EXPRESSION PROFILING OF HUMAN TUMORS pdf

1: Expression Profiling of Human Tumors: Diagnostic and Research Applications | Cancer Forum

A comprehensive review of the use of global gene expression profiling to understand human tumors. The authors focus on the analysis of human tissue samples for a variety of cancers, including breast, colorectal, lung, renal, ovarian, bone, and brain tumors, among others.

Expression Profiling of Human Tumors: Diagnostic and Research Applications Details: This is perhaps not surprising, for this approach lies at the intersection of three of the greatest technological advances of the late 21st century, namely molecular biology, robotics and bioinformatics. The fact that gene expression analysis emerged at a time when the hyperbole surrounding the human genome project was at its peak, also served to propel this nascent technology into the scientific limelight. Now, four to five years after the fruits of this technology were first reported in the scientific literature, it is timely that the process be reappraised. Expression Profiling of Human Tumours: Diagnostic and Research Applications, edited by Marc Ladanyi and William Gerald, is a page hardcover monograph which provides a clear and timely introduction to the promise and pitfalls of gene expression analysis in cancer. Each of these approaches is discussed in a separate chapter, in a readable and balanced manner. While inevitably there is some repetition and redundancy because of the multi-author approach of the book, these introductory chapters are commendable in that they provide a realistic appraisal of both the strengths and weaknesses of the technologies described. They are also clearly written with the non-scientist in mind, and as much as is possible in this complex area, they provide a description of the techniques that is accessible to most health professionals or other interested readers. The section on general technology is itself prefaced by a short introductory chapter by the editors, which provides a highly readable and refreshingly candid appraisal of the benefits that this technology may bring to our understanding of the problem of human cancer. Part one is rounded out by chapters on technologies that are complementary to the process of gene expression analysis, namely bioinformatics, tissue banking and the construction and use of tissue microarrays. Again these chapters are well written and would be of interest to a wide readership. In the second part of the monograph, individual chapters are devoted to a review of progress to-date using gene expression arrays in the setting of specific human cancers. Given the rapid pace of change, these chapters are likely to become redundant in a relatively short time, but they do provide insights into how the techniques have been used to address key questions in specific cancers. They also provide an excellent summary of both the current status of work, and the particular problems that arise in specific diseases. As such, these chapters would be of great interest to individuals currently involved in, or considering the initiation of, research in a particular form of malignancy. Overall, this is a concise, current, well-written and well-edited book. It provides a succinct description of the core technology of gene expression analysis, and a realistic appraisal of its strengths and weaknesses. It is a book that would appeal to a relatively wide range of readers, including clinical oncologists, pathologists, and other healthcare professionals with an interest in cancer and cancer genetics. It would also be of interest to scientists active in the area of cancer, since it provides a comprehensive overview of this challenging area, as well as an authoritative review of achievements to-date in a wide range of human malignancies.

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2: Gene expression profiling in cancer - Wikipedia

Expression profiling provides a supraexponential increase to the amount of gene expression data available on a given tumor, but lacks the topographical information of immunohistochemistry. Nonetheless, it is widely believed that the latter shortcoming will be more than compensated by the sheer multiplicity of the gene expression data.

