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Gene expression signatures may predict clinical outcome

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Context

Traditional pathological classification of breast tumours is based on a panel of established markers, especially hormone receptor status, axillary lymph node status and histological grade. Unfortunately these fail to accurately predict clinical outcome in some patients. As a result, many patients go on to receive unnecessary adjuvant therapy. The aim of this work was to use gene expression signatures to predict clinical outcome in a cohort of breast tumours.

Significant findings

Approximately 25,000 genes were analysed in 98 primary breast tumours, 5000 of these showed altered expression. Hierarchical cluster analysis revealed two distinct groups that were broadly classified into tumours of good or poor prognosis. Using knowledge of clinical outcome, a three-step 'supervised' cluster analysis identified genes that correctly predicted the development of metastasis. This poor prognosis signature consisted of genes regulating cell cycle, invasion, metastasis and angiogenesis. Interestingly, this was found in small primary tumours without node metastasis at presentation, suggesting these tumours are already "hard-wired" for a metastatic phenotype. To validate this, an additional cohort of 19 tumours was studied and resulted in only two incorrect classifications, indicating the predictive power of the prognosis classification.

Comments

The information from this and a related study (see Additional information [1]) show that so-called "molecular signatures" (see Additional information [2]) have the potential to allow more accurate prediction of the therapeutic requirements of breast cancer patients on an individual basis. It has long been the goal of clinicians involved in managing these patients to be able to predict disease course and to tailor therapy accordingly, thus eliminating the unnecessary adjuvant treatments that some patients have to endure. Molecular profiling offers the potential for this to become a reality.

Methods

DNA arrays, cluster analysis

Additional information

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2. Perou CM, Sorlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, Pollack JR, Ross DT, Johnsen H, Akslen LA, Fluge O, Pergamenschikov A, Williams C, Zhu SX, Lonning PE, Borresen-Dale AL, Brown PO, Botstein D: **Molecular portraits of human breast tumours.** *Nature* 2000,**406**: 747-752 ([PubMed abstract](#))

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