Offer #2024-08466

Analyzing cell state transition of tumor cells from tolerant to sensitive to cancer therapeutics, using single-cell data

Contract type : Fixed-term contract

Level of qualifications required : Graduate degree or equivalent

Fonction : Temporary scientific engineer

Level of experience : Recently graduated

About the research centre or Inria department

The Inria center at Université Côte d'Azur includes 42 research teams and 9 support services. The center's staff (about 500 people) is made up of scientists of different nationalities, engineers, technicians and administrative staff. The teams are mainly located on the university campuses of Sophia Antipolis and Nice as well as Montpellier, in close collaboration with research and higher education laboratories and establishments (Université Côte d'Azur, CNRS, INRAE, INSERM …), but also with the regional economic players.

With a presence in the fields of computational neuroscience and biology, data science and modeling, software engineering and certification, as well as collaborative robotics, the Inria Centre at Université Côte d'Azur is a major player in terms of scientific excellence through its results and collaborations at both European and international levels.

Context

The molecular mechanisms involved in tumor cell tolerance to immune cell killing or to cancer therapeutics contribute to the partial treatment efficacy and therefore represent potential targets for combination treatments. Identifying these molecular mechanisms is an essential task in the rational design of efficacious drug combinations.

It has been shown that drug-tolerant cells can emerge from transient differences in cellular contexts and we have established an approach to profile single-cell tolerance of non-genetic origins [1]. At the modeling level, we developed an approach to detect cellular mechanisms responsible for the amplification of transient and small differences, that ultimately lead to significant differences in single-cell signatures and dynamic response of sensitive or tolerant phenotypes [2].

The objective of this short project is to study and understand the cell state transition of tumor cells between sensitive and tolerant modes, by the analysis of RNAseq data as well as a set of kinetic parameters associated to a mathematical model. This work is funded by a collaborative project between M. Chaves at MACBES team at Inria Center of Université Côte d'Azur and J. Roux single-cell biology lab at the Institut de Pharmacologie Moleculaire et Cellulaire, CNRS.

Assignment

The first task is this project to use diffusion maps to analyze RNAseq data (see, for example, the R-package Destiny [3]). This will give us a landscape of genetic signatures covering both sensitive and tolerant cells, and we will investigate the adaptation of cells to a drug or an immune effector by detecting "pseudo-trajectories" between the two phenotypes.

The second task is to similarly analyse a set of kinetic parameters obtained from the mathematical models previously developed in our team. These models provide a set of parameters for each cell, which serve as a first distinction between sensitive and tolerant cell states. Here, we will look for features that separate the two groups in the parameter space.

Finally, we will systematize a method for comparison of the RNAseq data and kinetic parameter analysis and establish a link between genomic data and kinetic parameters.

References:
[1] Mickael Meyer, Agnès Paquet, Marie-Jeanne Arguel, Ludovic Peyre, Luis C. Gomes-Pereira, Kevin Lebrigand, Baharia Mograbi, Patrick Brest, Rainer Waldmann, Pascal Barbry, Paul Hofman, Jérémie Roux, Profiling the Non-genetic Origins of Cancer Drug Resistance with a Single-Cell Functional Genomics

Approach Using Predictive Cell Dynamics, Cell Systems, 11(4), 367-374.e5 (2020).

[2] Chaves, M., Gomes-Pereira, L.C., and Roux, J. Two-level modeling approach to identify the regulatory dynamics capturing drug response heterogeneity in single-cells. Sci Rep 11, 20809 (2021).

[3] Angerer P, Haghverdi L, Büttner M, Theis FJ, Marr C & Buettner F (2016) Destiny: Diffusion maps for large-scale single-cell data in R. Bioinforma Oxf Engl 32: 1241–1243

Main activities

1. Analysis of RNA seq data and kinetic parameters data, by application of different techniques such as diffusion maps.
2. Numerical simulations and analysis of the results.
3. Writing a report on the project.

Skills

The candidate should have some knowledge of ordinary differential equations and be familiar with a software such as Scilab, Matlab, Phyton, or equivalent.

Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (after 6 months of employment) and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Contribution to mutual insurance (subject to conditions)

Remuneration

From 2692 € gross monthly (according to degree and experience).

General Information

- **Theme/Domain :** Modeling and Control for Life Sciences
  Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city :** Sophia Antipolis
- **Inria Center :** Centre Inria d'Université Côte d'Azur
- **Starting date :** 2025-02-01
- **Duration of contract :** 6 months
- **Deadline to apply :** 2025-01-31

Contacts

- **Inria Team :** MACBES
- **Recruiter :**
  Chaves Madalena / Madalena.Chaves@inria.fr

About Inria

Inria is the French national research institute dedicated to digital science and technology. It employs 2,600 people. Its 200 agile project teams, generally run jointly with academic partners, include more than 3,500 scientists and engineers working to meet the challenges of digital technology, often at the interface with other disciplines. The Institute also employs numerous talents in over forty different professions. 900 research support staff contribute to the preparation and development of scientific and entrepreneurial projects that have a worldwide impact.

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Instruction to apply

Applications must be submitted online on the Inria website. Collecting applications by other channels is not guaranteed.

Defence Security :

This position is likely to be situated in a restricted area (ZRR), as defined in Decree No. 2011-1425 relating to the protection of national scientific and technical potential (PPST).Authorisation to enter an area is granted by the director of the unit, following a favourable Ministerial decision, as defined in the decree of 3 July 2012 relating to the PPST. An unfavourable Ministerial decision in respect of a position situated in a ZRR would result in the cancellation of the appointment.

Recruitment Policy :
As part of its diversity policy, all Inria positions are accessible to people with disabilities.