TEMES PER A TREBALLS DE FI DE GRAU (TFG)

GRAU EN CIÈNCIES BIOMÈDIQUES
Curs 2025-2026

DEPARTAMENT BIOENGINYERIA

1. Papel de la localización subcelular de la Triosa Fosfato Isomerasa (TPI) en el equilibrio proliferación-diferenciación de mioblastos: implicaciones para la Distrofia Muscular de Duchenne

La Distrofia Muscular de Duchenne (DMD) es un trastorno genético causado por mutaciones en el gen de la distrofina, caracterizado por una degeneración progresiva del tejido muscular para la que actualmente no existe cura. Aunque el tejido muscular posee cierta capacidad regenerativa mediante las células satélite, en la DMD este proceso es insuficiente para compensar la pérdida tisular constante. Por tanto, es crucial desarrollar nuevas estrategias terapéuticas enfocadas en potenciar la diferenciación eficiente de estas células satélite para rejuvenecer el músculo deteriorado.
Los mecanismos moleculares que regulan la decisión entre proliferar o diferenciarse en las células satélite son complejos. Datos recientes de nuestro laboratorio señalan a la enzima glicolítica triosa fosfato isomerasa (TPI) como un potencial regulador clave de este "interruptor" celular. Aunque clásicamente se considera una enzima citosólica, nuestros resultados preliminares en el modelo in vitro de mioblastos C2C12 revelan una dinámica de localización dependiente del estado celular: en condiciones de baja confluencia y alta proliferación, la TPI presenta una localización marcadamente nuclear. Por el contrario, cuando las células alcanzan una alta confluencia y disminuyen su tasa proliferativa —un paso previo necesario para la diferenciación—, la TPI se reubica mayoritariamente en el citosol, manteniéndose este patrón durante la formación de miotubos.
Esta relocalización dinámica nos lleva a la hipótesis de que la TPI nuclear podría estar ejerciendo una función no canónica, posiblemente interactuando con factores de transcripción para mantener el estado proliferativo, mientras que su exclusión nuclear sería necesaria para iniciar la diferenciación. El presente Trabajo de Fin de Grado tiene como objetivo caracterizar en profundidad el papel de la TPI en el destino celular de las C2C12. Para ello, emplearemos técnicas de cultivo celular combinadas con herramientas de biología molecular como western blot, regulación de la expresión de TPI mediante shRNA, co-inmunoprecipitación e inmunocitoquímica. Dilucidar cómo la TPI orquesta este delicado equilibrio podría no solo mejorar nuestra comprensión fundamental de la regeneración muscular, sino también revelar nuevas dianas terapéuticas para mitigar el impacto de la DMD.

Direcció: Dra. Marta Guerra Rebollo i Dr. Francesc Xavier Guix Ràfols

2. Avaluació de l'efecte de nanoformulacions funcionalitzades sobre la invasió i migració cel·lular en models de càncer de mama metastàtic

La invasió cel·lular i la metàstasi són processos clau que determinen el pronòstic del càncer de mama. Aquest projecte té com a objectiu avaluar els efectes biològics de nanoformulacions funcionalitzades amb material genètic terapèutic sobre la capacitat de migració i invasió cel·lular en models de càncer de mama metastàtic. Mitjançant l'ús de línies cel·lulars i assajos funcionals, es pretén determinar si el tractament pot inhibir processos relacionats amb la metàstasi, així com analitzar l'expressió de marcadors moleculars implicats en aquests mecanismes.
Metodologies utilitzades: Cultiu de línies cel·lulars de càncer de mama metastàtic, tractament amb nanoformulacions funcionalitzades, assajos de migració/invasió, proves de citotoxicitat, anàlisi de l'expressió de marcadors d'invasió i metàstasi mitjançant tècniques moleculars.

Direcció: Dra. Cristina Fornaguera Puigvert i Dra. Patricia González Sáenz

3. Prediction of nanoparticle uptake and endosomal escape using machine learning algorithms

Poly-β-amino esters (pBAEs) are biodegradable and biocompatible non-viral delivery vectors with efficient in vitro and in vivo transfection of genetic material (DNAs and RNAs). They have been shown to have high cellular uptake in a range of cancer and healthy cells, excellent endosomal escape and, as a result, high transfections efficiencies. The cellular uptake and transfection efficiency is cell- and formulation-dependent, and therefore time-consuming trial and error testing is required to find the optimal pBAE formulation for each new cell line of interest.
In a recent study, we developed a machine learning model to establish correlations between nanoparticle properties, gene expression of the target cell and cellular uptake of the nanoparticles. As a result, we can predict which pBAE nanoparticle formulation will have the most preferential uptake for a given cell population, easily enabling personalised medicine for cancer treatment.
In this project, we aim to 1) use this algorithm to widen the data set for biomaterial's inputs, by incorporating new formulations of pBAEs (eg., presence and concentrations of PEG and zwitterionic masks on the nanoparticles) and new cell lines (dendritic and tumoral cells), and 2) further develop the machine learning algorithm to predict not only cellular uptake but also endosomal escape once internalised in the cells.
Objective: Improvement of our ML model by incorporating more data points involving new biomaterial and cellular inputs. Widen the capability of the ML model to predict uptake of pBAE nanoparticles as a function of endosomal gene expression.
Technical skills: Nanoparticle fabrication and characterisation, tissue culture, fluorescence microscopy, machine learning.

Direcció: Dra. Núria Oliva Jorge, Dra Cristina Fornaguera Puigvert i Dr. Michael Bruyns-Haylett

4. Design and development of novel DNA nanotechnology for the selective and synergistic treatment of metastatic cancer

ASOs are short, synthetic, single-stranded DNA sequences that interact with RNA with high specificity to reduce, restore, or modify protein expression through several distinct mechanisms. They present several advantages over short RNAs (like siRNA or miRNA), the most important one being the enhanced stability of DNA compared to RNA. Matrix metallopeptidase 9 (MMP-9) is overexpressed mainly in metastatic cancer cells, but not healthy cells, with the exception of neutrophils, macrophages and fibroblasts under certain conditions. Hence, they are an attractive option for achieving high levels of selectivity to cancer cells, alongside therapeutic benefits like gene downregulation. Moreover, previous studies have also demonstrated that inhibiting MMP-9 prior to chemotherapy enhances drug toxicity, potentially enabling treatments with lower doses. We have computationally identified potential hairpin ASO sequences against MMP-9, and have validated their MMP-9 selectivity using our custom-made high-throughput validation platform. This project will build on the previous findings by studying the silencing capability of the selected hairpin ASOs, and their synergistic therapeutic effects in combination with drugs. The data collected will be combined with existing computational biophysical data into a machine learning model to establish non-linear correlations between cell gene expression, ASO properties and therapeutic outcomes.

Objective: Identify the optimal ASO sequence that elicits a selective and synergistic therapeutic effect in metastatic cancer cells and establish a ML model to predict silencing and therapeutic outcomes.
Technical skills: Nanoparticle fabrication and characterisation, tissue culture, RT-qPCR, microscopy, machine learning.

