Modeling dynamics of circulating tumor DNA for detecting resistance to targeted therapies

Ulysse Herbach [1]

[1]) Université de Lorraine, CNRS, Inria, IECL, F-54000 Nancy, France.

Targeted therapies represent a real advance in the treatment of patients with cancer. Most of these therapies are kinase inhibitors and require precise analysis of tumor DNA mutations to ensure the absence of primary resistance. Although tumours are often genetically heterogeneous with the presence of many subclones, they release circulating cell-free DNA (cfDNA) that can be directly extracted from basic blood samples: as sensitivity of measurements improves, such liquid biopsies increasingly appear as a mirror of tumour heterogeneity. In this context, we describe a promising statistical approach to analyze longitudinal cfDNA data, with the purpose of gaining a deeper understanding of the mechanism by which resistance develops in specific patients. While addressing the now classic problem of reconstructing the associated phylogenetic tree, this approach also describes production of cfDNA from the temporal dynamics of cells, in order to best exploit the longitudinal structure of the data.