Intrinsic subtyping enables fine-tuned prognosis and prediction of tumor behavior

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Aleix Prat, Principal Investigator of the Vall d'Hebron Institute of Oncology's (VHIO) Translational Genomics Group, Credit: Katherin Wermke

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Leader of translational genomics and targeted therapeutics in solid tumors at the August Pi I Sunyer Biomedical Research Institute (IDIBAPS), and Head of Medical Oncology at the Hospital Clínic in Barcelona, Aleix Prat has led a study showing the intrinsic subtyping of breast cancer by means of a genomic test as the most important prognostic factor in advanced or metastatic hormone-sensitive breast cancer.

Findings show that the genomic classification of tumors—the molecular subtyping of primary tumors, can predict the evolution of patients from the onset of metastasis and that this cancer intrinsic classification can better guide treatment decisions in the first-line metastatic setting.

Up until now, prognosis and treatment of patients with metastatic hormone-sensitive breast cancer has centered on unspecific variables such as age, number or type of metastasis, and previous treatment regimens.

Aleix Prat´s research has not only associated different molecular subtypes of breast cancer with disease prognosis and prediction of response to hormone therapy, but also now evidences intrinsic subtype as the most decisive prognostic factor to date within this particular setting. This work has been possible thanks to collaboration between physician-researchers at VHIO and IDIBAPS, along with colleagues at The Royal Marsden Foundation Trust, London UK, led by renowned medical oncologist Professor Stephen Johnston.

The biological heterogeneity of hormone-sensitive breast cancer

Studies over recent years have driven the classification of hormone-sensitive breast tumors into four distinct molecular sub-types: Luminal

A, Lumina B, HER2-enriched, and Basal-like. "Our group and others have demonstrated that hormone-sensitive breast cancers represent a highly heterogeneous group based on their biological and clinical make-up", explains Aleix Prat. "To better tackle such tumoral diversity, we must continue to render the classification of tumors yet more precise to be able to more finely tune the prognosis of each individual patient as well as use intrinsic biological intelligence to better guide important treatment decisions."

Insights into intrinsic biology of metastatic breast tumors imperative

Prat and study collaborators analyzed hormone-sensitive tumors, based on currently defined molecular criteria, from 821 patients enrolled in a phase III clinical trial, who were receiving hormonal therapy for advanced disease. Research centered on classifying the tumors according to different biological subtypes based on genetic expression and linking this sub- categorization to patient survival and response.

"In terms of prognosis, we observed that the intrinsic biology of each tumor represents the most important ´body´ of knowledge known to-date. More so than even patient age, number and type of metastasis, as well as previous treatment and performance status", affirms Prat. "As an example, in tumors classified as Luminal A, metastatic spread can be controlled with hormonal therapy in approximately fifty per cent of patients for almost 1.5 years. For patients with HER2-enriched or Basal-like tumors however, these cancers become resistant to hormonal therapy within the space of four to five months. Our discovery could therefore have immediate clinical implications since, up until now, we were unable to identify which patients with metastatic breast cancer should from the outset receive chemotherapy or hormonal treatment". He concludes, "Current phase III trials with new agents enrolling

thousands of patients with metastatic breast cancer do not consider the importance of intrinsic cancer biology. I think that from here on now, current and future therapeutic strategies should be based on the established biological subtype of a given tumor as opposed to clinical characteristics per se".

Primary tumor analysis to more accurately predict tumor behavior

Another important element of this present study is that 80% of samples analyzed derived from primary tumors as opposed metastatic lesions. "The intrinsic biology of tumors seems to represent a very stable biological process. By identifying this molecular make-up in the primary tumor we can establish what will happen to a patient who will over time unfortunately suffer disease recurrence through metastatic spread." observes Prat.

Genomic analysis of primary tumor cells could therefore become an essential yet basic tool to help make critical treatment decisions and predict the evolution of disease. Further, primary tumor analysis could be tremendously useful in cases where performing a biopsy would prove complicated given the particular location of metastasis.

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