarisation is required for host entry, and to map HIV assembly without prior knowledge of its distribution.

However, current tools struggle with the chaotic heterogeneity of biological systems. A bacterial cell scrambling its division machinery under drug stress or a pleiomorphic viral factory does not follow a rigid template. To capture this reality, this project aims to develop a shape-agnostic, AI-driven framework to map cellular architecture. Moving beyond deterministic template matching, we will employ self-supervised deep learning to project structural features into a high-dimensional latent space.

Within this latent space, the computational model will learn the ""morphological language"" of infection. This capability will enable detection of how viruses alter organelle structure or how bacteria redistribute internal organisation, thereby identifying subtle phenotypic signatures that may be overlooked by human observers. The project will operate at the intersection of microbiology, cell biology, and artificial intelligence, focusing on the development of open-source tools to quantify host-pathogen interactions. This technology aims to provide a unified platform for studying virulence mechanisms and screening treatments that restore healthy cellular architecture, with applications ranging from viral fusion to bacterial antibiotic resistance.

Catalytic Strategies for Greener Organic Synthesis

Laboratory: Organometallic Chemistry and Catalysis

Contact person: Beatriz Royo (broyo@itqb.unl.pt)

Project description: The transition toward a sustainable society is one of the defining scientific challenges of the 21st century. As fossil fuel reserves continue to decline, the chemical industry must pivot toward renewable feedstocks and energy-efficient processes. This project offers an exciting opportunity to contribute to that transformation by developing catalytic strategies that convert simple, bio-derived alcohols into high-value chemicals.

Alcohols obtained from biomass represent highly promising platform molecules. Their controlled functionalization, without relying on fossil resources, can unlock entire families of intermediates essential for pharmaceuticals, materials, and fine chemicals. In this project, you will explore the power of earth-abundant metal catalysts (e.g., Mn, Fe, Co) to drive two cutting-edge transformations: borrowing hydrogen (BH) and acceptorless dehydrogenative coupling (ADC). These methodologies enable efficient C–C and C–N bond formation using the inherent hydrogen content of the substrates themselves, avoiding wasteful oxidants or sacrificial reagents.

The work will combine catalyst design, mechanistic studies, and synthetic applications. Students will gain expertise across homogeneous catalysis, organometallic chemistry, sustainable synthesis, and modern analytical techniques. The overall goal is to build greener, scalable catalytic systems capable of transforming renewable alcohols into valuable products with minimal environmental footprint.

This project is ideal for students passionate about sustainable chemistry, renewable feedstock valorization, and innovative catalysis, and who want to be at the forefront of developing next-generation chemical technologies.

Development of an Engineered *Streptococcus mitis* Biotherapeutic to Prevent Pneumococcal Disease

Laboratory: Laboratory of Molecular Microbiology of Human Pathogens

Contact person: Raquel Sá Leão (rsaleao@itqb.unl.pt)

Project description: *Streptococcus pneumoniae* (the pneumococcus) remains a major global pathogen, causing otitis, pneumonia, bacteremia and meningitis, with high morbidity, mortality, and rising antimicrobial resistance. In contrast, its close relative *S. mitis* is a harmless commensal that naturally colonizes the human upper respiratory tract. Preventing pneumococcal colonization, a fundamental first step in disease, represents a promising strategy to reduce the risk of infection.

This project focuses on the development of MISSMI, an engineered *S. mitis* strain with probiotic traits and broad anti-pneumococcal activity. From a previous screen of 300 commensal streptococci, we identified seven strains producing diverse bacteriocins that inhibit a wide range of pneumococcal serotypes, although none provided complete coverage. MISSMI will overcome these limitations by constitutively expressing the most potent bacteriocins identified, together with their transport and immunity genes, integrated into the genome of the *S. mitis* F-ad chassis.

The F-ad strain is a naturally occurring human colonizer, amenable to genetic manipulation, and capable of colonizing the murine respiratory tract, enabling rigorous proof-of-concept studies. The project will include rational genome engineering to minimize lateral gene transfer and the emergence of bypass-resistant pneumococci, together with systematic evaluation of MISSMI activity *in vitro* biofilm models and in vivo colonization and infection models.