Direcció: Dra. Núria Oliva Jorge i Dr. Michael Bruyns-Haylett

5. Mechanistic validation of insulin-induced epithelial–mesenchymal transition (EMT) and protease activation in ovarian cancer cells

Chronic hyperinsulinaemia has been associated with increased tumour aggressiveness and metastasis in several cancer types. In ovarian cancer, insulin may promote epithelial–mesenchymal transition (EMT), enhancing cell motility and invasiveness through activation of insulin and insulin-like growth factor (IGF) receptors and downstream signalling pathways. Previous work in our group has shown that insulin stimulation alters the expression of EMT markers and increases MMP9 transcription in SKOV3 ovarian carcinoma cells. However, the specific receptor isoforms and signalling cascades mediating these effects remain unclear.
This project aims to mechanistically validate the role of insulin receptor isoforms (IR-A and IR-B), the IGF1 receptor (IGF1R), and key intracellular pathways in insulin-driven EMT. The study will quantify receptor expression (qPCR, Western blot), assess pathway activation (PI3K/AKT and MAPK/ERK), and test causality through pharmacological inhibition and gene silencing. Protein-level EMT markers (E-cadherin, N-cadherin, vimentin, ZO-1, SNAI1/2, TWIST1, ZEB1) will be analysed alongside morphological metrics to quantify EMT progression. The role of secreted mediators such as TGF-β1 will be assessed by ELISA, SMAD2/3 phosphorylation analysis, and neutralisation experiments. Finally, functional protease assays (gelatin zymography, DQ-gelatin degradation, TIMP rescue) will evaluate the impact on extracellular matrix remodelling.
Objective: Determine the receptor subtype, signalling pathway, and paracrine mediators responsible for insulin-induced EMT and protease activation in ovarian cancer cells, and establish whether pharmacological or genetic inhibition reverses these effects.
Technical skills: Tissue culture, qPCR, Western blotting, use of pathway inhibitors and siRNA, ELISA, phospho-protein analysis, gelatin zymography, DQ-gelatin degradation assay, fluorescence microscopy, image quantification.

Direcció: Dra. Núria Oliva Jorge

6. Polymer-based coating of lentiviral vectors for targeted T-cell therapy

Recent advances in immunotherapy, particularly Chimeric Antigen Receptor (CAR) T-cell therapy, are revolutionizing cancer treatment. By engineering a patient's own T-cells to recognize and destroy cancer cells, CAR T-cells have achieved remarkable success -especially in leukemia and lymphoma, where some patients reach complete remission. However, high costs and technical complexit limit their accessibility. The need to extract, modify, and reinfuse each patient's cells demands advanced infrastructure and coordination, making treatment expensive and logistically difficult. To overcome these barriers, we aim to develop a safer, more efficient, and cost-effective alternative using lentiviral vectors encapsulated in functionalized synthetic polymers. Direct injection of these vectors will enable in vivo reprogramming of T-cells, simplifying production, lowering costs, and improving both safety and therapeutic outcomes. The aim of this project will be first to create and optimize a protocol to purify CD8-positive T-cells from peripheral blood mononuclear cells. Second, lentiviral particles will be coated with different polymers and conjugated to targeting molecules. Finally, the specific

transduction of CD8 positive T-cells in complex cell samples will be tested by flow cytometry and fluorescence microscopy.
Methodologies: Coating of lentiviral vectors with polymers, Functionalization with targeting molecules, NTA measurements, DLS measurements, Cell isolation experiments, Transduction experiments, Cytometer measurements, Confocal microscopy, Cell viability assays

Direcció: Dra. Marta Guerra Rebollo

7. Caracterització de vesícules extracel·lulars de models de malaltia de Lafora com a nous biomarcadors

This project involves at least 80% experimental work. Lafora disease is a severe neurodegenerative disorder that begins in childhood and leads to death only a few years after symptom onset. Its diagnosis remains challenging, making the development of new diagnostic tools a top priority. This project addresses this urgent unmet need in the diagnosis of this fatal childhood disease. The aim of this thesis is to develop a novel, non-invasive diagnostic method based on the analysis of disease-specific markers contained in extracellular vesicles (EVs), which are increasingly recognized as promising biomarkers in other pathologies. The student will join an ongoing research project and will start by isolating extracellular vesicles from blood and tissue biopsies of mouse models of Lafora disease and characterizing the presence of these markers in purified EVs samples.
Methodologies used: Western blot, ELISA, confocal microscopy, flow cytometry, vesicle size characterization by light scattering, dot blot analysis

Direcció: Dr. Jordi Duran Castells, Dr. Francesc Xavier Guix Ràfols i Dra. Cristina Fornaguera Puigvert

8. in-silico protein engineering of an alpha-amylase for the treatment of lafora disease

Glycogen is a branched glucose polymer with roles in various tissues, including the CNS. In glycogen storage diseases, glycogen accumulates abnormally, causing toxicity. A key example is Lafora disease (LD), a severe neurodegenerative condition in adolescents, characterized by glycogen aggregates in neurons and astrocytes. LD progresses rapidly, with seizures, neurological decline, and dementia, leading to death within 5-10 years (1,2). With no effective treatment, efforts are focused on addressing this need. One promising pre-clinical approach is administering amylase, a protein that degrades glycogen aggregates (3). To maximize the efficiency of the amylase treatment, we are interested in tuning the pH dependence of the enzyme on catalytic activity.
Objective: The objective of this research project is to identify and/or design alternative amylase enzymes with different operational ranges of pH. First, functional annotation databases of enzyme parameters (such as BRENDA) will be screened for potential amylase enzyme candidates from different sources. Secondly you will explore different bioinformatics and molecular modelling tools (such as APBS) to measure pH dependence on enzymatic activity for the list of enzyme candidates. Finally, you will deploy a new metric to evaluate this pH dependence on full saturation libraries of mutants. This metric will be implemented into the BindScan algorithm developed in our Laboratory for computational enzyme design (4). The expected results of your project will be a list of new amylase enzyme candidates, together with a list of hot-spots that potentially control the desired activity of the enzyme. These new enzymes and hot-spots will later be tested experimentally in the laboratory.

1. Duran J, et al. Glycogen in Astrocytes and Neurons: Physiological and Pathological Aspects. Adv Neurobiol. 2019;23:311–29.
2.Duran J, et al. Astrocytic glycogen accumulation drives the pathophysiology of neurodegeneration in Lafora disease. Brain J Neurol. 2021 Sep 4;144(8):2349–60.
3. Brewer MK, et al. Targeting Pathogenic Lafora Bodies in Lafora Disease Using an Antibody-Enzyme Fusion. Cell Metab. 2019 Oct 1;30(4):689-705.e6.
4. Bissaro B, et al. Molecular design of non-leloir furanose-transferring enzymes from an alpha-L-arabinofuranosidase. ACS Catalysis. 2015;5(8): 4598-4611.
Methodology: *Molecular Modelling. Docking. Programming. More information:* link

Direcció: Dr. Jordi Duran Castells i Dr. Xavier Biarnés Fontal

9. Surface engineering of small molecule-modified nanoparticles for biomedical applications

This project focuses on the synthesis and physicochemical characterization of nanoparticles functionalized with small molecules or biomolecules to improve their stability, biocompatibility, and selective interaction with tumor environments, with. the final aim to becoma an immunomodulating therapy. It will include techniques from organic chemistry, nanoformulation and characterization and in vitro testing of RNA-loaded formulations.

