



Offer #2024-08121

Post-Doctoral Research Visit F/M Optimization of therapeutic strategies for pediatric cancers using mathematical modeling of intra-tumor heterogeneity

Contract type : Fixed-term contract

Level of qualifications required : PhD or equivalent

Fonction : Post-Doctoral Research Visit

Corps d'accueil : Ingénieur de Recherche (IR)

Level of experience : Recently graduated

About the research centre or Inria department

The Inria centre 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

This postdoc position will be located in the Inria-Inserm team COMPO (COMputational Pharmacology in Oncology), located in the La Timone health campus. The team is composed of mathematicians, data scientists, pharmacists and clinicians and is a unique multidisciplinary environment focused on developing novel computational tools for decision-making in clinical oncology.

The postdoc will join the INCa- (French National Cancer Institute) funded project COPYCAT: Combining Organoid technology with Mathematics to develop innovative models mimicking tumor cellular heterogeneity and plasticity for pediatric oncology. It is a collaboration between

- Laura Broutier's team (Cell death and childhood cancers team, Center of Research on Cancer of Lyon (CRCL), Inserm, CNRS)
- Eddy Pasquier's team (REMAP-4Kids, Center of Research on Cancer of Marseille (CRCM), Inserm, CNRS)
- COMPO (Inria and CRCM, Marseille)

He / she will also take part to the larger, INCa-funded, SouthRock consortium for pediatric cancers research between Lyon and Marseille.

The postdoc will be co-supervised by S. Benzekry and E. Ventre.

Assignment

Objective

To develop mechanistic mathematical models from patient-derived organoid data in order to propose novel drug combinations and scheduling regimen tackling intra-tumor resistance to treatment in pediatric rhabdomyosarcoma (RMS).

Data

From patients biopsies at diagnosis and relapse

- Molecular:
 - DNaseq 500X
 - bulk RNAseq

- MethylEpic
- scRNA-seq
- Histological images

Same from patient-derived RMS-organoids (RMS-O), both untreated and treated with multiple drugs and combinations, in addition to markers of differentiation, viability assays and qRT-PCR. in ≥ 3 genetically engineered RMS-O.

Part of the data has already been published in [1] and the other has been generated since the start of the project in 2023.

Methods

The mathematical and computational tools will be developed departing from existing methods:

- The [CARDAMOM](#) software for molecular data [2]
- Mixed-effects pharmacokinetics / pharmacodynamics modeling of tumor response / resistance [3]

[1] Savary, C. et al (Broutier, L.). Fusion-negative rhabdomyosarcoma 3D organoids to predict effective drug combinations: A proof-of-concept on cell death inducers. *Cell Rep. Med.* 4, 101339 (2023).

[2] Ventre, E., Herbach, U., Espinasse, T., Benoit, G. & Gandrillon, O. One model fits all: Combining inference and simulation of gene regulatory networks. *PLoS Comput. Biol.* 19, e1010962 (2023).

[3] Imbs, D. et al (Benzekry, S.). Revisiting Bevacizumab + Cytotoxics Scheduling Using Mathematical Modeling: Proof of Concept Study in Experimental Non-Small Cell Lung Carcinoma. *Cpt Pharmacometrics Syst Pharmacol* 7, 42–50 (2018).

Main activities

Main activities:

- Literature
- Bulk and single cell omics data analysis and modeling
- Pharmacokinetics / pharmacodynamics modeling of resistance to treatments
- Software development
- Interactions with the biological and clinical partners
- Writing scientific publications
- Communications in scientific events
- Responsibilities within COMPO (mentoring students,...)

Additional activities:

- Continuous integration / continuous deployment of the code
- Data visualization
- Statistical reporting to the partners
- Participation to the maintainment of COMPO software

Skills

Technical skills and level required :

- Excellent programming skills in a scripting language (R and/or Python)
- Hands-on experience with molecular data analysis (bulk / single-cell is a plus)
- Hands-on experience with real-world biological and clinical data analysis
- Strong background in applied mathematics and statistics
- Ideally, experience in mixed-effects modeling
- Strong motivation for biological and medical of computational methods
- Knowledge of biology and/or medicine is a plus
- Ability to work both independently and as a team, good relational skills

Additional:

- English speaking
- Strong academic writing skills
- Strong oral presentation skills

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 : 2788 € per month

General Information

- **Theme/Domain** : Computational Biology
Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city** : Marseille
- **Inria Center** : [Centre Inria d'Université Côte d'Azur](#)
- **Starting date** : 2024-12-03
- **Duration of contract** : 2 years
- **Deadline to apply** : 2024-11-30

Contacts

- **Inria Team** : [COMPO](#)
- **Recruiter** :
Benzekry Sebastien / Sebastien.Benzekry@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

You don't just apply the reference method to a given problem; instead, you are eager to thoroughly understand the information contained in the 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.

Instruction to apply

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

The position is open to:

- Inria internal mobility, remuneration according to statutory conditions
- mobility from other public body, by posting for a period of three years, renewable, remuneration according to statutory conditions
- in short term contract from service fixed-term

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.