2023-06501 - Post-Doctoral Research Visit F/M Modeling tumor cell response to immune effectors and cancer therapeutics

Contract type : Fixed-term contract  
Level of qualifications required : PhD or equivalent  
Fonction : Post-Doctoral Research Visit  
Level of experience : Recently graduated

About the research centre or Inria department

The Inria centre at Université Côte d'Azur includes 37 research teams and 8 support services. The centre'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 economy 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

Tolerant tumor cells can emerge after cancer treatments even when combination strategies are used and contribute to partial treatment efficacy. Identifying the molecular mechanisms involved in cell tolerance is thus an essential task in the rational design of efficacious drug combinations.

Several signaling pathways contribute to cell death, including the extrinsic apoptosis pathway which is triggered by drugs such as TRAIL. Tumor cells can also be eliminated through the activity of cytotoxic lymphocytes or natural killer cells, with the release of their immune effectors (granzyme B, TRAIL, and FasL). It has been recently observed that these different pathways respond to the drugs with very different timescales, and mathematical modeling of these pathways is essential to identify potential targets for drug combinations.

This is a project funded by ITMO Cancer (MIC-Mathématiques et Informatiques), where we will closely collaborate with the team of Jeremie Roux at IPMC (Institut de Pharmacologie Moléculaire et Cellulaire, CNRS, Sophia Antipolis) to develop a modeling workflow that uses single-cell response data and mathematical models to understand the dynamic interplay between immune effectors and other death signaling pathways and its role in tumor cell killing. The project runs for 12 months with a possibility of extension.

Assignment

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 : 2023-10-01
- Duration of contract : 1 year
- Deadline to apply : 2023-08-31

Contacts

- Inria Team : BIOCORE  
- 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.

The keys to success

A great motivation to work on mathematical models of biological networks, using a large range of tools from analysis of dynamical systems, numerical simulations, and comparison between models and experimental data.

Warning : you must enter your e-mail address in order to save your application to Inria. Applications must be submitted online on the Inria website. Processing of applications sent from other channels is not guaranteed.
Mathematical models for the extrinsic apoptosis pathway have been previously developed in our group (Pere et al., 2020; Chaves et al., 2021). Two main tasks are planned in this project:

1) The first task is to develop a mathematical model for the granzyme B pathway. Granzyme B is an immune effector released by natural killer (NK) cells. Cell death mediated by granzyme B occurs on average about 20 minutes after NK cell contact with the cancerous cell, a very fast timescale when compared to other death pathways (Prager et al., 2019). The signaling pathway triggered by granzyme B includes factors which are also present in the extrinsic apoptosis pathway triggered by TRAIL. In a first step, we will thus consider a model describing the common elements to both pathways, to be calibrated with kinetic data from the Roux team (Meyer et al., 2020).

2) The second task is to study the interplay between the granzyme B pathway and the slower extrinsic apoptosis pathway, where cell death is induced about 20-40 minutes later. By interconnecting the models of the two pathways, one of the problems to be studied is that of determining the contributions of each pathway in a combined signal. More specifically, we want to develop an algorithm to evaluate cell responses and classify the cell state in terms of a balance between the amounts of immune effectors and the presence of other pro-apoptotic proteins using analytical and possibly machine learning approaches (a short visit in Diego Oyarzun’s lab at the University of Edinburgh will be proposed to the candidate if desired, as part of an ongoing collaboration on this project).

References:

Main activities

- Mathematical modeling and analysis of a signaling network, by application of different techniques.
- Numerical simulations and analysis of the results.
- Writing scientific papers on the results and their communication at the main conferences in the area

Skills

- Experience on analysis and simulation of ordinary differential equations
- Experience using software such as Matlab, Scilab, Python, or equivalent
- Experience with models of biological networks
- Parameter estimation from experimental data
Some experience with or willingness to be using and exploring machine learning algorithms.

**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 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**
Gross Salary: 2746 € per month