In the field of functional taxonomy, we have completed our study in triple-negative breast cancer. We have interrogated the disease from the bimodal relapse pattern point of view, and performed a phosphoproteomic screening that would reduce the countless patterns of genomic, epigenomic and transcriptomic aberrations into a discrete number of patterns of hardwired signalling pathways. We found 6 kinases whose hyperactivity accounted for 94% of the relapsed cases. These kinases were grouped into a maximum number of 34 patterns, the largest of which (25%) was virtually associated with cure. This taxonomy was also useful because all the kinases in the final ‘relapse signature’ were also targetable.

Regarding the study of targeted therapies, we have observed that the generally assumed hypothesis of vascular normalisation upon exposure to antiangiogenics is not always true. In fact, resistance against antiangiogenics can originate after a vascular normalising or ‘abnormalising’ response. Whether a tumour experiences the former or the latter depends on the tumour type and the type of agent. What is quite important from the clinical point of view is that we can track, individually, whether a tumour experiences a normalising or an abnormalising response after less than 2 weeks of exposure to the agent, using a non-invasive imaging test with 18F-fluoromisonidazole. This has been demonstrated in animals and in patients. The applicability of this finding lies in the fact that we have also unravelled the mechanisms of resistance depending on whether the tumour reacts with normalisation or abnormalisation against antiangiogenics; in the first case, the tumour switches from glycolytic to mitochondrial metabolism, which is reversible by mitochondrial inhibitors. In the latter, the tumour experiences an immune-switch. Since both mechanisms are targetable, we can now individually track which pathway a tumour is undergoing upon exposure to antiangiogenics and tailor which synergistic agent that patient would need.

RESEARCH HIGHLIGHTS

In 2016, the Breast Cancer Group has tackled the mechanisms of resistance against antiangiogenics, implementing these findings into clinical trials.

- **Publications**

- **Awards and recognition**
  - 2016 AstraZeneca Award for Young Investigators, Spain.