By the end of the project, MISSMI will be established as a well-characterized engineered S. mitis strain with broad anti-pneumococcal capacity and strong potential as a simple, low-cost, and targeted live biotherapeutic to prevent pneumococcal colonization and disease.

Molecular simulation of the effect of the thylakoid pH gradient on the photoprotective protein PsbS

Laboratory: Molecular Simulation

Contact person: António M. Baptista (baptista@itqb.unl.pt)

Project description: Under strong sunlight, plants can avoid photooxidation by dissipating as heat the excess of absorbed energy. The dissipation is triggered by PsbS, a membrane protein sensitive to the light-induced pH changes in the thylakoid lumen. The mechanism of action of PsbS remains unknown, but experimental studies indicate that some of its Glu residues may act as pH sensors, its monomer-dimer equilibrium is sensitive to pH, and the dimer conformation may be affected by pH. Further molecular-level insight was recently provided by computational studies of the monomer [1] and the dimer (on-going), both involving the host lab and using our in-house constant-pH molecular dynamics (CpHMD) method that allows for explicit (de)protonations during the simulations. These two studies identified putative pH-sensing Glu residues, the pH-induced folding of a loop involved in dimerization, and lumen-stroma communication through correlated protonations, together making possible to quantify the pH-dependent dimerization equilibrium. Nonetheless, identical pH had to be assumed on both sides of the membrane.

The present proposal will add a level of realism to our previous studies of PsbS, namely by including the explicit effect of a pH gradient across the thylakoid membrane, using an extension of our CpHMD method. The pKa values, conformational dynamics, correlations involving conformation and/or protonation, and a pH-dependent profile of the dimerization equilibrium will be determined. These will shed light on the PsbS response mechanism to the gradual formation of a pH gradient, potentially opening new routes to control plant photoprotection and improve crops [2]. To our knowledge, this will be the first molecular dynamics study of a membrane protein with an explicit pH gradient.

Since the work includes methodological development, previous expertise with the CpHMD method is required.

[1] Liguori at al (2019) J. Phys. Chem. Lett. 10:1737. [2] Kromdijk et al. (2016) Science 354:857.

eCarbonCatchAir - Engineering a PEPC-based Bioreactor for Atmospheric CO_2 Capture Using an Enhanced Enzyme

Laboratory: Proteome Regulations in Plants

Contact person: Isabel A. Abreu (abreu@itqb.unl.pt)

Project description: Climate change mitigation urgently requires carbon-capture technologies that are scalable, low-energy, and compatible with distributed emission sources. CarbonCatchAir - a bioreactor concept based on enzymatic fixation of atmospheric CO_2 - offers a promising alternative to conventional, energy-intensive Direct Air Capture systems. Building on previous work developed in the lab, which characterized PEPC-driven carboxylation and established the first functional prototype, two major bottlenecks were identified: (i) insufficient delivery of CO_2 into the reactor, limiting bicarbonate availability, and (ii) the intrinsic instability of oxaloacetate (OAA), which rapidly decarboxylates under operational conditions. This project aims to develop the next generation of CarbonCatchAir by overcoming these constraints and creating a more efficient and economically relevant CO_2-fixation platform.

Task 1 will focus on understanding and solving inefficiencies related to CO_2 delivery. The student will quantify the impact of CO_2 hydration rate on reactor performance, using carbonic anhydrase, and optimize operational parameters such as flow rate and membrane material to enhance gas transfer across the contactor.

Task 2 will address product recovery and valorization by exploiting a malate-insensitive PEPC mutant coupled with malate dehydrogenase to convert OAA into malate, a stable and industrially relevant organic acid.

Task 3 will explore non-enzymatic strategies to increase overall system robustness: immobilizing PEPC on PEI-coated beads to improve enzyme stability and CO2 hydration, and screening hydrazine derivatives reactive with OAA under mild conditions to trap and stabilize the product in situ.

