Centre de Regulació Genòmica

1. Descripció del centre de recerca

El Centre de Regulació Genòmica (CRG) és un institut internacional de recerca biomèdica d'excel·lència, creat el juliol de l'any 2000. És una fundació sense ànim de lucre finançada pel Govern català a través del departament d'Empresa i de Coneixement i del departament de Salut, el Ministeri de Ciència i Innovació i la Fundació "la Caixa", i inclou la participació de la Universitat Pompeu Fabra.

La missió del CRG és descobrir i fer avançar el coneixement en benefici de la societat, la salut pública i la prosperitat econòmica. El CRG creu que la medicina del futur depèn de la ciència innovadora del present. Això requereix un equip científic interdisciplinari centrat en comprendre la complexitat de la vida, des del genoma fins a la cèl·lula i un organisme sencer, i la seva interacció amb l'entorn, oferint una visió integrada de les malalties genètiques.

- Adreça:

  Centre for Genomic Regulation (CRG)
  C/ Dr. Aiguader, 88
  PRBB Building
  08003 Barcelona, Spain

2. Descripció del projecte

En el cas del CRG s'ofereixen 4 projectes diferents, en els següents grups de recerca:

a) Computational Biology and Health Genomics

- **Group leader:** Dr. Roderic Guigó
- **Mentor:** Tamara Perteghella, PhD student
- **Summary of the project:** Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease that affects motor neurons in the brain and spinal cord. Motor neuron degeneration in ALS causes the loss of voluntary muscle control, severely impacting movement, speech, and breathing. Alternative splicing and isoform diversity play critical roles in neuronal function, and reconstruction of full-length transcript isoforms in disease-relevant cell types is crucial to understand the underlying biological mechanisms.

  With the aim of comprehensively characterise the transcriptional complexity associated to the disease, we generated ONT data from two samples: a healthy donor and a sample from patient's fibroblasts reprogrammed into motor neurons. Processing will require long reads quality check, mapping and transcript models reconstruction. We then want to assess the novelty and diversity with respect to the reference annotation and to conduct a preliminary investigation of differential isoform detection between the two conditions.

- **What kind of student profile is needed for your project (skills, knowledge, background...)?** The student should have a basic understanding of molecular biology concepts, particularly gene expression and RNA processing. Some familiarity with long-read sequencing technologies concepts is desirable, though no prior experience is expected. The ideal candidate is curious, motivated, and willing to learn new computational and analytical approaches. The project is designed as a guided, training-oriented experience, allowing the student to acquire hands-on skills in transcriptomic data processing, though basic proficiency in Linux/Unix environments, experience with command-line tools, and programming languages (R or python) would be an advantage.

b) Quantitative Cell Biology

- **Group leader:** Dr. Adel Al Jord
- **Mentor:** Julia Orio Tejada and Giulia Soggia, PhD students
- **Summary of the project:** Our research explores how physical forces shape nuclear organization and function, with a particular focus on biomolecular condensates, essential RNA-processing organelles within the nucleus. Our lab has pioneered the discovery that, in germ cells, cytoskeletal forces mechanically remodel nuclear condensates across scales, a process that is crucial for reproductive success. Whether a similar force-based mechanism operates in somatic cells remains unexplored.

  Our recent findings suggest that this mechanism is deployed by mammalian somatic cells within diverse physiological and pathological contexts. The research objective is to decipher how cytoskeletal forces impact nuclear dynamics across scales, from organelle remodeling down to RNA-processing regulation, and how this physical link influences somatic cell division and differentiation.
  To assess this aim, the student will use a multidisciplinary approach combining advanced microscopy, quantitative image analysis, spatial and high-throughput RNA profiling, force measurement and modulation assays. Working with multiple model systems, including mouse cell lines (muscle cells) and human cells (healthy and cancerous breast cells), the project will test the universality and functional relevance of this new undocumented mechanism.

- **What kind of student profile is needed for your project (skills, knowledge, background...)?** We are looking for a student with a background in Cell Biology, Molecular Biology, and/or Biophysics, who is interested and excited about the mysteries of the cytoskeleton, biomolecular condensates, and mechanobiology, as we are. Competences:
  - Curiosity and creative thinking
  - Excellent interpersonal, organizational, and communication skills
  - Broad interests with a passion for cross-disciplinary research in cell biology

c) Systems and Synthetic Biology

- **Group leader:** Dra. Nora Martin
- **Mentor:** Kye Hunter, PhD student
- **Summary of the project:** Within the group's focus on evolution and computational studies of the structure of genotype-phenotype maps and fitness landscapes, this project will most likely focus on investigating a specific computational model of a fitness landscape, its structure, and/or evolutionary dynamics. The project will involve writing code to run simulations and analyze the results, and interpreting the data to make conclusions. Important skills/interests for a candidate are evolution, genetics, computer science, and math/statistics. The project is not expected to include analyzing preexisting datasets (bioinformatics) or machine learning.

- **What kind of student profile is needed for your project (skills, knowledge, background...)?** Since the project is not within a "typical" field of undergraduate studies, the most likely situation might be a biology student with an interest in computational/theoretical research, or a math/physics/computer science student with an interest in genetics/biology. If they're enthusiastic about filling in the gaps, that should be enough!

d) Systems and Synthetic Biology

- **Group leader:** Dr. Luis Serrano
- **Mentor:** Karolina Guzauskaite, PhD student
- **Summary of the project:** Interferon-γ (IFN-γ) is a potent cytokine with well-established anti-tumour activity, making it an attractive therapeutic target. However, its clinical application in immunotherapy is severely limited by high systemic toxicity and extensive off-target effects. To address these challenges, masking strategies have been developed—an innovative approach based on engineering molecules that remain inactive under physiological conditions and become activated only within pathological environments, such as the tumour microenvironment (TME).

  Current masking approaches most commonly rely on fusion of the cytokine to nanobodies or soluble receptors via protease cleavable linkers. However, the effectiveness of these strategies is highly dependent on the specific domain fused to the target molecule, often making optimisation time-consuming.

  Here, we propose an alternative masking strategy based on closure of the molecule through the introduction of engineered cysteine bonds. This approach offers several advantages, including potential transferability to different cytokines and the potential to significantly extend protein half-life—another major bottleneck in the development of cytokine-based therapeutics.

The student's role will involve cloning the engineered constructs and validating their activity in vitro. During the project, the student will gain hands-on experience with a broad range of techniques, starting from fundamental molecular cloning techniques—such as primer design, PCR, gel electrophoresis, and bacterial transformation—to assays such as ELISA and Western blot. In addition, the student will be trained in working with Mycochassis and different cell lines.

- **What kind of student profile is needed for your project (skills, knowledge, background...)?** We are looking for a highly enthusiastic and motivated student eager to expand their scientific knowledge and develop wet-lab skills. Applicants should be pursuing a degree in a biology-related discipline and have a foundational understanding of molecular biology. Prior experience with basic molecular biology techniques is a plus, but training will be provided.