META-ANALYSIS OF THYROID CANCER EXPRESSION PROFILING STUDIES – IDENTIFICATION OF MOST PROMISING BIOMARKERS FOR TISSUE MICROARRAY ANALYSIS

Obi L. Griffith, Sam M. Wiseman and Steven J.M. Jones

Objective and Design

It is estimated that 5-10% of the population will develop a clinically significant thyroid nodule during their lifetime. In one third or more of these patients, pre-operative diagnoses by needle biopsy are inconclusive. In many cases, a patient will undergo unnecessary surgery for what ultimately proves to be a benign lesion. Thus, there is a clear need for improved diagnostic tests to distinguish malignant from benign samples. The recent development of tissue microarray techniques should allow the rapid evaluation of potential new markers. However, researchers are faced with an overwhelming number of potential markers from numerous thyroid cancer profiling and classification studies. We present a systematic and comprehensive selection of potential thyroid cancer biomarkers from published studies by meta-analysis for use in tissue microarray analysis (TMA).

Materials & Methods

A total of 20 published studies were identified from the literature. Each study reported differentially expressed genes (potential biomarkers) for at least one comparison type (eg. Normal versus PTC). The following information was recorded wherever possible: unique identifier (probe/tag/accession), gene name, gene description, gene symbol, tissue types compared, fold change (magnitude and/or direction), p-value, validation (RT-PCR, IHC, Western), and pubmed ID. Whenever possible, the mapping of clone accession, probe id or SAGE tag was updated using NCBI mapping files, Affymetrix annotation files, and the DiscoverySpace SAGE tag mapping tool respectively. A heuristic system was devised to identify the most promising markers, taking into consideration the number of studies reporting the potential marker, sample sizes, fold-change, p-value, and the type of tumour or condition for which the marker may be relevant.

Results

In total, 1,545 potential biomarkers were identified (not considering overlap) from 20 gene expression studies considering 27 different tumour or tissue type comparisons. This resource allows the identification of markers that consistently differentiate one tumour/tissue type (e.g. papillary thyroid cancer) from others (e.g. normal, benign, other thyroid cancer subtypes). From this analysis, an informed selection of markers will be made for tissue microarray analysis, optimizing the chance of finding clinically relevant markers.

Conclusion

Bioinformatics meta-analysis and tissue microarray analysis represents a powerful approach to identifying new thyroid cancer biomarkers. Such markers could prove invaluable for the diagnosis and prognosis of tumours in the clinical setting. The meta-analysis of published thyroid studies should prove a useful resource for many thyroid cancer researchers.

Contact Information:
Presenting Author:
Obi L. Griffith
Genome Sciences Centre, BC Cancer Agency
Suite 100 - 570 West 7th Ave, Vancouver, BC, V5Z 4S6
Phone: 604-707-5900 x.5401, Fax: 604-876-3561
Email: obig@bcgsc.ca

Sponsor:
Dr. Steven J.M. Jones
Genome Sciences Centre, BC Cancer Agency
Suite 100 - 570 West 7th Ave, Vancouver, BC, V5Z 4S6
Phone: 604-877-6083, Fax: 604-876-3561
Email: sjones@bcgsc.ca