The project will deliver an advanced, laboratory-validated CO_2-capturing module with enhanced catalytic efficiency and product valorization, contributing to next-generation climate-action biotechnology and reinforcing ITQB NOVA's commitment to sustainable innovation.

Killing Superbugs from Within: *Disarming Staphylococcus aureus* via Cell Wall Autolysins

Laboratory: Bacterial Cell Biology

Contact person: Mariana Gomes de Pinho (mgpinho@itqb.unl.pt)

Project description: As antibiotic resistance escalates into a major global health crisis, the bacterial cell wall remains a crucial, but still incompletely understood target. This fellowship focuses on the peptidoglycan cell wall of a major pathogen, Staphylococcus aureus, currently the second leading cause of death from antibiotic-resistant infections worldwide.

The bacterial cell wall is a protective barrier that maintains cell shape and integrity and allows cells to withstand high internal turgor pressure without bursting. Its major component, the peptidoglycan, is constantly remodelled by two sets of enzymes: the synthases that build it, and the hydrolases (also known as autolysins) that cut it. These activities must be perfectly balanced for the cell to grow, divide and separate into viable daughter cells. While most antibiotics target peptidoglycan synthesis, peptidoglycan hydrolases are equally crucial. When misregulated, these essential enzymes can become powerful "suicide proteins" that drive cell lysis from within. Understanding how autolysins work and how they are controlled is therefore key to uncovering new vulnerabilities in S. aureus and to designing innovative antibacterial strategies that make bacteria trigger their own destruction.

With this fellowship, you will investigate the function and regulation of key S. aureus autolysins using an integrated, multidisciplinary approach. The work will combine state-of-the-art super-resolution microscopy with advanced biochemistry, molecular biology and genetics, providing broad training at the interface of fundamental bacterial cell biology and translational antibiotic research. This fellowship is ideal for motivated students who want to understand fundamental bacterial cell biology while contributing to the fight against antibiotic resistance.

Development of metal- modified mRNA cap analogues

Laboratory: Bioorganometallic Chemistry

Contact person: Ana Petronilho (ana.petronilho@itqb.unl.pt)

Project description: One of the most important characteristics of eukaryotic mRNA is the presence of a cap structure. This cap consists of a N7-methylated guanosine connected to the first transcribed nucleotide by an unusual 5'-5'-triphosphate bridge. The cap is recognized by specific proteins, such as eukaryotic initiation factor 4E (eIF4E), involved in translation.

Modified cap analogues have can have a major role on the inhibition of cap-dependent translation and can also be employed to modify the 5'-end of mRNA for developing therapeutic mRNAs. Yet, the development of synthetic methods for modifying the cap structure is challenging, due to the difficulty of find selective procedures that are site specific. In this research project we will develop modified cap analogues based on transition metals, making use of common organometallic procedures, for the development of therapeutic mRNAs.

Structural and Computational Biology, Tuberculosis (TB), Drug-resistance and discovery TB

Laboratory: Membrane Protein Crystallography

Contact person: Margarida Archer (archer@itqb.unl.pt)

Project description: Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains one of the world's leading infectious diseases. An estimated one quarter of the population carries latent Mtb infection, and in 2024 alone more than 10 million individuals developed active disease, resulting in 1.2 million deaths (WHO report). The increasing prevalence of drug-resistant Mtb strains underscores the urgent need for innovative therapeutic strategies. Among the most compelling targets are enzymes involved in the biosynthesis of the mycobacterial cell envelope, a structure essential for bacterial growth, virulence, and intrinsic antibiotic resistance.

Our research group has recently determined high-resolution cryo-electron microscopy (cryo-EM) structures of several arabinofuranosyltransferases (AraTs), key enzymes in cell wall arabinan assembly. These structures elucidate the overall fold and catalytic site architecture of AraTs and reveal an unexpected interaction with Acyl Carrier Protein (ACP). The functional significance of ACP in this context—whether as a potential cargo carrier or as a modulator of AraT activity—remains an open and compelling question. We have also employed computational drug-repurposing strategies to select promising anti-TB candidates, which we subsequently validated through growth-inhibition assays in mycobacteria.