Direcció: Dra. Jennifer Fernandez-Alarcon i Dra. Cristina Fornaguera Puigvert

10. Study of the anti-senescent capacity of exosomes in human normal dermal fibroblasts (HNDF)

Replicative senescence is a phenomenon that occurs in adult cells once they have reached the maximum number of possible cell divisions, known as the Hayflick limit (Dr. Leonard Hayflick, 1960). This process is caused by the shortening of telomeres and factors that can produce genetic damage (oxidative stress and genotoxic agents), causing cells to lose their essential functions and accumulate in tissues, therefore promoting tissue failure that leads to aging. Although it has been proven that eliminating senescent cells from tissues using specific compounds, such as senolytic agents, promotes an increase in the proportion of normal cells and helps to increase tissue function, this way of combating aging can also accelerate it in the long term. In the first instance, the tissue will improve its function, but in the medium and long term, aging will accelerate. The reason is simple: by eliminating senescent cells with senotoxic agents, other neighboring non-senescent cells will necessarily enter cell division to maintain tissue mass and functional requirements, expending their proliferative capacity and generating general aging of the cell population. There may be a solution to this paradox. In principle, if cellular mechanisms are activated to maintain the Hayflick limit low, despite the proliferative increase by non-senescent cells in the tissue, tissue rejuvenation would be generated without shortening its lifespan. These epigenetic mechanisms would generate cellular reprogramming that would cause, among other things, a transient activation of telomerase, which would maintain the telomeres of the chromosomes at their normal size, extending the regenerative capacity of the tissue.
At the Tissue Engineering Laboratory we are developing a new potential therapeutic platform based in the use of exosomes and three-dimensional microenvironments to promote reduction of the senescent proportion of dermal derived fibroblasts. We have observed significant non-senolytic reduction of senescence in fibroblast cultures and we are actively studying the possible mechanism of action.

Objective: The prospective TFG student will actively analyze by western blots and immunofluorescence the specific markers (up-regulated and down-regulated) of the senescence or anti-senescence process undergoing in the cell cultures.
Methodology: molecular biology tools (wester blots), cell culture (immunofluorescence), tissue engineering (3D-cultures), etc.

Direcció: Dr. Carlos Semino

11. Exploring tumor formation in homeostatic and regenerating planarians

The relation between cancer development and tissue regeneration has long been hypothesized, with some studies suggesting that regenerative tissues are less prone to tumor formation. Freshwater planarians, known for their whole-body regenerative capacity, offer a unique model to study this connection. These animals rely on the presence of pluripotent adult stem cells (neoblasts) to regenerate and maintain tissue homeostasis. Despite of the presence of continuous stem cell division, planarians rarely form tumors. However, their exposure to carcinogens can lead to the formation of both benign and malignant tumors. Your TFG project aims to connect cancer biology and regenerative processes by exploring tumor formation at the cellular and molecular levels in regenerating and non-regenerating planarians exposed to chemical and genetic insults.

This TFG implies at least 70% of experimental work.

Techniques and methodologies used: Planarian culture; planarian microinjection; observation and documentation of the effects of planarian exposure to chemical and genetic compounds; molecular biology techniques (RNA extraction, PCR, double-stranded RNA synthesis, riboprobe synthesis); immunostaining, in situ hybridization, confocal microscopy.

Direcció: Dra. Loli Molina Jiménez

12. Functional characterization of cancer-related genes in planarians

Planarians possess adult pluripotent stem cells, known as neoblasts, which confer their remarkable regenerative capacity. Interestingly, despite the continuous proliferation of these stem cells, planarians rarely develop tumors, suggesting the existence of strong regulatory mechanisms controlling cell division and differentiation.
Previous experiments have revealed that silencing *cbp3*, a histone acetyltransferase involved in chromatin regulation, results in accumulation of undifferentiated neoblasts and alters the expression of several cancer-related genes, highlighting its potential role in maintaining genomic and cellular stability. Building on these findings, your TFG project aims to investigate the oncogenic and tumor-suppressive potential of genes affected by *cbp3* silencing in planarians. By integrating molecular and RNAi functional analyses, your project seeks to identify key genes whose deregulation contributes to abnormal stem cell behavior. Ultimately, this study will provide a functional link between epigenetic regulation and tumorigenesis, offering valuable insights into how chromatin modifiers like CBP3 influence stem cell dynamics.

This TFG implies at least 70% of experimental work.

Techniques and methodologies used: Planarian culture; planarian microinjection; *in vivo* imaging; RNA interference, molecular biology techniques (RNA extraction, PCR, double-stranded RNA synthesis, riboprobe synthesis); immunostaining, *in situ* hybridization, confocal microscopy.

Direcció: Dra. Loli Molina Jiménez

13. Análisis crítico de las posturas negacionistas frente a la pandemia de la COVID-19 un lustro después. Ejemplo de crisis sanitaria que deja huella

Breve descripción y objetivos: En este TFC, se te propone desarrollar un análisis crítico de las posturas negacionistas frente a la pandemia de la COVID-19, como ejemplo de cómo las crisis sanitarias influyen en la percepción pública de la ciencia, la salud y las políticas sanitarias.
Objetivos: i) examinar los argumentos negacionistas, incluyendo argumentos sociales y políticos que deberán ser contrastados desde una perspectiva biomédica, científica y económica; ii) analizar el papel del negacionismo en la percepción pública de la ciencia y las medidas de salud pública; y iii) reflexionar sobre el impacto del negacionismo en la confianza en las instituciones científicas en contextos de crisis sanitaria, especialmente en relación con la equidad, la vulnerabilidad y la toma de decisiones informadas.

Metodología: Investigación bibliográfica y análisis de datos.

Direcció: Dra. Montserrat Agut Bonsfills

14. Enfermedades infecciosas importadas y reemergentes en Cataluña: análisis epidemiológico, causas y retos para la salud pública

Breve descripción y objetivos: En las últimas décadas, Cataluña ha experimentado un aumento significativo en la incidencia de enfermedades infecciosas importadas y reemergentes. Este fenómeno está estrechamente vinculado a factores como la globalización, el cambio climático, los flujos migratorios, el turismo internacional y la resistencia antimicrobiana. El estudio de estas patologías es esencial para comprender los nuevos desafíos que enfrenta el sistema sanitario español y para diseñar estrategias eficaces de prevención, diagnóstico y tratamiento. En este trabajo propongo: i) identificar las enfermedades importadas y reemergentes más frecuentes en España; ii) analizar los factores que contribuyen a su aparición y propagación; iii) evaluar el impacto en la salud pública y los retos para el sistema sanitario, para poder finalmente proponer en las conclusiones de este trabajo algunas medidas de vigilancia, prevención y control.

