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. Specifically, our research areas cover the:

- Study of the mechanisms of resistance against CDK inhibitors.
- Role of FGFRI in cancer progression and therapeutic resistance in hormone-positive cancer.
- Study of the implications of hypoxia in response to immunotherapy.

“We have provided clinical proof-of-concept of the synergy between antiangiogenics and mitochondrial inhibitors in breast cancer, which we previously described in animal models.”

RESEARCH HIGHLIGHTS

The following highlights some of the achievements of the Breast Cancer Clinical Research Unit during 2020:

- We demonstrated that PD-L1 inhibitors in combination with antiangiogenics in advanced breast cancer restrict their activity to those cases in which antiangiogenics normalise tumour hypoxia and vasculature.
- We confirmed our preclinical findings regarding acquired resistance against antiangiogenics: in those cases where antiangiogenics normalise tumour hypoxia and vasculature, a targetable mitochondrial switch takes place. Consequently, mito-inhibitors were found to synergise with antiangiogenics. We confirmed the findings in a clinical trial in early breast cancer.
- In parallel, in the preclinical setting, we are solving the mechanism of escape against antiangiogenics that increases vascular abnormality and tumour hypoxia. Preliminary data suggested that hypoxic areas are excluded from the antitumor immune response. Diverse therapeutic avenues are being explored to induce immune re-infiltration in hypoxic areas.
- We characterised FGFRI as a driver of acquired resistance to combined treatment with hormonal and CDK inhibitors. We found that in FGFRI-amplified or overexpressed tumour models, the triple combination of FGFRI, CDK4/6 and RR blockade is the only one able to completely suppress RB phosphorylation.
- Completion of the first phosphoproteomic screening in a randomised clinical trial in early breast cancer treated with paclitaxel monotherapy revealed that elevated P70S6K phosphorylation.
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