



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
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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



Dr. Morag Park

BSc Glasgow University 1978

PhD Glasgow University 1983

**James McGill Professor, Dept. of Oncology, Biochemistry and
Medicine**

Director, Molecular Oncology Group MUHC

Research Interests

Increasing evidence supports the concept that the malignant behavior of some tumors is sustained by the deregulated activation of growth factor receptors. Although much is known about the signal transduction pathways that are activated following acute stimulation of cells by growth factors, little is known about the steady state balance achieved by each signal in tumor cells following receptor deregulation, and the consequence of this for tumor formation and metastasis.

My interests focus on the molecular mechanisms of oncogenic activation of receptor tyrosine kinases and mechanisms for cell transformation. We and others have demonstrated that the activity of the hepatocyte growth factor (HGF) receptor is frequently altered in human cancer. We have proposed new models for its oncogenic activation. Our research goals aim at identify the critical molecular signals regulated by the HGF/SF receptor and receptor tyrosine kinases in general, that contribute to tumor progression, and are suitable targets for therapeutic intervention. For these aims we have developed epithelial, fibroblastic and mouse models to study signals that (i) are required for epithelial morphogenesis and (ii) promote the breakdown of organized epithelial structures, anchorage independent growth, tumorigenesis and invasion.

<http://www.mcgill.ca/mog/research/park/>



Dr. Michael Hallett

PhD, University of Victoria, 1996

**Associate Professor, School of Computer Science and McGill Center for
Bioinformatics**

Associate Member, Department of Biochemistry

Research Interests

My group mainly uses tools from statistical inference and algorithm design to address problems arising in biological and medical research. My research currently focuses on Breast Cancer (with W. Muller, M. Park, P. Siegel, Molecular Oncology), the Endoplasmic Reticulum interactome (with D. Thomas, E. Chevet, K. Gehring, J. Bergeron, Biochemistry/Cell Biology), and Cystic/Pulmonary Fibrosis (with C. Haston, Medicine). Each of these projects contains many interesting statistical and computational problems and solid, pragmatic solutions to these problems can have significant impact on our understanding of the underlying biology.

<http://www.mcb.mcgill.ca/~hallett/>



Dr Morag Park

B.Sc., Glasgow University (1978)
Ph.D., Glasgow University (1983)

Professeur James McGill

**Directeur du Département d'oncologie, de biochimie et de médecine,
Groupe d'oncologie moléculaire du CUSM**

But de la recherche

Il est de plus en plus établi que le comportement malin de certaines tumeurs est soutenu par l'activation dérégulée des récepteurs des facteurs de croissance. On connaît bien les voies de transduction du signal qui sont activées par suite d'une stimulation aiguë des cellules par les facteurs de croissance. Par contre, on connaît peu l'équilibre d'état régulier atteint par chaque signal dans les cellules tumorales après la dérégulation des récepteurs et ses conséquences sur la formation des tumeurs et les métastases.

Je m'intéresse aux mécanismes moléculaires de l'activation oncogénique des récepteurs tyrosine kinases et aux mécanismes de la transformation cellulaire. Nous avons établi, ainsi que d'autres chercheurs, que l'activité du récepteur du facteur de croissance hépatocytaire (HGF) est fréquemment altérée dans le cancer humain. Nous avons proposé de nouveaux modèles pour son activation oncogénique. Nos objectifs de recherche sont d'identifier les signaux moléculaires critiques régulés par le récepteur HGF/SF et les récepteurs tyrosine kinases en général, qui contribuent à la progression tumorale et constituent des cibles adéquates d'intervention thérapeutique. À ces fins, nous avons développé des modèles épithéliaux, fibroblastiques et murins pour étudier les signaux i) qui sont nécessaires à la morphogenèse épithéliale et ii) qui favorisent la dégradation des structures épithéliales organisées, la prolifération indépendante de l'ancrage, la tumorigenèse et l'invasion.

<http://www.mcgill.ca/mog/research/park/> (version anglaise seulement)



Dr Michael Hallett

Ph.D., University of Victoria (1996)

Professeur agrégé à l'École d'informatique et au Centre de Bioinformatique de McGill

Membre agrégé du Département de biochimie

But de la recherche

Mon groupe de recherche utilise principalement des outils d'inférences statistiques et de conception algorithmique pour aborder les problèmes découlant de recherches biologique et médicale. Mes travaux de recherche se concentrent actuellement sur le cancer du sein (avec W. Muller, M. Park, P. Siegel, en oncologie moléculaire), l'interactome dans le réticulum endoplasmique (avec D. Thomas, E. Chevet, K. Gehring, J. Bergeron, en biochimie/biologie cellulaire) et la fibrose kystique/pulmonaire (avec C. Haston, en médecine). Chacun de ces projets comporte de nombreux problèmes intéressants d'ordre statistique et informatique et le fait d'en arriver à des solutions sûres et pragmatiques pourrait avoir un effet considérable sur notre compréhension de la biologie sous-jacente.

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