Direcció: Dra. Montserrat Agut Bonsfills

15. Developing an optogenetic gene expression system for light-switchable control of transcription

Optogenetics is an emerging discipline that uses light to control genetic circuits in living cells, and it is pioneering research in neurobiology and optopharmacology. In contrast to chemical inducers, light provides fast and reversible responses (millisecond scale diffusion rate) with spatial resolution. Light-switchable control of gene expression typically uses two genetically-encoded proteins that are able to sense the light and transduce this signal into target promoters. We are developing novel synthetic photosensors in microalgae to control the production of high-value bioproducts like recombinant

therapeutic proteins and vaccines. Recently, our group has developed a modular cloning kit to facilitate construction of complex multigenic vectors (Melero-Cobo et al 2025).
Objective*:* You will contribute to the construction and analysis of a novel light-switchable sensor in microalgae chloroplasts based on blue-light sensing VIVID and red/far-red sensing phytochrome photoreceptors. These photoreceptors are fused to either LexA-based or Opto-T7 RNA Polymerase split transcriptional effectors. Through light-regulated control of VIVID and Phytochrome photodimerization, the split effectors reassemble and are able to bind promoter and activate the expression of reporter gene. This project should contribute to create new synthetic biology tools for the precise control of recombinant gene expression in microalgae chloroplast synthetic chassis.
Methodology: *Optogenetics and photobiology, gene cloning, gene expression (qRT-PCR, western blot, reporters). More information:*
https://planaslab.iqs.edu/research/synthetic-biology-and-molecular-biotechnology-in-green-microalgae/

Direcció: Dr. Pau Leivar Rico i Dra. Elena Monte

16. Discovering enzymes and lectins that target human glycans for therapeutic applications

Glycans, the complex sugars decorating the surface of cells, play key roles in biological recognition, immune defense, and infection. Aberrant glycan formation is a hallmark of many cancers, where it influences tumor progression, metastasis, and immune evasion. Similarly, some pathogens, such as *Pseudomonas aeruginosa*, exploit specific human glycans to adhere to host cells and avoid immune detection. The proteins involved in these processes include not only enzymes that build or degrade glycans (*Carbohydrate-Active enZYmes*, or CAZymes), but also *lectins*, which recognize and bind them.
In this project, you will explore both enzyme and lectin families to discover new proteins with biomedical potential. Using artificial intelligence and molecular modeling, you will predict how these proteins interact with human glycans and identify those that could be targeted to prevent infection or modulate immune responses.
Objective: To identify and characterize new CAZymes and lectins guided by their recognition of human glycan structures relevant to infection and immunity.
Methodology: Protein structure prediction (AlphaFold, Boltz-2); molecular docking (AutoDock); programming and data analysis (Python, Bash).
Expected learning outcomes: You will gain experience in AI-assisted discovery of biomolecular interactions, molecular modeling, and bioinformatics. You will learn how protein–glycan recognition shapes infection and immunity, and how computational tools can guide therapeutic discovery. Full time dedicated.

Direcció: Dr. Xevi Biarnés Fontal

17. Data mining of carbohydrate active enzyme's function and structure for the training of an artificial intelligence model

Structural and functional information of enzymes is disseminated in many different public web resources. Researchers aimed at gathering useful data for a particular family of enzymes usually experience the lack of consistency in the data among these different resources. At the Laboratory of Biochemistry we are particularly interested in carbohydrate active enzymes (CAZYMES). In previous

years we have initiated the development of a database that integrates functional annotations from CAZY, BRENDA and PDB databases.
Objective: To deploy a data model to allocate functional information on carbohydrate active enzymes gathered from different public repositories and implement a web-based interface to facilitate accessing the data to users of our Laboratory and other researchers. You will also preliminarily explore different machine learning algorithms suitable for the compiled data in order to train an artificial intelligence model for the prediction of protein function in CAZYMES.
Methodology: Text mining. Machine Learning. Programming (SQL or PowerQuery, python, R). *More information:* link
Expected learning outcomes: You will gain experience in integrating and curating heterogeneous biological data to extract meaningful patterns and relationships between enzyme structure and function. The project will foster skills in data management, programming, and machine learning, encouraging a critical and innovative approach to computational problem-solving in the life sciences.

Direcció: Dr. Xevi Biarnés Fontal

18. New-to-nature glycosidases as bio-orthogonal tools in metabolic labelling and enzyme prodrug therapies

Non-natural modified sugars (such as 6'-modified glucosides or ring expanded septanosides) have the potential to be transformative glycomimetics with application in chemical biology and medicinal chemistry. Such modified sugars are insensitive to degradation by hydrolytic enzymes. Therefore, engineering the active site of a glycosidase to be active on these non-natural glycosides will generate a bio-orthogonal non-natural sugar/engineered hydrolase pair. Transfected cells expressing the engineered glycosidase will allow the highly selective and time-resolved delivery of molecular cargoes inside cells. We are particularly interested in applying the pairs to "antibody directed enzyme prodrug therapy" (ADEPT) and time-resolved intracellular release of conjugates for metabolic labeling studies. First application will address ADEPT that intentionally adds an enzyme as part of the therapeutic modality to specifically liberate the bioactive compound. Competing background reactions from endogenous enzymes and the immunogenicity of the enzyme being introduced can hamper these efforts. Our contribution is the development of a platform that will deliver a specific biorthogonal glycosylated small molecule – engineered enzyme pair ready for application to prodrug development efforts. The pair will enable the spatiotemporal targeted activation of anti-cancer drugs to solid tumors with greater selectivity in the cleavage of the prodrug and the ability to better tune properties related to both the enzyme and the substrate followed by conjugation to the carrier antibody.
Objective: In this project, we will contribute to engineer a novel (new-to-nature) glycosyl hydrolase (bioorthogonal glycosidase) that selectively cleaves 6'-modified glycosides or septanosyl glycosides *in vitro* and in cells that recombinantly produce the enzyme. We have recently shown that fluorescent-labelled septanosides are uptaken by cells (Pote et al.2021) enabling *in vivo* selection strategies. You will develop and implement a targeted directed evolution approach by Iterative Saturation Mutagenesis (ISM) combined with fluorescence-assisted cell sorting (FACS) screening of large libraries using the fluorogenic substrates recently synthesized in collaboration with Dr. M. Peczuh (University of Connecticut, USA. The novel bioorthogonal hydrolase will be characterized for the bioorthogonal unmasking of functional probes *in vivo*. You will work in close collaboration with Dr. Karel Hernández, postdoctoral researcher in the group.
Methodology: *molecular biology, gene library preparation, HTS by FACS and robotic platfom, protein expression, enzyme kinetics and characterization.*

Direcció: Dr. Antoni Planas Sauter

19. Transcriptomic analysis of duchenne muscular dystrophy mouse models using nanopore sequencing to identify candidate biomarkers for personalized genetic therapies

