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## Phosphoproteomic screening for biomarkers and novel targets finding in early breast cancer

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Breast cancer is a heterogeneous entity. The different changes in the genetic code, gene expression levels and micro-environmental perturbations converge into certain degrees of hyper- or hypo-activation of the kinome. The kinome and the phosphoproteins are the effector layers of regulation of the tumor phenotype. We hypothesized that a phosphoprotein based interrogation of certain phenotypes (i.e., aggressive vs. indolent cases, resistant vs. sensitive to a given drug etc) could generate taxonomic clusters in a similar way as gene expression or other high-throughput tools do but with the unique property of pinpointing targetable nodes since there are more than 100 clinical-grade kinase inhibitors under development. Using frozen banked tissue and metal-based purification chromatography coupled with mass spectrometry we have profiled a set of triple-negative breast cancer cases and cell lines that has allowed us to identify a few hundreds of phosphopeptides that discriminate the good from the bad-prognosis cases. By linear-motif domain consensus sequence prediction we have identified the driving kinases of the aggressive and indolent cases. Currently we are testing the therapeutic value in preclinical models of the 5 top kinase hits predicted by this approach with promising results. In addition, we have used a similar approach to study the acquired resistance against a multikinase anti angiogenic agent, nintedanib in preclinical models and 130 patients of early breast cancer. We will present the hits and the druggable targets driving resistance in this setting identified with this approach that will converge in the design of a second-generation trial based on phosphoproteomic screening.

### Biography

Miguel Quintela-Fandino completed his MD, PhD degree in 2000 at the Universidad Complutense, Madrid. He trained as a Medical Oncologist and did a Clinical Fellowship in Drug Development in the Princess Margaret Hospital, Toronto. He then worked as a Post-doctorate Researcher under the supervision of Professor Tak Mak at the Ontario Cancer Institute. He is the Director of the Breast Cancer Program at the CNIO, Spain, since 2011. He has authored more than 20 papers in clinical and preclinical journals.

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