Project goal

The main goal of this project is to enable constant monitoring of triple negative breast cancer (TNBC) evolution and response to treatment, using only patients' blood. Circulating tumor cells (CTCs) represent a very strong candidate for following cancer using minimally invasive techniques (e.g., blood sample). Currently, very little is known about these CTCs in patients with TNBC, and mostly about the so-called protein-coding repertoire. We wish to also unlock the remaining portion of the transcriptome, the elusive non-coding transcriptome.

Description of research

We will study the blood, and the primary tumor, from patients with triple negative breast cancer (TNBC). We will isolate very rare cancer cells from the blood which are released from the tumor (so-called CTCs). We will study each one of these CTC cells, as a single cell, and measure all of the coding and non-coding RNAs (transcriptome) within each cell. In parallel, we will also study the transcriptome of each single cell in the primary tumor, including not only the cancer cells, but also the cells from the tumor microenvironment. For these measures we will use a state-of-the-art technique called "vast transcriptome analysis of single cells by dA-tailing" (VASA-seq), which captures both non-polyadenylated and polyadenylated RNAs, from each separate cell, using droplet microfluidic. We will study the CTC transcriptome before surgery, during therapy and beyond, at single cell level and in each patient, to understand how CTCs are related with the evolution and progression of the disease, and with the response of the cancer to treatment.

Reasons for attempting a particular research topic

The potential of using CTCs is far greater than that of other prototypical non-invasive types of liquid biopsies (e.g., circulating tumor DNA), since the latter can not be traced directly to tumor cells, unless it has been mutated.

Furthermore, the CTC potential is also far larger than that of traditional solid biopsies, as CTCs are less invasive, less expensive, and easier to obtain in a timely manner. In addition, CTC sampling at single cell level will yield, in principle, a more complete and robust representation of the TNBC tumor, and metastasis, than routine biopsies. We will be able to relate back the CTCs to the primary tumor and to identify any other mutation which might have originated during cancer evolution.

As a result of this project, the therapy and management of TNBC (and possibly that of other subtypes of breast cancer) will be significantly advanced by a successful outcome of this project.

Substantial results expected

The application of VASAseq to characterize the CTCs from TNBC patient's blood represents the forefront of personalized molecular medicine, and will enable the study of cancer progression in each patient. At the same time, accurate assessment of the impact of therapy on the cancer will be performed, in a far superior manner to what has been possible, up until now.

Our research proposal will allow for the first time, the single-cell characterization of the non-coding and coding transcriptome, somatic mutations, for each CTC in TNBC patients and, with them, the longitudinal study of the cancer evolution during treatment.

Additionally, a successful outcome of this project will open novel avenues, including early detection of cancer using blood and CTCs. This novel method represents also a significant cost-reduction from traditional methods with the potential of significantly increased efficacy in the management of TNBC, as well as the potential for commercialization.