

## Gene expression test distinguishes btw breast cancer patients at high and low risk of late recurrence

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A test that measures the expression levels of 58 genes in oestrogen receptor-positive breast cancers can effectively differentiate between patients who are at higher and lower risk for having their cancer recur elsewhere in the body more than five years after diagnosis, researchers report.

The new findings show that better individual <u>risk prediction</u> for women with these cancers is getting nearer, says study author Prof Michael Gnant from the Medical University of Vienna, Austria.

Prof Gnant reported the findings at the 5th IMPAKT <u>Breast Cancer</u> Conference in Brussels, Belgium. The IMPAKT meeting presents cutting edge, 'translational' <u>breast cancer research</u> that is beginning to have an impact for <u>patients</u>.

Metastasis after 5 years of follow-up is an important research issue, particularly in hormone-receptor positive breast cancer, Prof Gnant explains.

"Despite all great progress we have made in the treatment of this most frequent subtype of breast cancer, some patients develop metastasis many years after their initial diagnosis. Extending adjuvant endocrine therapy to prevent this is an option, but comes with substantial sideeffects and cost for society, and should therefore be reserved for those



patients who really need it. Thus, better defining individual risk for late metastasis is an important medical and scientific need," Prof Gnant says.

The PAM50 Risk of Recurrence (ROR) score used by the researchers in this study directly measures the <u>expression levels</u> of 58 different genes (50 discriminator genes and 8 controls).

Prof Gnant and colleagues performed the PAM50 analysis on 1,478 patients who had taken part in the ABCSG-8 trial, which ran from 1996 to 2009. They found that the PAM50 ROR score provided significant prognostic information in addition to clinical factors with respect to late distant-relapse-free survival.

After 11 years of median follow-up, of patients who were classified by the test as having low risk, 98.7% had not had a late metastasis between 5 and 10 years of follow-up, compared to 91.5% of those with a high PAM50 ROR score. This was true both for node-positive and node-negative disease.

"It makes a huge difference whether a patient looks at an individual risk of 1.3% or 8.5% between years 5 and 10. This is more than six times as much risk. Such important information may well be implemented into individual treatment decisions," Prof Gnant says.

The researchers conclude that the PAM50 ROR score can successfully be used to differentiate patients with respect to their risk for late metastasis, in addition to established clinical and pathological risk factors.

This ability to predict late metastasis may be used in the future to identify patients with endocrine-responsive breast cancer who need or alternatively who can be spared extended adjuvant therapy, they say.



"We have to admit that at this point we cannot prove definitely that we will improve the outcome in patients we have now identified as high risk by extending their adjuvant therapy, but it appears logical that this may be the case. At least as important, if we can define an individual patient reliably as low risk, we can spare her the burden of unnecessary treatment extension," Prof Gnant says.

Commenting on the results, Dr W Fraser Symmans, Professor and Director of Research Operations, Department of Pathology at the University of Texas M.D. Anderson Cancer Center, USA, said they were important for prognostic testing of early breast cancers and for confidently limiting the duration of endocrine therapy to 5 years for women with low-risk disease.

"In the last 6 months it has become clear that three prognostic tests, including the PAM50 ROR score, have similar prognostic utility that holds for up to 15 years after initial diagnosis. It is particularly exciting for the diagnostic community that such newer tests could be offered by pathology laboratories, and might not require centralised testing. I look forward to seeing the results of studies that report the inter-laboratory consistency of these tests for determining the long-term prognosis for early breast cancer patients who received 5 years of adjuvant endocrine therapy," Dr Symmans said.

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