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ITMO Cancer

PROGRAM

First international THE workshop : Mathematical Modelling of Tumour Heterogeneity in Tumoral Environments, and its Impact on Therapies

INTS auditorium 6, rue Alexandre Chabanel, Paris – Tuesday, February the 28th

10:00 – 10:15	**Introduction**
10:15 – 11:15	**Probabilistic/statistic models for inferring tumour heterogeneity and phylogeny** - Gregory Nuel, CNRS, LPMA, UPMC, Sorbonne Universités, FR
11:15 – 12:15	**Mathematical modelling of tissue growth** - Benoît Perthame, LJLL, UPMC, Sorbonne Universités, FR
12:15 – 13:45	**Lunch**
13:45 – 14:45	**Quantification of cancer evolutionary dynamics using multi-scale mathematical modelling of genomic data** - Trevor Graham, Queen Mary University of London, UK
14:45 – 15:45	**Multi-scale modelling of cell-microenvironment interactions and cell competition during angiogenesis and tumour progression** - Roeland Merks, CWI, NL
15:45 – 16:15	**Coffee break**
16:15 – 17:15	**Unravelling the impact of heterogeneity on tumour responses to treatment** - Helen Byrne, Oxford, UK
17:15 – 17:30	**Conclusion**

ABSTRACTS

Gregory Nuel, CNRS, LPMA, UPMC, Sorbonne Universités

The purpose of this talk is to present the general principle of the statistical inference of tumor heterogeneity from molecular data. We first explain how somatic mutations frequency might be used to identify clonal sub-populations and proportion through mixture models. The alteration of copy number is also discussed along with identifiability issues. Finally, phylogeny models for reconstructing the clonal process are also presented. We end with a discussion on the challenges and perspectives of such approaches.

Benoît Perthame, LJLL, UPMC, Sorbonne Universités

Models of tumor growth have been used to understand the evolution of cancers, based on images for instance.

These models serve to predict the evolution of the disease in medical treatments, to understand the biological effects that permit tumor growth and decide of the optimal therapy.

These models contain several levels of complexity, both in terms of the biological and mechanical effects, and therefore in their mathematical description. The number of scales, from molecules to the organ and entire body, explains partly the complexity of the problem.

A more recent subject is to explain emergence of resistance to drug and its implication in therapeutic failures and raises the question of the optimal scheduling when several therapies are used.

Trevor Graham, Queen Mary University of London

The apparently simple question of 'how does a tumour grow?' is surprisingly hard to answer. The difficulty comes from the fact that it is nearly always impossible to sample a tumour over time, and so the only information we have is from the end of the process when the tumour ends up on the specimen table. To tackle this problem, we attempt to read the 'secret diary' of a tumour's growth that is surreptitiously written in the cancer genome. Each time a cell divides, it accumulates a few new mutations, and so the frequency and spatial distribution of these mutations within a tumour are a record of how the tumour grew. To read the secret diary, we use multiscale modelling to specify potential models of how a tumour grew, and then use statistical inference against genomic data to determine the most likely mode of tumour growth. Surprisingly, our analysis shows widespread neutral tumour evolution, but in the cases where there is subclonal selection, the subclones experience extremely large (>20%) increases in fitness.

Helen Byrne, Oxford University

There are multiple sources of heterogeneity within solid tumours and each of these can affect the response to radiotherapy.
For example, an irregular distribution of blood vessels may create tumour regions with low oxygen concentrations and decreased radio sensitivity. Alternatively, the tumour may comprise distinct cellular populations, each with different intrinsic radiosensitivity.
In this talk, I will present recent results from several complementary mathematical and computational models that we are developing in order to understand the impact of cellular and vascular heterogeneity on tumour responses to radiotherapy.