The selected fellow will contribute to a multidisciplinary effort involving bacterial culture, protein purification, structural analysis of AraT variants lacking ACP, and computational approaches including in silico screening to identify novel compounds and to probe mechanisms underlying Mtb drug resistance.

This project will be conducted in the Membrane Protein Crystallography Laboratory at ITQB NOVA, under the supervision of Doctor Margarida Archer, in close collaboration with the Instituto Nacional de Saúde Doutor Ricardo Jorge (INSA) and Accelbio, a non-profit association supporting drug discovery initiatives.

Antibiotic resistance/cell division – When resistance breaks the ring: how vancomycin-adaptive changes perturb cell division in *clostridioides difficile*

Laboratory: Microbial Development

Contact person: Adriano O. Henriques (aoh@itqb.unl.pt)

Project description: Vancomycin (VAN) inhibits cell-wall synthesis by binding lipid II/D-Ala–D-Ala. Mutations that reduce susceptibility often disrupt peptidoglycan (PG) architecture and cell division. The human pathogen *Clostridioides difficile* remains VAN-sensitive despite carrying a resistance operon, suggesting bottlenecks that limit resistance acquisition. Preliminary data indicate one such barrier is division: VAN-adaptive mutations cause elongated cells and defective septation. This project will define genetic routes to reduced susceptibility, dissect divisome malfunction, and link septal PG alterations to resistance.

CENTRAL HYPOTHESIS: Mutations that increase VAN tolerance, via modified stem-peptides, de-regulated PG enzymes, or two-component-mediated gene expression shifts, impair divisome function, causing morphological defects and fitness trade-offs.

AIM 1: Identify VAN-resistant cell division mutants through stepwise laboratory evolution. Screen clones by microscopy in planktonic and biofilm conditions; map mutations by whole-genome sequencing.

AIM 2: Validate causality by reconstructing mutations. Quantify MICs, growth, cell shape, division, and nucleoid organization using time-lapse microscopy and microfluidics.

AIM 3: Link PG chemistry to divisome malfunction. Characterize PG composition and enzyme activity; test whether altered lipid II disrupts FtsZ-ring assembly, FtsW, or PBP localization.

AIM 4: Define mechanistic and evolutionary trade-offs. Probe epistasis with multi-mutation reconstructions, assess fitness across environments, manipulate divisome components to evaluate rescue or exacerbation of defects, such as synthetic lethality.

These studies will reveal how VAN-adaptive changes compromise division in *C. difficile* illuminating constraints on resistance evolution and anticipating therapeutic solutions.

New molecular targets to combat foodborne infections

Laboratory: Control of Gene Expression

Contact person: Cecilia Arraiano (cecilia@itqb.unl.pt) and Rute Matos (rmatos@itqb.unl.pt)

Project description: Foodborne pathogens present a significant worldwide threat, leading to multiple infections and compromising food safety and human health. Campylobacter jejuni is a foodborne bacterial pathogen that, according to the World Health Organization, is the leading cause of human bacterial gastroenteritis worldwide. Infections are related with the development of dreadful and potentially fatal secondary disorders, like the Guillain-Barré or Miller-Fisher syndromes. C. jejuni ability to persist and grow at low temperatures is a major problem for food safety and public health. As such, it is crucial to study new ways to eradicate or reduce the infections caused by this bacterium.

As an invading pathogen, it is exposed to different stresses imposed by the gastrointestinal tract and immune system of the host. Consequently, it needs to rapidly respond to stress conditions and readjust its gene expression profile. Ribonucleases (RNases), enzymes that process and degrade RNA, are important players in this process. They are found in all domains of life and play a central role in the control of gene expression, degrading RNA that is not required for the cell and recycling nucleotides to synthesize new molecules.

