Post-Doc

Development of statistical models for oncology applications

Contact: Marc Lavielle, Research Director at Inria, head of the Xpop team, Marc.Lavielle@inria.fr,

Duration: 12 months (with the possibility of extension)

Laboratory: The postdoc will join the center of applied mathematics at Ecole Polytechnique CMAP (http://www.cmap.polytechnique.fr). He will be integrated into the joint Inria - CMAP team Xpop, a team mainly dedicated to the statistical modelling for life sciences.

Project description: the postdoc will participate in two research projects:

1) Statistical modelling of metastase free survival

Project in collaboration with the Biochimistry Laboratory of Ecole Polytechnique and Curie Institute, supported by INCa (Institut National du Cancer).

In cancer, the most dreadful event is the formation of metastases that disseminate tumor cells throughout the organism. WAVE complexes are molecular machines composed of 5 subunits, most of which can be encoded by paralogous genes. In several cancers, a high level of subunit expression has been associated with high grade and poor prognosis.

qRT-PCR has been used to systematically analyze the expression of all 11 genes encoding WAVE complex subunits in breast tumors from a retrospective cohort of patients with known clinical parameters and outcome. We could derive an optimal multivariate Cox model of metastasis-free survival (MFS) using expression levels of only two subunits, NCKAP1 and CYFIP2. Experimental results thus validated the prediction of the MFS statistical model and revealed an unexpected anti-migratory function of the paralogous CYFIP2 subunit.

The very satisfactory results of this approach in breast cancer have incited us to apply it for cutaneous melanoma. Indeed, cutaneous melanoma is a cancer, where the primary tumor can easily be removed by surgery. However, this cancer is of poor prognosis because melanomas metastasize often and rapidly.

The objective is therefore to extend the method previously developed in breast cancer in order to build a metastasis-free survival model for cutaneous melanoma.

2) Statistical analysis of spectrum data for therapeutic monitoring of anti-cancer molecules

Project in collaboration with the Pharmacy Service of the European Hospital Georges Pompidou (APHP) and the team of Pharmaceutical Analytical Chemistry, University Paris Sud.

Therapeutic drug monitoring (TDM) is based on the measurement of blood concentrations to adjust the dosage of drugs. It is one approach to personalized medicine; it is still not widely used in oncology. However, in view of their narrow therapeutic margins, the significant inter-individual pharmacokinetic variability, and the relationships between concentration and described clinical response, anticancer drugs are excellent candidates for the individualization of dosage regimens to optimize management and reduce the risks of toxicity.

The aim of this project is to develop a new fast, sensitive and reliable analytical tool for the TDM of anti-cancer drugs. The objective is to combine the contribution of nanotechnologies and computational statistics to the development of robust prediction models in order to offer patients the possibility of real-time TDM of these molecules.

The postdoc will contribute to the development of classification models (prediction of the molecule in solution) and regression models (prediction of the concentration of this molecule) in order to guarantee the physico-chemical quality of the drugs prepared in hospital.

To build these models, experimental Raman spectrum data will be acquired from samples containing increasing and known amounts of molecules of interest covering their therapeutic concentrations.