Increasing the Number of Thyroid Lesions Classes in Microarray Analysis Improves the Relevance of Diagnostic Markers

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Increasing the Number of Thyroid Lesions Classes in Microarray Analysis Improves the Relevance of Diagnostic Markers

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Background
Genetic markers for thyroid cancers identified by microarray analysis have offered limited predictive accuracy so far because of the few classes of thyroid lesions usually taken into account. To improve diagnostic relevance, we have simultaneously analyzed microarray data from six public datasets covering a total of 347 thyroid tissue samples representing 12 histological classes of follicular lesions and normal thyroid tissue. Our own dataset, containing about half the thyroid tissue samples, included all categories of thyroid lesions. Methodology/Principal Findings Classifier predictions were strongly affected by similarities between classes and by the number of classes in the training sets. In each dataset, sample prediction was improved by separating the samples into three groups according to class similarities. The cross-validation of differential genes revealed four clusters with functional enrichments. The analysis of six of these genes (APOD, APOE, CLGN, CRABP1, SDHA and TIMP1) in 49 new samples showed consistent gene and protein profiles with the class similarities observed. Focusing on four subclasses of follicular tumor, we explored the diagnostic potential of 12 selected markers (CASP10, CDH16, CLGN, CRABP1, HMGB2, ALPL2, ADAMTS2, CABIN1, ALDH1A3, USP13, NR2F2, KRTHB5) by real-time quantitative RT-PCR on 32 other new samples. The gene expression profiles of follicular tumors were examined with reference to the mutational status of the Pax8-PPARγ, TSHR, GNAS and NRAS genes. Conclusion/Significance We show that diagnostic tools defined on the basis of microarray data are more relevant when a large number of samples and tissue classes are used. Taking into account the relationships between the thyroid tumor pathologies, together with the main biological functions and pathways involved, improved the diagnostic accuracy of the samples. Our approach was particularly relevant for the classification of microfollicular adenomas.
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