In several human pathogens, RNases have been implicated in virulence and can be critical for microbial survival. However, RNA degradation remains largely unexplored from the perspective of antibiotic drug target discovery. Until date, not much is known regarding RNA degradation in C. jejuni, meaning that there are still many questions to address regarding the role of RNases in this important foodborne pathogen. Our main goal is to uncover virulence mechanisms regulated by RNases and support the development of strategies to control C. jejuni infections based on these proteins. The mechanisms discovered may also apply to other bacterial pathogens, thereby amplifying the translational impact of this project towards novel antimicrobial therapies.

Foldamer glycoconjugates for bacterial adhesion inhibition

Laboratory: Bio-oriented Supramolecular Chemistry

Contact person: Pedro Mateus (pmateus@itqb.unl.pt)

Project description: Antimicrobial resistance (AMR) is one of today's most urgent global health threats. Antivirulence strategies—those that disarm pathogens instead of killing them—offer a promising route to bypass antibiotic resistance. [PMID:28337021] Because many pathogens adhere to host cells through proteins that recognise multiple carbohydrates, [PMID:23799663] multivalent glycoconjugates have attracted great interest. [PMID:27341003, 26875976] Yet few systems allow precise control over the number, spacing, and orientation of these carbohydrate units.

In this project you'll develop arylamide foldamers as a new molecular platform for multivalent carbohydrate display. These molecules adopt stable helical conformations in solution, whose stability, [PMID:22531290] tunability, [PMID:25803472] ease of synthesis, [PMID:37024428] and structural elucidation, [PMID:31863707] make them ideally suited to control the number, nature, and orientation of glycoligands with high precision. Their ability to incorporate proteinogenic side chains [PMID:24288253] also opens the door to selective targeting of specific bacterial adhesins and toxins.

The foldamer–glycoconjugates you'll develop will mimic natural glycoprotein patterns on host cells to block recognition by pathogen virulence factors. Targets include LecA/LecB from P. aeruginosa, FimH from E. coli, and the TcdA/TcdB toxins of C. difficile.

You will gain robust training in organic synthesis, heterocyclic chemistry, solid-phase synthesis, analytical and semi-preparative HPLC, and a range of structural and biophysical characterisation techniques, equipping you for future academic and industrial careers.

This provides an opportunity to work at the forefront of molecular design, developing complex synthetic architectures with precise control over structure and function, and applying them to biologically targets with real impact in the fight against AMR.

Molecular Engineering of Nitrogen Use Efficiency in Rice: Promoter Optimisation and Gene Regulatory Networks for Sustainable Production

Laboratory: Plant Gene Regulation

Contact person: Nelson Saibo (saibo@itqb.unl.pt)

Project description: Rice is the staple food for half of the world's population and an important crop for Portugal. A major limitation to production is nitrogen-deficient soils, which require fertilisation to ensure yield and grain quality. Improving nitrogen-use efficiency (NUE) is essential to increase productivity while reducing fertiliser waste and environmental pollution. At the molecular level, NUE depends on coordinated processes: nitrogen uptake through transporters (e.g., OsNRT), rapid assimilation via glutamine synthetase and glutamate synthase, and effective remobilisation of leaf proteins to the grains. Each step offers genetic opportunities for improvement. By characterising key genes, regulatory networks, and natural variation, we can rationally develop rice varieties requiring 20–30% less nitrogen without compromising yield.

NUE is closely linked to light and photosynthesis, since 25–50% of leaf nitrogen is allocated to Rubisco and thylakoid proteins. Efficient plants balance nitrogen investment and photosynthetic output, maximising CO_2 fixation while maintaining plant performance. In Portugal, where low nitrogen availability is a problem, improving NUE has a major agronomic and environmental impact. CRISPR-based enhancement of nitrogen transport or assimilation genes can generate varieties optimised for low-input systems, improving sustainability, reducing fertiliser runoff, and increasing farmer profitability. It will also support a climate-smart rice production.

Main objectives:

1- Improve Nitrogen Use Efficiency in Portuguese varieties. Using CRISPR/Cas9, we will modulate gene expression to obtain higher-NUE rice.
2- Investigate NUE in wild rice species. Screening diverse wild species will identify mechanisms associated with superior NUE and support targeted rice improvement.
3- Investigate how NUE is influenced by light and photosynthesis. Understanding regulatory links between light, photosynthesis, and nitrogen utilisation to support advances in crop performance.

