The aim of the laboratory is to understand the molecular pathology of breast cancers, especially triple-negative breast cancers, to identify and validate therapeutic targets.

Breast cancers are the leading cancers in women with about 50,000 new cases per year in France. Breast cancers are composed of molecularly distinct subtypes with different clinical outcomes and responses to therapy. The efficacy of their therapeutic management has improved considerably in recent years. However, the subgroup of patients with “triple-negative” breast cancer (TNBC), due to the absence of expression of estrogen and progesterone receptors and Her2 overexpression, maintains a poor prognosis. Indeed, they respond well to current therapeutic strategies based on conventional chemotherapies, but they still represent a large proportion of breast cancer deaths, because of a high recurrence rate of residual resistant tumor cells. Alternative treatments are therefore needed to bypass resistance to chemotherapies and to improve the survival rate of TNBC patients.

Our goal is to identify and validate drug targets to offer new ways to treat TNBC. To achieve this aim, we have analyzed a cohort of 200 samples including biopsies of the different breast cancer subgroups, healthy breast tissues and TNBC cell lines. The collected data (DNA, RNA, microRNA, protein) have been analyzed in collaboration with the Bioinformatics (Unit U900) of Institut Curie, in order to provide us with lists of candidate therapeutic targets.

Our team has focused on several of these targets for further validation studies, particularly kinases such as PI3K/AKT, TTK and PLK1 (see Figure 1), as well as TIPIN, a protein involved in DNA replication. Recently, our results led to a phase I clinical trial with a TTK inhibitor. The team is currently analysing the protein arginine methyltransferases and the Wnt signalling pathway in TNBC.
Figure 1: A PLK1 inhibitor, in combination with chemotherapy, impairs tumor relapse in a TNBC-derived xenograft model. A combination of chemotherapy (adriamycin + cyclophosphamide), used for the management of TNBC patients, leads first to complete response (CR); however the tumor relapses after stopping chemo treatment (gray line). Treatment with a PLK1 inhibitor (BI-2536) leads to the stabilization of the size of the tumor, but the tumor grows again after cessation of the treatment (orange line). The combination of AC with BI-2536 (blue line) induces 100% CR, which are observed earlier than CR induced by AC treatment alone. BI-2536 + AC combination impairs tumor relapse in contrast to AC alone. At day 200, mice were still tumor-free and could be considered as cured (Maire et al., Cancer Research, 2013).

Key publications

Year of publication 2021

Samyuktha Suresh, Solène Huard, Thierry Dubois (2021 Jan 24)
CARM1/PRMT4: Making Its Mark beyond Its Function as a Transcriptional Coactivator.

Year of publication 2020

Olivier Zajac, Renaud Leclere, André Nicolas, Didier Meseure, Caterina Marchiò, Anne Vincent-
Salomon, Sergio Roman-Roman, Marie Schoumacher, Thierry Dubois (2020 Jan 23)
**AXL Controls Directed Migration of Mesenchymal Triple-Negative Breast Cancer Cells.**
*Cells:* [DOI: 10.3390/cells9010247](https://doi.org/10.3390/cells9010247)

- **Year of publication:** 2019

**Protein arginine methyltransferase 5: A novel therapeutic target for triple-negative breast cancers.**
*Cancer medicine:* 2414-2428 : [DOI: 10.1002/cam4.2114](https://doi.org/10.1002/cam4.2114)

- **Year of publication:** 2015

Sylvie Maubant, Bruno Tesson, Virginie Maire, Mengliang Ye, Guillem Rigaill, David Gentien, Francisco Cruzalegui, Gordon C Tucker, Sergio Roman-Roman, Thierry Dubois (2015 Apr 8)
**Transcriptome analysis of Wnt3a-treated triple-negative breast cancer cells.**
*PloS one:* e0122333 : [DOI: 10.1371/journal.pone.0122333](https://doi.org/10.1371/journal.pone.0122333)

- **Year of publication:** 2013

**TTK/hMPS1 is an attractive therapeutic target for triple-negative breast cancer.**
*PloS one:* e63712 : [DOI: 10.1371/journal.pone.0063712](https://doi.org/10.1371/journal.pone.0063712)

- **Year of publication:** 2012

**Polo-like kinase 1: a potential therapeutic option in combination with conventional chemotherapy for the management of patients with triple-negative breast cancer.**
*Cancer research:* 813-23 : [DOI: 10.1158/0008-5472.CAN-12-2633](https://doi.org/10.1158/0008-5472.CAN-12-2633)