Advanced Search Abstract Objective: We sought to investigate the expression patterns of miRNA in all major types of thyroid tumors, including tumors carrying distinct oncogenic mutations, and to explore the utility of miRNA profiling for the preoperative diagnosis of thyroid nodules. All tumors were genotyped for most common mutations. Various histopathological types of thyroid tumors, including those deriving from the same cell type, showed significantly different profiles of miRNA expression. Oncocytic tumors, conventional follicular tumors, papillary carcinomas, and medullary carcinomas formed distinct clusters on the unsupervised hierarchical clustering analysis. Significant correlation between miRNA expression patterns and somatic mutations was observed in papillary carcinomas. In this study, we demonstrate that various histopathological types of thyroid tumors have distinct miRNA profiles, which further differ within the same tumor type, reflecting specific oncogenic mutations. A limited set of miRNAs can be used diagnostically with high accuracy to detect thyroid cancer in the surgical and preoperative FNA samples. Specific subsets of overexpressed or down-regulated miRNAs have been identified in various cancer types, suggesting that aberrations in miRNA expression may be important in tumor development and progression 6 â€” 8. Many miRNAs are expressed in a tissue-specific manner and exhibit expression profiles that are different between normal and neoplastic tissues and between tumors with distinct biological properties 6 , 9 , Some data suggest that miRNA profiles allow reliable identification of the cell origin of tumors 11 , In this regard, thyroid cancer represents an attractive model to study because it encompasses several histopathological tumor types originating from the same cell and tumors with distinct levels of differentiation. Most thyroid carcinomas originate from thyroid follicular cells and are subdivided into well-differentiated papillary carcinoma PC and follicular carcinoma FC the latter further subclassified into conventional and oncocytic type Follicular adenomas FAs are benign thyroid tumors and can be of either conventional type or oncocytic type. Although several recent studies have assessed the miRNA expression profiles in specific types of thyroid cancer 14 â€” 17 , miRNA expression signatures of all major types of thyroid neoplasms have not been analyzed and compared in a single study to our knowledge. Significant information has been accumulated on carcinogenic mutations in thyroid cancer It is not known, however, whether miRNA expression profiles are different among tumors carrying specific oncogenic mutations. One of the main diagnostic problems in the thyroid field involves the preoperative assessment of thyroid nodules. Some improvement in the diagnostic accuracy can be achieved by additional testing of the FNA material for somatic mutations known to occur in thyroid tumors 23 , 24 , although its sensitivity is limited because a significant proportion of PCs and FCs do not have any known mutations. Therefore, additional methods to improve the preoperative diagnosis are highly desirable and would result in a major impact on the clinical care. In this study, we 1 determined and compared miRNA expression profiles of all major types of thyroid tumors, 2 explored the correlation between miRNA expression patterns and specific oncogenic mutations, and 3 determined the diagnostic utility of the detection of specific miRNAs in the preoperative assessment of thyroid nodules. Materials and Methods Thyroid tissue samples Snap-frozen tissue from surgically removed thyroid samples was collected at the Department of Pathology, University of Cincinnati following the University of Cincinnati Institutional Review Board approval or obtained through the Cooperative Human Tissue Network. The age of patients ranged from 21â€”79 yr, and the female to male ratio was 3. All tumors were classified according to the widely accepted diagnostic histological criteria RNA samples that did not show intact 18S and 28S ribosomal bands were excluded from the study. One tumor sample PTC30 was assayed twice to test the reproducibility of the detection. A good correlation 0. Two endogenous controls were used for the normalization of RNA input: To evaluate the appropriateness of these endogenous controls for use in thyroid tissue, their expression levels were determined in 16 random thyroid tumor and normal samples. All samples demonstrated low variability in

the expression levels of let7a and RNU44, validating their use as normalization controls. Two nonhuman miRNAs, ath-mira and cek-lin-4, were used as negative controls. The data are presented as the fold change of miRNA expression in tumors relative to normal thyroid tissues after normalization to an endogenous control let7-a or RNU Statistical analysis Agglomerative hierarchical clustering between thyroid specimens was performed in R software. The purpose of the filtering was to remove miRNAs with no detectable expression across all thyroid specimens that may introduce noise to the clustering. A subset of 59 miRNAs remained after filtering and was used for hierarchical clustering. The software integrates selection of predictive miRNAs while constructing the prediction model and performs fold cross-validation. Linear discriminant analysis was used for the class prediction of the set of individual miRNAs without feature selection. Principal component analysis PCA was applied to provide an unsupervised visualization and investigation of the relationship between miRNA expression and mutation type. For each pair of mutation-specific groups, PCA was performed to project the samples to the first principal component, and a simple t test was applied to test for significance of separation between the two groups. Expression of miRNAs in various types of thyroid tumors To determine whether different histopathological types of thyroid tumors have distinct miRNA profiles, the unsupervised hierarchical clustering analysis of miRNA expression was performed. It revealed four major clusters: The first three clusters were located closer to each other, whereas the MC cluster was at the greatest distance, consistent with their different cell type origins, i. The oncocytic tumor cluster was most segregated of the three follicular cell-derived tumor clusters. Less differentiated tumors PDCs and ACs did not form distinct clusters and were situated either close or within the papillary or follicular clusters or separately, supporting their origin from the well-differentiated PCs and FCs and their propensity for profound dedifferentiation. Cluster dendrogram of miRNA expression of thyroid tumors showing four major clusters: View large Download slide Cluster dendrogram of miRNA expression of thyroid tumors showing four major clusters: Next, we searched for individual miRNAs that had the highest levels of overexpression in specific tumor types. The top 10 up-regulated miRNAs in each type of malignant and benign thyroid tumor are shown in Tables 1 and 2. There was virtually no overlap in the highly expressed miRNAs between MCs and the rest of the tumors, all of which derive from thyroid follicular cells. Seven miRNAs, miR, miR, miR, miRb, miRb, miR, and miR, were most consistently overexpressed in all follicular cell-derived carcinomas, although their expression levels varied significantly between individual tumor types. Additionally, miRNA, miR, and miR were highly expressed in oncocytic follicular carcinomas. Among benign adenomas, tumors of conventional type and oncocytic type had quite distinct sets of mostly up-regulated miRNAs, with miRa being at the top of the list in conventional follicular adenomas and miR in oncocytic adenomas. Ten most up-regulated miRNAs in various thyroid tumors:

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