Health Biotechnology - Advanced Therapeutic Medicinal Products

Laboratory: Cell Line Development & Molecular Virology

Contact person: Ana Coroadinha (avalente@itqb.unl.pt)

Project description: Gene therapy has transformed modern medicine by providing the direct delivery of genetic material to a patient. Several gene therapy products are already approved and used clinically. Central to the success of gene therapy are vectors capable of delivering genetic material safely and efficiently to the target cells.

Adeno-associated virus (AAV) vectors are widely used due to their safety and extensive clinical validation. However, despite their success, AAV vectors possess important limitations. Their small packaging capacity, restricted to approximately 3.5 kb, precludes the delivery of many therapeutically relevant genes. In addition, AAV vectors exhibit low transduction efficiency, with only about 1 in 100,000 particles achieving a therapeutic effect. These limitations necessitate the use of extremely high clinical doses, which increases the risk of adverse events and creates significant challenges in manufacturing.

Our group aims to develop next-generation technologies to expand the versatility, efficiency, and therapeutic reach of AAV vectors for gene, cell, and genome-editing applications. To achieve this, we are investigating the intracellular trafficking barriers that limit AAV transduction both in vitro and in vivo, with the goal of identifying and overcoming the major bottlenecks. In parallel, we are engineering novel AAV vectors by modifying capsid proteins and viral genomes using pioneering molecular approaches. These vectors undergo comprehensive biophysical, biochemical, and functional characterization, including in vitro evaluation and in vivo testing. We collaborate closely with translational laboratories targeting muscular, neurodegenerative, and retinal diseases.

The development of the novel, highly efficient AAV vectors, will significantly expand their use in gene therapy for the treatment of a vast number of genetic disorders. Its broader applicability to a larger number of patients will make them cost-effective and accessible to all.

Exploring Ancestral Copper Radical Oxidases for Sustainable Biocatalysis

Laboratory: Microbial and Enzyme Technology

Contact person: Lígia Martins (lmartins@itqb.unl.pt)

Project description: Copper Radical Oxidases (CROs) catalyze the oxidation of alcohols to aldehydes using molecular oxygen, representing key transformations in green and sustainable chemistry. Although CROs are widespread in nature, only a small fraction has been experimentally characterized, leaving significant unexplored potential for biocatalysis, biomass valorization, and the production of bio-based chemicals.

Ancestral Sequence Reconstruction (ASR) offers a powerful strategy to access this hidden diversity. By computationally inferring and resurrecting extinct protein sequences, ASR often yields enzymes with enhanced thermostability, broadened substrate scope, or distinct catalytic features lost in modern homologs. These properties make ancestral enzymes particularly promising starting points for developing robust biocatalysts able to withstand industrially relevant conditions.

This project will explore the functional and molecular features of ancestral CROs by expressing, purifying, and characterizing synthetic ancestral enzyme variants derived from a curated phylogenetic analysis. Comparative studies between ancestral and contemporary CROs will uncover evolutionary trends and provide insights into their catalytic mechanisms and structure-function relationships, thereby supporting the discovery of new, stable, and efficient biocatalysts for industrial applications.

The project integrates evolutionary biology, protein engineering, and structural and biochemical characterization, offering a unique opportunity to investigate how nature's past innovations can inform future advances in green chemistry. Depending on the student's background and interests, the work may also incorporate computational modeling and structure-guided analysis to support the exploration of enzyme function and guide experimental design.

The role of the cell-envelope in *Staphylococcus epidermidis* response to endogenous antimicrobial fatty acids: comparison between pathogenic and commensal strains

Laboratory: Proteomics of non-model organisms

Contact person: Ana Varela Coelho (varela@itqb.unl.pt)

Project description: Staphylococcus epidermidis (SE) is the most representative coagulase-negative staphylococcus skin resident. Despite many benefits as a commensal, SE has emerged as an opportunistic pathogen, accounting for 80% of medical device-associated infections, which when becoming chronic can lead to bacteraemia. Development of new preventive and therapeutic strategies is urgently needed.