Duchenne Muscular Dystrophy (DMD) is a severe X-linked genetic disorder caused by mutations in the dystrophin gene, resulting in absence of dystrophin and leading to progressive muscle degeneration and premature death. Despite advances in diagnosis and management, there is still no definitive cure, and current therapeutic approaches only partially mitigate disease progression. Understanding the molecular mechanisms underlying DMD is therefore essential for developing effective and personalized genetic therapies.
Recent transcriptomic studies confirm that the molecular landscape of DMD includes widespread abnormalities in cytoskeleton and extracellular matrix organization, calcium homeostasis, immune and oxidative stress pathways (Gorji *et al*., 2025). Human studies show variability in disease progression linked to differential gene expression in healthy muscle groups and changes in the proportions of muscle fibre types, satellite cells and fibroadipogenic progenitors (Suárez-Calvet *et al*., 2023, Nieves-Rodríguez *et al*., 2023). Understanding these transcriptional signatures is critical to identifying novel biomarkers and therapeutic targets.
Recent advances in third-generation sequencing technologies, such as Oxford Nanopore Technologies (ONT), allow full-length transcriptome sequencing and real-time analysis of RNA molecules. Unlike traditional short-read sequencing, ONT-based transcriptomics provides comprehensive information about transcript isoforms, splicing variants, and gene expression dynamics, which are critical to understanding the complex molecular landscape of DMD.
This project aims to perform comparative transcriptomic analyses between well-characterized Duchenne and healthy mouse models using Nanopore sequencing. The goal is to identify gene expression changes and novel transcript isoforms associated with disease pathology and to discover candidate biomarkers that could serve as potential targets for future personalized genetic therapies.
References: https://doi.org/10.1038/s41598-025-14756-9; https://doi.org/10.1038/s41419-023-06103-5;
https://doi.org/10.3389/fgene.2023.1216066
Objective: To identify transcriptomic biomarkers associated with Duchenne Muscular Dystrophy using Oxford Nanopore sequencing technology and assess their potential as therapeutic targets for personalized genetic interventions.
Methodology: RNA extraction from muscle tissues of Duchenne and healthy mouse models; cDNA library preparation; Nanopore-based transcriptome sequencing (ONT); differential gene expression and identification of candidate biomarkers.

Direcció: Dra. Marta Guerra Rebollo i Dra. Norma Fàbregas Vallvé

20. Enzyme discovery by third-generation sequencing of bacterial genomes using nanopore

Third-Generation Sequencing (TGS) using Nanopore technology represents a cutting-edge approach to obtaining complete bacterial genomes. Nanopore sequencing is an advanced genomic technology that analyzes DNA by guiding single DNA molecules through nanoscale protein pores, without the need for DNA amplification. The MinION device by Oxford Nanopore is a portable genome sequencing instrument no larger than a smartphone that can be connected to a desktop computer and , that offers real-time sequencing and analysis capabilities. As this instrument directly senses native, individual DNA fragments without the need for amplification, it can sequence extremely long fragments (>10 kilobases) of DNA without a reduction in sequence quality.

Generating high-quality, complete reference genomes is essential for functional genomics, taxonomic classification, and the identification of novel genes with biotechnological and biomedical relevance. This project aims to obtain a complete genome of the isolated bacterial species using Oxford Nanopore sequencing, with the goal of identifying functional enzymes with biotechnological and biomedical interest. This study involves three main objectives: (i) Nanopore sequencing technology (ii) predicting protein-coding sequences (CDS) within the genome of the bacterial species, and (iii) screening the new genome for functional enzymes by means of bioinformatics analysis (BLAST, HMM and AlphaFold).
Objective: To sequence the whole genome of specific bacterial species producing a complete high-quality reference genome with TGS using Nanopore, and to perform bioinformatic analyses to discover new enzymes for potential biotechnological applications.
Methodology: Molecular biology: genomic DNA extraction, DNA quantification and quality control using spectrophotometry and gel electrophoresis, library preparation following Oxford Nanopore protocols. Nanopore sequencing: DNA sequencing using the Oxford Nanopore MinION platform. Bioinformatic analysis/pipeline: Genome assembly, CDS prediction, Homology-based searches, 3D protein modelling).

Direcció: Dra. Norma Fàbregas Vallvé i Dr. Xevi Biarnés Fontal

21. Targeting aberrant glycans in tumor cells by enzymatic hydrolysis

Protein glycosylation is a widespread eukaryotic post-translational modification in extracellular and membrane anchored proteins. Protein glycosylation pathways are frequently altered in cancer cells, resulting in aberrant glycan structures that are well-known tumoral markers. Preventing the formation of such abnormal glycans has been reported to diminish tumor progression.
One of such aberrant glycan structures is the formation of highly branched structures. These are the result of enhanced expression of MGAT4 and MGAT5 genes by oncogenic transcription factors. Cells with increased MGAT5 expression show increased frequency of metastasis, whereas cells lacking this gene lose the metastatic phenotype. Therapeutic strategies aimed at preventing the formation of such branched glycans have been attempted and are under current research efforts.
Objective: The objective of this research project is to express and characterize a glycosyl hydrolase that specifically hydrolases branched glycans. You will recombinantly express a selection of enzymes that potentially cleave the glycosidic bonds present in highly branched glycans. Previous bioinformatics analysis of the carbohydrate active enzymes database (CAZY) has identified a list of gene candidates with enzymatic activities close to the desired one. You will clone, express, purify and characterize the enzymatic activities of a short selection of genes from this list. The outcome of your investigations will be the characterization of a lead glycoside hydrolase that potentially targets aberrant glycans in tumor cells. This lead enzyme can further be optimized by protein engineering and/or assessed for functionality in cellular studies.

Methodology: Molecular biology, recombinant protein expression and purification, enzymatic characterization.

Direcció: Dra. Magda Faijes Simona i Dr. Xevi Biarnés Fontal

22. Human milk oligosaccharides (hmo) as functional prebiotics. enzyme engineering by directed evolution for hmos production

Human milk oligosaccharides (HMO) furnish breast-fed infants with a number of health benefits as prebiotics and antimicrobial agents as well as exerting immunomodulation effects. There is a huge

interest in the health and food sector to supplement infant formula milk with functional HMOs, requiring biotechnological approaches for their production. Lacto-N-tetraose is one of the main core structures that is further extended and functionalized with fucosyl and/or sialyl units at different positions. Using hydrolases involved in HMO catabolism by Bifidobacteria, we aim at engineering GH20 glycosidases into synthetic enzymes by modulating the transglycosylation to hydrolysis ratio towards efficient biocatalysts. By a structure-guided mutagenesis approach of Lacto-N-biosidase from Bifidobacterium bifidus we have been able to introduce transgycosylation activity for the enzymatic synthesis of the major type 1 HMO, lacto-N-tetraose (LNT) up to a 30% yield (Castejón et al, 2021). A step further is to evolve this mutant to reach high preparative yields. Here you will develop different mutants with different affinities and activities at genetic level and expressed them. Hits will be biochemically characterized and crystallized in collaboration with Dr. Shinya Fushinobu from University of Tokyo (Japan)

