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Measuring progesterone receptor expression to improve hormone-receptor-positive cancer management

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American and Spanish researchers have found potential ways for doctors to improve the treatment of hormone receptor-positive breast cancer even if they lack access to costly multi-gene tests, as they report at the 4th IMPAKT Breast Cancer Conference.

Because breast cancer is a biologically and clinically varied disease, doctors aim to choose appropriate treatments based on the characteristics of each patient's individual tumor. In the past, this has been done using pathology-based biomarkers; however these do not capture the full diversity of cancers.

"In this context, tests based on multi-gene expression have been shown to provide valuable information beyond the pathology-based biomarkers," says Dr Aleix Prat from the University of North Carolina, Chapel Hill. "However, multi-gene tests are not readily available in most of the world due to cost, assay turnaround times and other logistic issues."

Dr Prat and colleagues addressed this problem by trying to improve the current pathology-based biomarkers to better represent data coming from a particular multi-gene test known as the PAM50 breast cancer intrinsic classifier.

"The PAM50 breast cancer intrinsic classifier identifies two major groups of hormonal receptor-positive breast cancer known as the

Luminal A and Luminal B subtypes. These two molecular entities have different risks of relapse and responses to chemotherapy," Dr Prat said.

Alongside the development of this multi-gene assay, clinicians have devised pathology-based surrogate assays for the identification of both the Luminal A and Luminal B subtypes. "In the absence of multi-gene assays, the pathology-based assays are clinically valuable," Dr Prat explained. "However, we observed that the current pathology-based definitions of the Luminal A and Luminal B subtypes still show a 30-40% discordance rate compared to multi-gene tests such as the PAM50 breast cancer intrinsic classifier."

The researchers examined differences in gene expression patterns between Luminal A and Luminal B tumors using the PAM50 test. They also collected clinical-pathological features from 2,950 primary tumors across four independent studies. Using statistical methods, they tested the independent prognostic significance of those features.

They found that the expression of progesterone receptor was one of the most discriminatory molecules. "Addition of quantitative scoring of the progesterone receptor into the current pathology-based Luminal A definition appears to better identify the subgroup of patients that have an outstanding survival when treated with endocrine therapy alone, and therefore do not need systemic chemotherapy," Dr Prat said. "This subpopulation of patients is likely to represent around 30% of the patients with low-risk pathology-defined Luminal A tumors."

"Current pathology-based definitions of the Luminal A and Luminal B subtypes are valuable, but can be improved for the management of hormonal receptor-positive breast cancer," the researcher concluded. "We believe that we have an improvement based upon the progesterone receptor, and given that progesterone receptor is widely used, our improvement could be widely and quickly adopted, if further validated."

According to Dr Di Leo, Hospital of Prato, Italy, former IMPAKT Chair, this is an important study with practical implications, because it tells us that the evaluation of the progesterone receptor along with the evaluation of other biomarkers, such as the estrogen receptor, proliferation markers and c-erbB2, may be relevant to better define the biological profile of the tumor. "This is a critical step towards a personalized medicine approach in breast cancer. It will be important to test the progesterone receptors according to a standardized approach across the pathology departments. One potential concern, in fact, could be the use of different techniques for the progesterone receptors evaluation, which might lead to discordant results between different pathology labs."

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