Human skin SE populations consist of two main clonal lineages, A/C and B. Lineage A/C, including both commensal and pathogenic strains, resides in superficial and broader niches. Conversely, lineage B, enriched in commensal strains, survives better in lipid-rich environments (hair follicles/sebaceous glands). These findings are corroborated by our studies that have determined higher anti-microbial activity of skin endogenous antimicrobial fatty acids (AFAs) against pathogenic SE strains (submitted publication).

This project aims to elucidate the mechanisms of AFAs antimicrobial activity against SE commensal and pathogenic strains, enabling development of pathogen-specific antimicrobials. We hypothesize that pathogenic and commensal SE strains exhibit differential AFA susceptibility due to distinct cell envelope compositions.

The main objectives include studying: a) Temporal changes in exolipidome composition by GC-MS, focusing on AFA uptake; b) Cell membrane lipid and protein compositions using lipidomic and proteomic approaches; c) Cell membrane structure and fluidity following fluorescent membrane dye incorporation by spectroscopy and microscopy (single-cell analysis); d) Cell wall composition (peptidoglycan, teichoic acids, proteins) by LC-MS and MALDI-MS.

Insights on AFA mode of action on SE cell envelope will be crucial for developing strategies to selectively control pathogenic SE strains while promoting healthy skin colonization by commensal strains, informing topical formulations or medical device coatings.

Sugar signalling in plants

Laboratory: Plant Cell Biotechnology

Contact person: Ana Confraria (ana.confraria@itqb.unl.pt)

Project description: Being sessile organisms that continuously develop throughout their lifetime, plants must tightly coordinate development with the environment. One of the mechanisms contributing to this coordination is a tight regulation of their sugar status, which is highly dependent on environmental conditions. In plants, sugars play key roles as energy sources, as building blocks, and as signals, regulating cellular processes, growth, storage, and nutrient remobilization across different plant tissues.

One of the major sugar signalling pathways in plants involves the conserved heterotrimeric protein kinase complex SnRK1 (Snf1-Related Kinase 1). SnRK1 is important under stress, when sugars are typically scarce; sugar starvation activates SnRK1, triggering vast metabolic and transcriptional changes that promote stress tolerance and survival. In contrast, sugar abundance inactivates SnRK1. And in addition to its role during stress, SnRK1 is also essential for normal plant growth and development in higher plants, as full knockout mutants have not been isolated so far. Despite its crucial and diverse roles and the remarkable progress of the field in recent years, only a few SnRK1 targets have been discovered and characterized so far.

With our work, we aim to dissect the mechanisms underlying SnRK1's role in developmental processes that affect yield. Through a combination of molecular biology, biochemistry, phenotyping, and genetics approaches, we have been mostly focusing on shoot branching, using Arabidopsis thaliana as a model, due to the wide availability of genetic resources and amenability to transformation. We are currently also trying to establish tomato as a model in the lab and are generating plants with modified SnRK1 levels. Overall, we aim to contribute with mechanistic knowledge about the effects of sugar signalling on plant developmental programmes, which we think is important to identify precise targets that can be manipulated in crops in the future.

Deciphering the role of iron-sulfur clusters in DNA repair

Laboratory: Structural Genomics

Contact person: Elin Moe (elinmoe@itqb.unl.pt)

Project description: We are interested in understanding the molecular mechanisms underlying DNA repair. In particular, we study Endonuclease III (EndoIII) DNA glycosylase from D. radiodurans and its human homologue, hNTH1, which is associated with cancer development. The enzymes are structurally related and possess iron-sulfur (FeS) clusters, whose role is debated. Additionally, hNTH1 has an N-terminal extension with an unknown function. Based on insights from structural and biophysical approaches, we recently hypothesized that the N-terminal domain and the FeS cluster may be involved in damage screening and serve as a scaffold for DNA binding, respectively.