Methodology: molecular biology, protein purification, enzyme kinetics, crystallization

Direcció: Dra. Magda Faijes Simona, Dr. Xevi Biarnés Fontal i Dr. Antoni Planas Sauter

23. Bioprocess development for the production of cosmetic ingredients in Plant Stem Cells (VEG4COS)

Platform development for the biotechnological production of ingredients for cosmetic applications based on *in vitro* culture of plant stem cells as an alternative to extracting ingredients from plants' biomass, to produce anti-aging, anti-oxidants, and other ingredients with cosmetic activity.
The interest of companies focused on the production of cosmetic ingredients is moving fast from the classical ingredient extraction from plants to biotechnological-based bioprocesses that allow the no stationary production, improve reproducibility and product quality. The student will join a team of the project VEG4COS composed by 2 PhD candidates. The project has granted by Acció (Nuclis, Genralitat de Catalunya) in collaboration with Biogründl SL (https://biogrundl.es/), a well stablished company of the cosmetic ingredients sector.
Up to date, Plan Stem Cells have been induced from explants of the of the species of interest (*Ocimum basilicum*) and cultured in callus and in suspension. The final goal is to produce Flavonoids and Polyphenols and test their antioxidant and antiaging activity *in vitro* using hNDF (human fibroblasts).
The main aim is to stablish the bases of the bioprocess based on Plant Stem Cells at bench scale bioreactors (from shake flasks up to 5-liter Bioreactor). This work will include the study of the main culturing and bioprocessing conditions, the development of bioprocess monitoring tools, bioprocess intensification to increase productivities, and if possible, production of different batches of the ingredient of interest and its characterization.
The objective of this Final Degree Project is to explore the use of plant stem cells as a sustainable source of bioactive compounds for cosmetic applications. Starting from differentiated cell lines derived from explants, the project involves a process of selection and screening to identify the most resilient, fast-growing, and productive cell cultures. These selected lines will then be transferred to suspension cultures, where different elicitation methods will be tested to enhance the production of flavonoids and polyphenols. In the most promising cases, biochemical assays will be carried out to evaluate the antioxidant activity of the produced molecules, which will also be tested in an *in vitro* platform using human cell models (hNDF). The overall aim is to contribute to the development of innovative and environmentally responsible cosmetic ingredients through plant cell biotechnology.

Direcció: Dr. Martí Lecina Veciana i Dr. Pau Leivar Rico

24. Development of a platform to engineer small extracellular vesicles for peptide-based therapies targeting AAT deficiency

The working hypothesis is that small extracellular vesicles (sEVs) can serve as an efficient delivery system for therapeutic proteins and peptides, which can be endogenously loaded by engineering the donor cell lines. Specifically, the present proposal focuses on developing an innovative therapeutic approach that employs small extracellular vesicles (sEVs) as a delivery system for functional alpha-1 antitrypsin (AAT) to protect alveoli from enzymatic degradation in patients sulfureting of AAT deficiency. This innovative treatment can be administrated via inhalation, directly to the lungs.
Building on this hypothesis, the primary goal of the project is to design endogenous loading strategies by expressing recombinant fusion proteins composed of hATT and sEVs specific markers. To achieve this goal, the proposal identifies four milestones that address key challenges in the development of EV-based therapeutics: **a)** achieving efficient protein (AAT) loading on/into EVs, **b)** overcoming limitations in scalable and efficient EV purification methods, **c)** ensuring effective delivery of EVs to pulmonary tissue, and **d)** establishing a robust, scalable biomanufacturing process for EV production. To achieve this goal, we have defined three specific objectives:
The **first objective** focuses on the engineering of HEK293 cells to produce esEVs efficiently loaded with AAT. This objective involves the expression of AAT fused to LAMP2B or TSG101. The strategy includes the expression of cleavable HisTag/StrepTag on the esEV surface to facilitate esEVs purification.

This proposal belongs to the project **TherPeEVs** kindly founded by the Ministerio de Ciencia e Innovación (Plan Estatal de Investigación Científica y Innovación). The student will work within a research group together with a Polish PostDoc researcher, so a good level of English is essential.

Direcció: Dr. Martí Lecina Veciana

25. Development of a bioprocess platform for the large-scale production and purification of small extracellular vesicles (sEVs) derived from HEK293 cells

This Final Degree Project is part of the *TherPerEVs* project, funded by the *Ministerio de Ciencia e Innovación* under the *Plan Estatal de Investigación Científica y Técnica y de Innovación*. The overarching goal of *TherPerEVs* is to develop a therapeutic platform based on engineered small extracellular vesicles (sEVs) for peptide- and protein-based therapies targeting alpha-1 antitrypsin (AAT) deficiency. Within this framework, the proposed project focuses on the bioprocess development required for the efficient and scalable production of sEVs using HEK293 cell cultures.
The student will work on establishing and optimizing upstream and downstream processes, with special emphasis on the design and operation of high-density culture systems in bioreactors. The upstream phase will involve applying different process strategies—including *fed-batch*, *perfusion*, and intensified continuous culture modes—to enhance cell growth, productivity, and sEV yield. Process parameters such as nutrient feeding profiles, oxygen transfer, and shear stress control will be systematically studied to identify the optimal operating window.
In the downstream phase, the student will implement and evaluate a purification workflow based on a multi-step tangential flow filtration (TFF) cascade coupled to an affinity chromatography. This system will be designed to ensure efficient clarification, concentration, and polishing of sEVs while maintaining their structural and functional integrity. The ultimate aim is to integrate upstream and downstream operations into a consistent and scalable continuous manufacturing process.
Experimental work will be conducted using a prototype Single-Use Bioreactor (SUB) developed in collaboration with an industrial partner, offering the opportunity to work with state-of-the-art technology in process intensification and advanced biomanufacturing.

The project provides practical training in mammalian cell culture, bioreactor operation, process monitoring, and EV purification. The student will join the Bioprocessing Lab at the Department of Bioengineering, under the supervision of Dr. Martí Lecina, and will collaborate closely with a Polish postdoctoral researcher. Therefore, a good level of English is essential for effective communication and documentation.

