



Offer #2023-05678

Post-Doctoral Research Visit F/M --- Molecular mechanisms of cancer cell adaptation to targeted therapies: novel insights into the biology of drug-tolerance.

Contract type : Fixed-term contract

Level of qualifications required : PhD or equivalent

Fonction : Post-Doctoral Research Visit

About the research centre or Inria department

The Inria research centre in Lyon (previously the Lyon branch of the Inria centre in Grenoble) is the 9th Inria research centre, formally created in December 2021. It brings together approximately 270 people (including 110 Inria employees) in 15 research teams and research support services.

Its staff are distributed at this stage on 2 campuses: in Villeurbanne La Doua (Centre / INSA Lyon / UCBL) on the one hand, and Lyon Gerland (ENS de Lyon) on the other. A third site should be opened in the course of 2022. The teams are mainly hosted with our partners. The centre's teams work closely with research and higher education institutions (ENS de Lyon, UCBL, INSA Lyon, etc.), their laboratories, and other research organisations in Lyon (CNRS, INRAE, competitiveness clusters, etc.), but also with Lyon and regional economic players. Many international collaborations are also underway.

The Lyon centre is active in the fields of software, distributed and high-performance computing, embedded systems, quantum computing and privacy in the digital world, but also in digital health and computational biology.

Context

A two-year postdoctoral position is available in team BEAGLE at Inria Lyon. At BEAGLE, we study cellular systems through computational models and bioinformatic data analysis, in order to better understand their organizational principles. In our team, we value working together, being innovative, and providing opportunities for professional and personal growth.

The position is within the framework of project CLAIRE, a collaboration between Inria's team BEAGLE and research groups at the Cancer Research Center of Lyon (CRCL). The overall goal of this project is to better understand the emergence of drug tolerance during treatment of lung cancer. You will be advised by Anton Crombach (Inria) and Sandra Ortiz-Cuaran (CRCL), whilst working together with other members of the project. You will be located at Inria's La Doua site and regularly visit the CRCL.

You will benefit from the expertise at BEAGLE regarding bioinformatic data analysis and computational modelling of biological systems; and you will profit from world-class knowledge at CRCL regarding cancer biology. Overall, the project will foster your career in terms of building up cutting-edge expertise on high-dimensional data analysis, network inference, statistical and machine learning, and data visualization techniques – areas that are strongly demanded in academia and industry.

Assignment

The CLAIRE project focuses on the identification of molecular mechanisms associated with drug-tolerance. Despite the encouraging outcomes observed in cancer patients treated with targeted therapies, tumor responses are only partial and are followed by acquired resistance. It is thought that resistance emerges from drug-tolerant cells that survive treatment through an adaptive response, that does not involve genetic resistance mutations. These drug-tolerant cell populations are considered the main drivers of the partial tumor response observed in patients. In this context, oncogene-driven lung cancer is a paradigm system of the success and limitations of targeted therapy, and thus makes for a relevant system to identify molecular regulatory mechanisms of adaptive survival to therapy.

Your goal within the project will be to use single-cell network inference to predict candidate genes, genetic interactions, and/or regulatory pathways that can interfere with the establishment of drug-tolerant cancer cell populations. Moreover, systematic comparisons of the inferred networks will allow for the identification of a "core" transcriptional regulatory program underlying cancer cell states.

To model the trajectories that individual lung cancer cells take between drug-sensitive and drug-tolerant states, you will reconstruct pseudo-time trajectories and infer regulatory networks that take pseudo-time into account. Trajectory inference will suggest how transcriptional states change and will

serve to identify proliferative drug-tolerant cells and allow the identification of the factors triggering state transitions.

In summary, through single-cell data analysis, network inference, and pseudo-time trajectory analysis, the you will generate candidate genes, genetic interactions and/or other regulatory pathways that are suitable for developing pre-clinical therapeutic rationales.

Main activities

The goal of this two-year postdoctoral research position is to better understand how drug tolerance manifests itself in gene regulatory processes. This means your main activities are:

- apply cutting-edge network inference tools to generate regulatory networks,
- explore the application of network inference tools that are pseudo-time aware
- perform systematic differential network analysis
- use differential analyses to predict genes and genetic interactions linked to drug-tolerance

Finally, you disseminate your work through publications in international journals and by presenting it at national and international conferences.

Skills

The project requires skills in computer science, mathematics, and (cancer) biology. A successful candidate has experience in one or more of the following areas: single-cell data analysis, network inference, statistics and machine learning, programming in Python/R. Affinity with cancer biology and the challenge of acquired drug-tolerance is considered a real advantage. Good oral and written communication skills in English are essential.

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 (90 days / year) 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
- Social security coverage under conditions

Remuneration

2653€ brut / mois

General Information

- **Theme/Domain** : Computational Biology
Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city** : Villeurbanne
- **Inria Center** : [Centre Inria de Lyon](#)
- **Starting date** : 2023-05-01
- **Duration of contract** : 2 years
- **Deadline to apply** : 2023-09-30

Contacts

- **Inria Team** : [BEAGLE](#)
- **Recruiter** :
Crombach Antonius / anton.crombach@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

The applicant should have a strong basis in computer science/mathematics and biology (PhD degree or equivalent), ideally oriented toward bioinformatic data analysis. An essential quality for this project is a keen interest to apply one's computational skills to help answering biological questions. An interest in

single-cell technologies and network inference is considered a real asset, as is wanting to communicate and collaborate with experimental biologists that study cancer.

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.

Instruction to apply

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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.