Considerable data have been accumulated across the past decades on the role of mutations in cancer. However, while a number of genetic mechanisms driving tumor progression or resistance processes has been discovered, in many cases genetic mechanisms driving these processes cannot be found, raising the possibility of non-genetic plasticity or rare cell variability. Hence, besides genetic mechanisms, mounting efforts now concentrate on non-genetic and particularly epigenetic mechanisms that may account for the adaptability of cancer cells to environmental, metabolic or therapy-related stresses. In the lab, we focus on the study of chromatin landscapes, and develop approaches to study the heterogeneity and dynamics of chromatin landscapes at single-cell resolution both in vitro and in vivo in breast cancer. Our goal is to reveal the timing of occurrence of chromatin alterations, address their stability over time, and their association to the cellular phenotype.

Deregulation of epigenetic mechanisms often occurs in cancer, with recurrent mutations of epigenetic players or massive redistribution of epigenetic marks throughout the cancer cell genome. Given the dynamic nature of epigenetic changes, epigenome rewiring might give cancer cells the opportunity to delineate a rapidly evolving malignant transcriptional program, more plastic than through the acquisition of genetic events. Upon cancer treatment, this inherent plasticity may allow epigenetic alterations to be easily acquired and play a key role in the emergence of resistant phenotypes. Yet the contribution of epigenetic plasticity to the biology of cancer cells remains unclear, and means to target it rather unspecific and inefficient, due to the lack of in vivo datasets and relevant cellular models that would be able to capture the dynamic nature of epigenetic alterations.

The research projects we are leading in the group aim at grasping the dynamics of epigenetic deregulation in cancer cells during **two time frames in triple-negative breast cancer**:
Response to chemotherapy and resistance to treatment, using patient-derived xenografts and patient samples

Tumor progression, using mouse models of breast tumorigenesis and patient samples

For both time frames, we combine tailored integrative data-mining approaches for the identification of key chromatin features and the design of a unique image-based single-cell monitoring tool to move towards the targeted reversal of these key epigenetic traits thanks to high-throughput drug and CRISPR screens. We want to grasp the dynamics of chromatin deregulation during tumor progression and the acquisition of resistance to cancer treatment. Our aims are:

- to reveal the timing of occurrence of epigenetic alterations,
- address their stability over time,
- relate them to the cellular and clinical phenotype, especially resistance to treatment
- identify compounds with epigenetic remodeling potential

The team is focusing on the study of breast cancer, considering its high incidence (it is the most common cancer in women worldwide, 1.7 million new cases are diagnosed each year, representing 25% of all female cancers) and the frequent occurrence of epigenetic remodeling events in this tumor type. Thanks to collaborations with other groups at Institut Curie, we are working with a wide panel of models: breast cancer cell lines, patient-derived animal xenografts (PDX), tumor samples and mouse model of breast cancer.

The specificity of our team relies on how it works at the interface between translational and basic science. We have been selected as one of the four labelled SiRIC groups (Site de Recherche Intégrée contre le Cancer) of the Institut Curie precisely because we ask fundamental biological questions with direct clinical perspectives. We want to understand how and when long-range epigenetic alterations occur in breast cancer, and whether they are stably maintained in tumor progression, to elucidate whether they can be considered as reliable therapeutic targets. Moreover, we have a deep interest in performing drug screening to identify FDA-approved compounds that could have effect on the tumor epigenome.

Another key aspect in the group is to have in-house extensive expertise in both data mining and biology. We are developing intensive bioinformatics and statistics analyses to achieve proper understanding and modeling of our working models.

The team is a SiRIC group (Site de Recherche Intégrée sur le Cancer) and is supported by the ATIP-Avenir program and an ERC Starting Grant. We are looking for Postdocs and M2 students trained in biology and/or bioinformatics & statistics.

France Culture: program “la Méthode Scientifique” 2021
Céline Vallot – Epimédicaments

CNRS: Movie about the lab for the CNRS Bronze Medal 2018
Céline Vallot – Bronze Medal CNRS 2018
Dynamics of epigenetic plasticity in cancer
UMR3244 – Dynamics of Genetic Information

France Culture: program “la Méthode Scientifique” 2017
Céline Vallot- Epigénétique reportage

Our data analyses pipelines
Vallot Lab Github repository

Key publications

Year of publication 2021

Marsolier, Justine Prompsy, Pacôme Durand, Adeline Lyne, Anne-Marie Landragin, Camille Trouchet, Amandine Bento, Sabrina Tenreira Eisele, Almut Foulon, Sophie Baudre, Léa Grosselin, Kevin Bohec, Mylène Baulande, Sylvain Dahmani, Ahmed Sourd, Laura Letouzé, Eric Marangoni, Elisabetta Perié, Leïla Vallot, Céline (2021 Jan 4)
**H3K27me3 is a determinant of chemotolerance in triple-negative breast cancer**
bioRxiv: DOI: 10.1101/2021.01.04.423386

Year of publication 2020

Pacôme Prompsy, Pia Kirchmeier, Justine Marsolier, Marc Deloger, Nicolas Servant, Céline Vallot (2020 Nov 12)
**Interactive analysis of single-cell epigenomic landscapes with ChromSCape.**
Nature communications: 5702: DOI: 10.1038/s41467-020-19542-x

**Tuning parameters of dimensionality reduction methods for single-cell RNA-seq analysis.**

Year of publication 2019

Kevin Grosselin, Adeline Durand, Justine Marsolier, Adeline Poitou, Elisabetta Marangoni, Fariba

**High-throughput single-cell ChIP-seq identifies heterogeneity of chromatin states in breast cancer**

*Nature Genetics* : 51 : 1060-1066 : [DOI : 10.1038/s41588-019-0424-9](https://doi.org/10.1038/s41588-019-0424-9)

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Céline Vallot, Catherine Patrat, Amanda J Collier, Christophe Huret, Miguel Casanova, Tharvesh M Liyakat Ali, Matteo Tosolini, Nelly Frydman, Edith Heard, Peter J Rugg-Gunn, Claire Rougeulle (2017 Jan 5)

**XACT Noncoding RNA Competes with XIST in the Control of X Chromosome Activity during Human Early Development.**

*Cell stem cell* : 102-111 : [DOI : 10.1016/j.stem.2016.10.014](https://doi.org/10.1016/j.stem.2016.10.014)

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Céline Vallot, Jean-François Ouimette, Mélanie Makhlouf, Olivier Féraud, Julien Pontis, Julien Côme, Cécile Martinat, Annelise Bennaceur-Griscelli, Marc Lalande, Claire Rougeulle (2015 Apr 30)

**Erosion of X Chromosome Inactivation in Human Pluripotent Cells Initiates with XACT Coating and Depends on a Specific Heterochromatin Landscape.**

*Cell stem cell* : 533-46 : [DOI : 10.1016/j.stem.2015.03.016](https://doi.org/10.1016/j.stem.2015.03.016)