



# Postdoctoral position: Characterization and functional validation of epigenetic changes implicated in the response to breast cancer immunotherapy

## Description of the project

Breast Cancer (BC) is the first cause of cancer-related death in women worldwide. Breast cancer is classified into well recognized molecular subtypes. Despite solid pre-clinical evidence, only some patients benefit from administering drug combinations, an indication that patient and tumor heterogeneity is still present in the current stratification. Out of the numerous possible combinations of approved drugs, only a few have been actually tried, and the choice of tested combinations has been to some degree arbitrary. The EU H2020 funded project RESCUER (Resistance under combinatorial treatment in ER+ and ER- breast cancer) seeks to develop new approaches and identify mechanisms of treatment resistance at systems level, exploring how the effectiveness of specific targeted therapies applied in different clinical trials is affected by patient- and tumor-specific conditions. For this purpose, the project will gather and integrate multidimensional data from ongoing clinical trials to discover molecular signatures of resistance and predict patient response to combinatorial therapies. The overarching goal is to develop computer “xenograft model” as a cost-efficient and better alternative in terms of ethics, availability to everyone, and animal use.

In the framework of the RESCUER project, the Laboratory for Epigenetics and Environment of the CEA – CNRGH will identify and functionally validate epigenetic changes in tumor-relevant immune cell populations correlating and potentially predicting treatment response in breast cancer patients in current cancer immunotherapy trials.

The work performed by the successful candidate will consist of 1) isolating tumor relevant immune cell populations from circulating or tumor infiltrating lymphocytes from patients included in clinical trials for breast cancer (mainly immunotherapy) with a differing response; 2) expand these populations by short term cell culture and characterize them at multiple molecular levels (RNA, miRNA, chromatin accessibility, histone modifications) to identify molecular changes correlating with and potentially predicting treatment response; and 3) validate the functional relevance of the observed changes as well as

promising leads identified by other members of consortium using transfection and perturbation experiments in the cultured primary cells as well as in tumor explants.

## Description of the host laboratory

The Laboratory for Epigenetics and Environment (LEE), headed by Jörg Tost, focuses on the development and application of technologies to analyze DNA methylation, smallRNAs and other epigenetic modifications at high resolution at target loci and genome-wide as well as the development of bioinformatic tools for the processing of such data. The main focus of the LEE has been the analysis of epigenetic modifications and associated functional assays of immune cells implicated in complex diseases including cancer and inflammatory and autoimmune and diseases. The laboratory has over the last ten years produced more than 150 scientific publications. The National Center of Human Genomics Research (CNRGH), of which the LEE is part, is a department of the François Jacob Institute of Biology (IBFJ) within the Fundamental Research Division (DRF) of the CEA. The CNRGH's main objective is to advance research of the genetics/genomics of human diseases. The National Center for Research on Human Genomics, is extensively equipped for genomic studies and among the top 3 European sequencing facilities with a platform of high and medium throughput Illumina sequencers as well as a Chromium platform (10X Genomics) allowing easily to generate a large variety of sequencing data. Data analysis can be done at the CNRGH that is fully equipped to cope with big data. The CNRGH has three fully equipped state-of-the art safety level 2 laboratories for culture and transfection of cell lines and primary cells as well as for the handling of human blood samples. For cell sorting two cell sorters are available: 1) a BD Bioscience MELODY equipped with two lasers allowing to isolate a single cell population at a time and 2) a Beckman Coulter MOFLO Astrios with 5 lasers and 17 filters allowing parallel sorting of up to six cell populations based on up to 16 parameters.

## Expected profile of the candidate

The candidate must have a PhD in immunology, molecular biology or cellular biology. The candidate should have a solid background in immunology and experience in the use of flow cytometry-based cell sorting and cell culture of primary human cells. Knowledge on genomic technologies such as NGS including library preparation as well as some competence in analyzing data from NGS experiments is a strong asset. The candidate should have good communication skills and be fluent in English to interact with the other partners of the European consortium participating in the described tasks, have good reporting capabilities and be motivated to learn and implement new cutting-edge technologies in partner laboratories (e.g. culture, treatment and analysis of tumor explants).

**Type of Contract:** CDD 36 months, potentially renewable up to total of 48 months

**Salary:** according to experience and qualifications

**Localization:** Evry, France

**Start date:** October/November 2021

Please send your CV and a cover letter with references to [tost@cnrgh.fr](mailto:tost@cnrgh.fr)