Gene marker identification for prognostic prediction of Acute Mieloid Leukemia (AML) from gene expression data.

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Motivation

Today many clinical feature and laboratory parameters are used for the prognosis of Acute Mieloid Leukemia (AML). Currently used prognostic indicators include age, cytogenetics, white-cell count, and the presence or absence of an antecedent hematological disorder (e.g., myelodysplasia). Among these, cytogenetics represents the most powerful prognostic factor. The karyotype can be used to classify patients as being at low (t(8;21), t(15;17), or inv(16)), intermediate (e.g., a normal karyotype or t(9;11)), or high risk (e.g., inv(3), -5/del(5q),-7, complex karyotypes). Nevertheless, there is substantial heterogeneity within these risk groups. Thirty-five to 50 percent of patients have a normal karyotype, but molecular markers such as mutations in the fms like tyrosine kinase 3 (FLT3) gene and the mixed-lineage leukemia (MLL) gene allow a stratification of this group and provide potential targets for molecular therapies. Despite the effectiveness of clinical diagnosis and risk stratification, there is no consensus on the risk group pertaining to AML patients with a normal karyotype.

Several research works demonstrated how gene expression profiles, obtained using high-throughput technologies (e.g., microarray), can represent a powerful tool for classifying hematopoietic neoplasm. With a specific regard to AML, it has been demonstrated that transcriptional fingerprints distinguish cytogenetically homogeneous groups.

Methods

In the present study we selected two public available gene expression datasets (Affymetrix and Stanford spotted arrays) from AML adult patients. Transcriptional data were correlated with survival information or the course of the pathology (alive/dead or diagnostic/relapse). We applied a meta-analysis approach and statistic tools to identify a list of genes related to prognostic prediction for those cases of AML not classifiable using the common diagnostic criteria (e.g. cytogenetics).

Results

We built a list of genes associated to poor outcome (dead or relapse) in patients with normal karyotype. This list will be validated using real-time quantitative RT-PCR on a group of AML patients available in some Italian hospitals. These results could be useful to build tools for clinic diagnosis of AML using cheaper and handier tools than microarrays (e.g. real-time quantitative RT-PCR analysis).

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