Direcció: Dr. Martí Lecina Veciana

26. Induction, generation and characterization of novel plant cell culture lines to produce bioactive compounds

Historically, plants have been used for or a wide range of food, pharmaceutical, and cosmetic applications. Today, plant-derived products remain essential worldwide and are gaining popularity as sustainable alternatives to synthetic compounds. However, traditional methods for obtaining plant extracts often face limitations related to environmental dependency, resource use, and low yield.
Recent advances in biotechnology have enabled the use of plant tissue, callus, and cell suspension cultures as innovative systems for the controlled production of bioactive compounds. These cultures, derived from totipotent plant stem cells obtained through phytohormone-induced dedifferentiation, represent a renewable and scalable source of valuable biomolecules with cosmetic, pharmaceutical, or nutraceutical potential. Previous work in our group has successfully implemented the first plant cell cultures at IQS to produce bioactive compounds in specific plant species.
This project aims to contribute to the development and characterization of new plant cell culture lines capable of producing bioactive compounds. Through the induction of calli from different explants and the development of cell suspension cultures, we will optimize growth and elicitation conditions to enhance metabolite production at the Erlenmeyer flask scale. In addition, we will also characterize the established plant cell cultures at the transcriptomic and metabolomic levels.
Objective: To develop and optimize novel plant cell culture lines for the sustainable production of bioactive compounds.
Methodology: Induction of calli from explants (leaves, stems, or flowers); establishment of cell suspensions from generated calli; optimization of elicitation conditions to increase biomolecule production at the Erlenmeyer flask scale; preliminary transcriptomics and metabolomics analyses.

Direcció: Dr. Martí Lecina Veciana, Dr. Pau Leivar Rico i Dra. Norma Fàbregas Vallvé

DEPARTAMENT BIOENGINYERIA / DEPARTAMENT QUÍMICA ANALÍTICA I APLICADA

27. In vivo identification of lea protein complexes using immunoprecipitation coupled to mass spectrometry

Climate change is one of the most urgent global challenges, leading to more intense droughts and high salinity levels in agricultural soils. These environmental stressors significantly threaten ecosystems and agricultural productivity. A deeper understanding of how plants perceive, respond and adapt to drought and salt stress is therefore critical for the development of stress-resilient crops. While numerous genes, proteins, and metabolites involved in stress signaling responses have been identified, the *in vivo* functional relevance of many of these components remains largely unknown.
A clear example is the case of the Late Embryogenesis Abundant (LEA) proteins, a family of hydrophilic proteins known to accumulate in response to stress. The LEA proteins show strong

correlation with stress responses, yet the *in vivo* localization, dynamics and functional roles during stress remain poorly understood.
In our group, we have previously characterized a group of LEA proteins and identified their protein interactors using co-immunoprecipitation followed by liquid chromatography coupled to mass spectrometry (LC/MS/MS). Our preliminary data indicate that LEA proteins interact with several well-known proteins involved in salinity and drought stress responses.
This project aims to further investigate LEA protein interaction networks under different water-deficit stress conditions. To achieve this, *LEA:GFP* transgenic lines will be exposed to various stress treatments, followed by co-immunoprecipitation using anti-GFP antibodies and LC-/MS/MS proteomic analysis to identify the candidate LEA interactors. By including appropriate negative controls and biological replicates, we aim to generate high-confidence protein–protein interaction datasets. Identifying LEA protein interactors *in vivo* will provide key insights into their functional roles in plant stress adaptation.
Objective: To identify novel LEA protein interactions in response to water-deficit stress.
Methodology: *In vitro* plant growth under controlled stress treatments (e.g., salt stress, osmotic stress, high temperature), protein extraction and immunoprecipitation, western blotting, protein digestion and peptide sample preparation for LC/MS/MS, proteomic data analysis.

Direcció: Dra. Norma Fàbregas Vallvé i Dra. Margalida Artigues Cladera

28. Application of a metabolomic LC-QTOF method for the control of bioengineered cosmetic ingredient production

The cosmetic industry is increasingly embracing sustainable and environmentally responsible approaches. One key direction involves the use of natural raw materials and biotechnological strategies to develop high-value cosmetic ingredients with minimal environmental impact. Among these strategies, the use of bioengineered plant stem cells cultivated in bioreactors offers a promising alternative for the controlled production of active compounds. In this context, the present project focuses on the application of a previously developed metabolomic method based on liquid chromatography coupled with high-resolution mass spectrometry (LC-QTOF). The method will be used to monitor and control the metabolite profiles generated by various bioengineered plant stem cell lines cultivated under different elicitation treatments. These treatments aim to promote the biosynthesis of metabolites with cosmetic relevance. By comparing the metabolic fingerprints of cultures exposed to different elicitors, this work seeks to identify key metabolic changes associated with enhanced production of target compounds. The results will contribute to a deeper understanding of plant cell metabolism in bioreactors and provide a robust analytical framework for process optimization and quality control in the development of sustainable cosmetic ingredients.

Direcció: Dra. Margalida Artigues Cladera i Dr. Martí Lecina Veciana

DEPARTAMENT BIOENGINYERIA / DEPARTAMENT QUÍMICA ORGÀNICA I FARMACÈUTICA

29. Production of Vaults: a virus-like-particle with a lock-open mechanism allowing the cargo of therapeutical as a novel drug delivery system

Precision personalized medicine seek for next-generation biomaterials to serve as drug delivery systems with “smart” functional properties, including accurate recognition, self-organization and adaptability. Several strategies are currently inspired by the prospect of controlling the precise protein architectures as an alternative to the classic delivery systems. Among them, a particular virus like particles (VLP) named vaults represent a particularly attractive case, being about 40 nm -width-, 70 nm -length in size. Their natural function is not yet completely elucidated, although several functions related to nuclear transport, immune response, and drug multiresistance in cancer cells have been hypothesized. These nanocapsules are composed of different protein constituents and they can be produced in large quantities by expression of recombinant versions of the “major vault protein” (MVP) alone. Importantly, the vault particle represents an assembly of half-vaults. Under acidic conditions, the vaults can be reversibly opened and loaded with small molecules or biopharmaceuticals.
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Direcció: Dr. Martí Lecina Veciana i Dra. Ana Belén Cuenca González

30. Microscopy image of isolated Vaults, and vault 3D reconstruction

The project consists in engineering HEK293 (human cell line) to produce engineered vaults with improved functionalities for cell tracking, quantification and specific purification. Initially, heterologous expression of MVP protein will be performed in HEK293 cells, and then purified by SEC and characterized by means of cytometry, western blot, NTA (nano-tracking analysis) and cryo-TEM. Once purified, vaults will be loaded with a small reporter molecule to assess functionality and loading capacity. Then, vaults uptake by recipient wild-type HEK293 cells will allow the assessment of vaults functionality and the potential of vaults to be used as delivery systems. Once purified, Vaults can be loaded with drugs/mRNA, by taking advantage of the dynamics of the nanoparticle (can be opened by lowering the pH).

The second part of the project consists in modifying MVP protein expression by fusing eGFP to N terminus of MVP to provide a fluorescent labelling to vaults, and StrepTag to the C-terminus (located outside the cupula structure), what will ease vaults purification, tracking and quantification. Also

targeting peptides will be fused to MVP to provide specific cell targeting to direct the drug delivery to specific recipient cells.

This piece of work will be conducted in collaboration with a PhD student and Dr Ana Belén Cuenca, head of Pharmaceutical Chemistry Department, whose team will further chemically modify the produced vaults to provide with improved features.