In this project, we aim to test this hypothesis by studying two EndoIII-like enzymes from the yeast S. cerevisiae, yNTH1 and yNTH2, of which only yNTH2 contains a FeS cluster. This makes them ideal for exploring the cluster's role in DNA repair. Both enzymes recognize oxidation damaged bases in DNA; however, yNTH1 is localized in mitochondria, while yNTH2 is in the nucleus. Like their human counterpart, they also have an N-terminal extension.

We have expressed, purified, and biochemically characterized both enzymes and analyzed the spectroscopic properties of yNTH2's FeS cluster. Next, we aim to study chimera enzymes, engineered by a) adding the FeS cluster to yNTH1 and b) removing the cluster from yNTH2. This will provide more information on the cluster's importance for catalytic activity, substrate specificity, and enzyme stability. Additionally, we aim to determine the three-dimensional structures of native and chimera enzymes using X-ray crystallography, and investigate the in vivo effects of swapping the locations of these enzymes in yeast under oxidative stress.

The project is supervised by Dr. Elin Moe at the Structural Genomics Lab and collaborates with Dr. Smilja Todorovic from the Raman BioSpectroscopy Lab, ITQB NOVA, and offers opportunities to work in European laboratories and participate in international consortia.

Catalysis, Peptides, Liquid-liquid phase separation

Laboratory: Bioinspired Peptide Systems

Contact person: Ana Pina (ana.pina@itqb.unl.pt)

Project description: The fellowship will focus on advancing the use of catalytic peptides as microreactors for green aldol condensation reactions. Specifically, short peptide sequences, designed for intrinsic disorder and liquid-liquid phase separation (LLPS) will be screened to form microcompartments, also known as coacervates, and characterized for their ability to catalyze aldol condensation between simple ketones (e.g., acetone, cyclohexanone) and aldehydes. The approach leverages peptide confinement within coacervate droplets, creating microenvironments that promote both substrate concentration and catalytic activity, mimicking enzyme-like function in water. Studies show such peptides can yield products with improved efficiency, with the added advantage that microreactor compartmentalization can further boost reaction rates and selectivity. The methodology will involve solid-phase synthesis of peptide libraries, turbidity and microscopy assays to confirm LLPS, and colorimetric/NMR assays for tracking reaction progress and selectivity. The preliminary data will demonstrate the feasibility of peptide-based coacervates as robust, tunable catalysts for sustainable aldol condensation, laying the foundation for subsequent doctoral work and scalable green chemistry applications.

Engineering LLPS-Enhanced Enzyme Condensates for Phenylketonuria Therapy and Biosensing

Laboratory: Dynamic Structural Biology

Contact person: Tiago Cordeiro (tiago.cordeiro@itqb.unl.pt)

Project description: Phenylketonuria (PKU) is a serious metabolic disorder requiring lifelong dietary management and limited treatments. Current enzyme replacement therapies face challenges such as instability and rapid degradation. This PhD project aims to utilize Liquid-Liquid Phase Separation (LLPS) technology to develop "smart enzyme microreactors" – self-assembling condensates that improve enzyme stability and therapeutic performance.

The candidate will engineer therapeutic enzymes to achieve controlled phase separation, creating dynamic compartments that concentrate enzymes and enhance catalytic efficiency.

Key Activities:

1. Design and characterize LLPS-enzyme chimeras using computational tools and advanced biophysical techniques.

2. Develop a miniaturized biosensor for rapid PKU monitoring, incorporating LLPS-stabilized enzymes.

3. Validate therapeutic candidates in 3D human hepatic organoid models.

This project spans ITQB NOVA, University of Lisbon, and iBET, providing access to advanced facilities and collaboration with experts in protein engineering and bioengineering.

Impact: This research establishes enzyme condensate technology as a platform for treating metabolic disorders, with potential clinical applications. We seek motivated candidates with a Master's degree in biochemistry, molecular biology, or bioengineering. An interest in protein engineering and prior experience in structural biology or biosensor development is advantageous.