The laboratory aims at investigating the clinical relevance of tumor biomarkers that are related to the tumor dissemination and metastatic process.

**background**
In our institute, the first research program on disseminated tumor cells (DTC) detection in the bone marrow of early breast cancer patients was initiated in the late 90’s; with about a thousand patients included, we constituted one of the largest cohort ever reported and contributed to the landmark report that established bone marrow DTC as a level-of-evidence 1 prognostic factor in early breast cancer (Braun, N Engl J Med 2005).

Bone marrow aspiration being somehow invasive, we then investigated whether the detection of circulating tumor cells (CTC) in the blood could be used as a biomarker of early tumor relapse or progression. Our team was the first to report that a single CTC detected in the blood of early breast cancer patients was associated with a higher risk of metastatic relapse (Pierga, Clin Cancer Res 2008). In patients with metastatic breast cancer, our large multicenter study confirmed that CTC can be used as a prognostic marker and that dynamic early changes during chemotherapy are associated with the treatment outcome (Pierga, Ann Oncol 2012). Our team then coordinated a large European analysis which included about 2,000 patients, allowing CTC to reach a level-of-evidence 1 for clinical validity, and demonstrating its superiority over standard serum markers (Bidard, Lancet Oncol 2014).

Our laboratory recently developed an interest in circulating tumor DNA (ctDNA), which may be
used to determine the mutational landscape of a given tumor. While an in-house (MH Stern’s team) developed technique (biPAP-PCR) showed exquisite sensitivity for uveal melanoma mutations (Madic, Clin Cancer Res 2012), we developed other ctDNA techniques (ddPCR and NGS-based techniques). Our latest report showed an excellent agreement for mutation detection between invasive biopsies and ctDNA (Lebofsky, Mol Oncol 2015).

The dissemination of our findings was also performed through key reviews on these research subjects (Bidard, Nat Rev Clin Oncol 2013; Bidard, Sci Transl Med 2013)

Main projects for 2015

- Several multicenter interventional trials are ongoing to demonstrate the clinical utility of CTC detection:
  - CirCe01: randomized phase 3 coordinated by our team, metastatic breast cancer.
  - STIC CTC: randomized phase 3 coordinated by our team, metastatic breast cancer.
  - CirCe T-DM1: single arm phase 2 coordinated by our team, metastatic breast cancer.
  - TREAT CTC: randomized phase 2 coordinated by EORTC, early breast cancer.

- International MEta-analysis of breast cancer patients treated by NEOadjuvant chemotherapy (IMENEO study).
- Observational studies on ctDNA clinical validity:
  - CirCA01 prospective cohort: TP53 mutations detection in BRCA01 mutation carriers.
  - Other cohorts collected in “CTC-CEC-ctDNA” and “ALCINA” umbrella protocols.
  - Ancillary ctDNA detection in national studies (e.g. SAFIR02 breast, COMET02 coordinated by UNICANCER)

- Technological developments on CTC and ctDNA detection

Key publications

Year of publication 2020

Alexandre Eeckhoutte, Alexandre Houy, Elodie Manié, Manon Reverdy, Ivan Bièche, Elisabetta Marangoni, Oumou Goundiam, Anne Vincent-Salomon, Dominique Stoppa-Lyonnet, François-Clément Bidard, Marc-Henri Stern, Tatiana Popova (2020 Apr 22)

ShallowHRD: detection of homologous recombination deficiency from shallow whole genome sequencing.
Amanda Bortolini Silveira, François-Clément Bidard, Amélie Kasperek, Samia Melaabi, Marie-Laure Tanguy, Manuel Rodrigues, Guillaume Bataillon, Luc Cabel, Bruno Buecher, Jean-Yves Pierga, Charlotte Proudhon, Marc-Henri Stern (2020 Mar 17)

**High-Accuracy Determination of Microsatellite Instability Compatible with Liquid Biopsies.**

*Clinical chemistry*: 606-613 : [DOI: 10.1093/clinchem/hvaa013](https://doi.org/10.1093/clinchem/hvaa013)

Year of publication 2018

Manuel Rodrigues, Lenha Mobuchon, Alexandre Houy, Alice Fiévet, Sophie Gardrat, Raymond L Barnhill, Tatiana Popova, Vincent Servois, Aurore Rampanou, Aurore Mouton, Stéphane Dayot, Virginie Raynal, Michèle Galut, Marc Putterman, Sarah Tick, Nathalie Cassoux, Sergio Roman-Roman, François-Clément Bidard, Olivier Lantz, Pascale Mariani, Sophie Piperno-Neumann, Marc-Henri Stern (2018 May 16)

**Outlier response to anti-PD1 in uveal melanoma reveals germline MBD4 mutations in hypermutated tumors.**

*Nature communications*: 1866 : [DOI: 10.1038/s41467-018-04322-5](https://doi.org/10.1038/s41467-018-04322-5)