Direcció: Dr. Martí Lecina Veciana i Dra. Ana Belén Cuenca González

31. Low-dose insulin in dermatological formulations for skin regeneration and wound healing

This Final Degree Project focuses on the development of a dermocosmetic cream formulation containing low concentrations of insulin, aimed at evaluating its potential regenerative and wound-healing properties on superficial skin injuries. The study includes the in vitro assessment of insulin efficacy as a healing agent in human dermal fibroblasts (hDF), as well as the design, preparation, and physicochemical characterization of the topical formulation. Additionally, the stability and skin safety of the product will be investigated. This project seeks to provide an innovative approach to the use of bioactive pharmaceutical ingredients in topical products intended for skin repair and regeneration.
Objective: Assess the effects of insulin on wound healing and develop a dermocosmetic cream formulation to release insulin in wounds.
Technical skills: Tissue culture, wound healing assays, formulation technology

Direcció: Dr. Carles Bofill Bonet i Dra. Núria Oliva Jorge

DEPARTAMENT BIOENGINYERIA / ENGINYERIA QUÍMICA I CIÈNCIA DE MATERIALS

32. Disseny de microagulles recobertes de multicapes de polímer pel seu ús com a vacunes transdermals de mRNA

Aquest és un treball amb un mínim del 80% de dedicació experimental. El seu objectiu és desenvolupar un sistema d'alliberació controlada d'àcids nucleics basat en una platforma de microagulles. Partint de resultats preliminars del grup on ja s'ha dissenyat la plataforma i s'han fet les primeres proves de concepte, s'espera que l'alumne incorporat/da faci les validacions in vitro de seguretat i eficàcia, així com algunes proves de caracterització pendents.
Metodologies utilitzades: caracterització de mida de vesícules per dispersió de llum, nanotecnologia, síntesis de nanopartícules polimèriques i estudis d'encapsulació, treball in vitro amb cultius cel·lulars, assajos de viabilitat, tècniques de biologia molecular per veure l'expressió de marcadors associats, química de superfícies.

Direcció: Dra. Cristina Fornaguera Puigvert i Dr. Robert Texidó Bartés

33. Investigating the Role of Beta-Amyloid and Tau Propagation through Extracellular Vesicles in Alzheimer's Disease

Alzheimer's Disease (AD) is a neurodegenerative disorder characterized by the deposition of beta-amyloid (Aβ) plaques and tau protein aggregation, leading to progressive cognitive decline. Evidence suggests that the interaction between extracellular Aβ aggregates and intracellular tau proteins may trigger the propagation of tau pathology across neurons via extracellular vesicles (EVs). The spread of pathological tau forms across the brain in Alzheimer's disease patients is closely linked to the progression of symptoms. Thus, understanding the molecular mechanisms governing this process is crucial for developing new therapeutic strategies This project aims to explore the deposition of Aβ as a trigger for tau aggregation and its neuron-to-neuron spread through EVs, contributing to AD pathology. Additionally, we will investigate the mechanical differences between healthy and Alzheimer's brains, which may influence protein propagation. To study tau propagation, a model of neuroblastoma cells cultured in gelMA scaffolds will be developed.
This project aims to shed light on the molecular and mechanical pathways contributing to tau pathology and Alzheimer's disease progression.

Objectives:

1. Characterise Mechanical Properties in Alzheimer's and Healthy Brains: review literature on mechanical property differences in AD brains versus healthy brains, with a focus on how stiffness or elasticity may affect disease progression.
2. Develop and characterise a 3D model of Alzheimer's and healthy brain using gelatin methacryloyl (gelMA) scaffolds to simulate the brain microenvironment and evaluate how mechanical properties of the scaffold affect tau aggregation and EV-mediated propagation.
3. Isolate EVs from cells in 3D models and characterize EVs using nanoparticle tracking analysis (NTA) and immunodetection with antibodies specific to tau and EV markers.

Technical skills: 3D printing, mechanical characterisation, tissue culture, fluorescence microscopy, nanoparticle tracking analysis and immunostaining.

Direcció: Dr. Francesc Xavier Guix Ràfols, Dra. Núria Oliva Jorge i Dr. Robert Texidó Bartés

34. Comparison of mechanical and structural properties of adult and paediatric human bone: Assessment to guide bioprinted bone tissues design for paediatric reconstructive surgery

Most bone repair and implant solutions currently under development are designed for adults and are not suitable for paediatric patients. This is because, in paediatric reconstructive surgery, engineered bone constructs must not only integrate with the host tissue but also grow and remodel alongside the patient. At the same time, the few tissue-engineering approaches focused on paediatric applications are often based on adult bone properties, without accounting for the intrinsic mechanical and structural characteristics of paediatric bone. This limits the physiological relevance of bioprinted constructs designed for this use. Therefore, it is essential to establish a clear understanding of how paediatric bone differs from adult bon.
Hence, this study aims to identify and quantify these differences, providing essential reference data to define the design requirements for bioprinted bone tissues tailored to paediatric reconstructive surgery.

Objective: To determine the mechanical and structural differences between adult and paediatric bone that can inform the design and fabrication of bioprinted bone constructs optimized for paediatric reconstructive surgery.
Methodology: The project will begin with a literature review to identify the main mechanical, structural, and compositional parameters differentiating paediatric from adult bone and to define the most relevant experimental assays. Representative bone samples from both age groups will then be characterised through basic mechanical tests under physiological conditions. When feasible, complementary analyses will be performed to correlate structure and composition with mechanical performance. The collected data will finally be analysed to extract key differences and translate them into design criteria and material specifications for bioprinted bone constructs suitable for paediatric applications.

Direcció: Dra. Núria Agulló Chaler i Dra. Glòria Nieva Esteve

DEPARTAMENT BIOENGINYERIA / DEPARTAMENT DE MATEMÀTIQUES I ANALÍTICA DE DADES

35. Geometry-driven classification of protein–glycan interfaces

Protein-carbohydrate interactions are fundamental to a wide range of biological processes, from cell-cell communication and immune response to infection and cancer progression. Glycans are the most structurally diverse biomolecules, and their recognition by proteins plays a crucial role in numerous physiological and pathological mechanisms. Despite their importance, many aspects of protein-glycan interactions remain elusive due to the intrinsic complexity of glycans, their dynamic nature, and the challenge of studying their binding mechanisms at high resolution. In this project you will contribute to advance the molecular understanding of protein–glycan recognition. By integrating structural biology, mathematical modeling, and data science, this project has the potential to accelerate the discovery of new glycan-targeted therapies and to support innovations in biotechnology, biomedicine, and sustainable industry.
Objective: To develop computational methods to identify and classify glycan-binding sites based on the geometric properties of protein surfaces. You will analyze the surface patches around known monosaccharide binding sites, compute curvature and geometric descriptors, and represent them using simplified shape coefficients.
Methodology: Structural Bioinformatics. Data Analysis and Machine Learning. Programming (python). *More information:* link
Expected learning outcomes: You will learn how to analyze protein structures and surfaces using computational tools. You will also gain experience in Python programming, data visualization, and in connecting biochemical concepts with mathematical and computational approaches. Full time dedicated.

Direcció: Dr. Xevi Biarnés Fontal i Dr. Giovanni Dalmasso