**BREAST CANCER CLINICAL RESEARCH UNIT**

**Clinical Research Unit Head**  
Miguel Quintana-Fandino

**Research Scientists**  
María José Bueno, Leonardo Garma (since April), Silvana A. Mouron

**Clinical Research Fellows**  
Desiree Jimenez (since February)

**Post-Doctoral Fellows**  
Rebeca G. Jimeno (until March), Ana M. Roncero

**Clinical Research Fellow**  
José Luis Ruiz (until November)

**Students in Practice**  
Pien Debets (until August) (Master’s Thesis, University of Amsterdam, The Netherlands), William Murray (March-June) (Universidad Carlos III, Madrid, Spain)

**Technicians**  
Verónica Jiménez, Manuel Muñoz, Ángela Sánchez (since February) (TS) *  
*Titulado Superior (Advanced Degree)

**Visiting Scientists**  
Andrea Gutiérrez (until November) (Hospital Universitario de Fuenlabrada, Madrid, Spain), Rocío Moreno (Hospital Universitario 12 de Octubre, Madrid, Spain), Berta Nassarre (Peaches Biotech, Madrid, Spain), Mai Tolba (February-May) (Science by Women Programme)

---

**OVERVIEW**

The Breast Cancer Clinical Research Unit (BCCRU) focuses on the translational interface of therapeutic development. Breast cancer is a heterogeneous disease and, thus, there are large inter-patient variations in terms of disease course, prognosis, relapse, and resistance to conventional or targeted therapeutics. Our activities are directed towards personalised treatment and range from preclinical models to correlative studies and clinical trials.

Our current research areas are to:

- Study the implications of hypoxia for immunotherapies.
- Understand the individual factors regulating response to immunotherapy in breast cancer, taking advantage of an advanced, personalised “tumouroid” platform.
- Tackle mechanisms of resistance against novel therapies in advanced breast cancer.
- Incorporate our findings into concept-driven clinical trials.
- Develop the new discipline of High-Definition Oncology.

“At the Breast Cancer Clinical Research Unit, we are focused on individualising therapy for patients with advanced breast cancer.”
In 2023, we started a new major line of research – High-Definition Oncology. Currently, precision oncology is largely based on genomics and performs poorly outside the context of matching targeted agents with oncogene addiction driving alterations. Outside this context, next-generation sequencing (NGS) panels are able to provide a solution in less than 10% of the cases. The problem is that many factors explain interpatient heterogeneity beyond genomics. These factors include, for example, the patient's exoposome (explained by factors such as diet or the environment), and translated into changes in the plasma metabolome), microbiome; plasma proteome; individual germline genetic variations that drive different pharmacodynamic or pharmacokinetic traits; co-morbidities or concurrent medications; and habits, mood or cognitive factors, among others. In addition, current medical approaches are based on single-point observations or probing at distant points in time, obtaining only snapshots of what it is in reality a disease trajectory. To take into account these factors, we launched a project consisting of longitudinal omic sampling, combined with electronic data capture from medical records and continuous physiological monitoring via a smartphone, and habits of life tracking through an application built ad hoc and installed on the patients' smartphones. The ultimate goals of this grant–supported research are to (1) establish and understand female patients' disease trajectories in advanced breast, lung or colorectal cancer; and (2) build a prototype of a cancer “Patient Digital Twin”.

Still in the area of precision medicine, we published a high-impact manuscript regarding the real-world impact of NGS panels in oncology. Among all common situations in which clinicians order NGS panels, only a few have demonstrated clinical utility. Advanced tumours in which several targets need to be determined, such as lung, melanoma or colorectal cancer; rare cancers; patients screened for clinical trials; or exceptional responders. In most other situations, NGS panels are simply not justified. (B) Kaplan-Meier curves showing the progression-free survival of patients in which an NGS panel was ordered in the indicated categories (blue chart) versus patients in which this panel was ordered in other situations (green).

Another area of relevance within the field of treatment personalisation is the role of diet as an adjunct treatment in cancer management. Traditionally, cancer nutrition has focused only on cancer cachexia or other tangential aspects such as anorexia or dysphagia. However, in recent years, robust evidence (at various preclinical and clinical levels) has been generated about how specific metabolic modulations can actually have therapeutic effect in cancer. Because of cancer mutations, tumours harbour metabolic alterations that render nutrients essential for the tumour but disposable for healthy cells; additionally, some nutrients can specifically damage the tumour and be innocuous to healthy cells. We have created an algorithm that takes into account the tumour type, treatment type, known mutations, co-morbidity, certain microbiota parameters, and even patient dietary preferences, and that is able to deliver a unique set of dietary patterns for each patient. Through the translation of these patterns into a specific diet, we can deliver therapeutic nutrition to each cancer patient. This diet is based on the premise that cancer cells are different from healthy cells: they actually have therapeutic effect in cancer. Because of cancer mutations, tumours harbour metabolic alterations that render nutrients essential for the tumour but disposable for healthy cells; additionally, some nutrients can specifically damage the tumour and be innocuous to healthy cells. We have created an algorithm that takes into account the tumour type, treatment type, known mutations, co-morbidity, certain

**PUBLICATIONS**


