



A breast cancer prognostic test for enhanced clinical outcome

Information Summary

Reference code:	ROI 07033
Technology overview:	Stroma-derived gene-expression breast cancer prognostic markers
Application:	Clinical test for risk of recurrence and outcome
Validation:	Predictive power validated in independent whole tumor-derived gene expression datasets
Inventors:	Morag Park ; Michael Hallett et al.
Contact:	Giovanna Sebastiani Ph.D. 514-398-6138 Giovanna.sebastiani@mcgill.ca

Technology Description

The invention teaches that the stromal environment of cancer is pivotal to breast cancer progression. By comparing gene expression profiles from laser capture-microdissected tumor-associated to matched normal stroma, they derived transcriptional profiles strongly associated with clinical outcome. The stroma-derived prognostic predictor (SDPP) identifies a hypoxic and angiogenic transcriptional response associated with poor outcome (non-responsiveness to chemotherapy), and the recruitment of, immune response, NK and activated T cells associated with good outcome (no tumor metastasis and migration).

Advantages

- **New information to stratify breast cancer; predicts recurrence and clinical outcome independently of other prognostic factors** - The test is independent of ER and HER2 status, lymph node involvement, grade, age, chemotherapy and hormonal therapy as well as other expression based predictors.
- **Increased accuracy compared to other available tests** - The SDPP shows increased accuracy compared to the FDA approved 70-gene predictor MammaPrint, the wound response, hypoxia and SFT/DTF signatures. Furthermore

combining the SDPP with these predictors leads to further improvement of prognosis value.

- **Better prognostic value in multiple clinical subtypes including lymph node negative patients** – The test was validated in whole-tumor derived gene expression datasets including the Rotterdam set that included only node negative patients. Therefore the test is predictive of outcome before detectable lymph node involvement.
- **Potential for prognosis in HER2 positive patients** – Using the same cohort on which MammaPrint was developed, the SDPP was 5.96 times more likely to identify a 'true' poor outcome patient with HER2 positive breast cancer than MammaPrint.
- **Ease of integration into current clinical practice** – The minimal size, maximal accuracy SDPP is based on the expression of only 26 genes and therefore can be easily adapted for use on the Formalin Fixed Paraffin Embedded tissue routinely used in clinical pathology.

Medical Need and Opportunity

Breast cancer is a complex disease and represents a significant cost to healthcare systems worldwide. Breast cancer already benefits from the development of new clinical diagnostic tests for early diagnosis, proper therapeutic decision making and overall reduction in health care cost through a more personalized management of the disease. Biomarkers such as hormone receptor status and the HER-2 receptor are currently used to support treatment decisions. However, it is clear that additional biomarkers are required for better stratification of patients, and improving the selection of appropriate treatment. There is currently no assay available to further stratify the 20 to 30% HER2-positive patient subset. These patients are at increased risk of invasive cancer and often have poor clinical outcome. The SDPP can enhance the ability of clinicians to better stratify patients for systemic adjuvant therapy, reducing both morbidity and expense due to over-treatment and unnecessary mortality occasioned by under-treatment

Additional reference material

Finak, G. et al, 2008, Nature Medicine 14: 518