GENETICS

Gene-expression profiling in leukemia—a valuable diagnostic tool

A comprehensive data set to address whether gene-expression microarrays are capable of complementing current diagnostic algorithms (for the identification of different leukemia subtypes) has been generated by the international Microarray Innovations in Leukemia (MILE) study group. "We demonstrated that gene-expression profiling is a robust technology for the diagnosis of hematologic malignancies with high accuracy," commented joint-lead researcher Torsten Haferlach, of the Munich Leukemia Laboratory.

A combination of different methods is required to diagnose and subclassify leukemias under standard laboratory procedures. Over the past decade investigators have observed that, in hematologic malignancies, gene-expression profiling allows the characterization of distinct disease subtypes. In light of these findings, the MILE study group "sought to find a technical solution that would allow an objective, fast and operator-independent diagnostic assessment," Haferlach explains. Thus, in 2005 the MILE study group was formed and a multicenter study was initiated to assess the clinical utility of gene-expression profiling as a single test to subclassify leukemias.

The MILE study was carried out in 11 laboratories across three continents, and included 3,334 patients with leukemia. In the first stage of the study—designed for biomarker discovery—2,143 whole-genome microarray analyses were performed. Gene-expression profiles were generated from 18 clinically relevant recognized categories of leukemias and myelodysplastic syndrome (including one control category of nonleukemic and healthy bone marrow samples). Relative to the 'gold-standard' diagnosis, gene-expression profiles achieved a 92.2% classification accuracy with a median specificity of 99.7%.

The diagnostic accuracy of gene-expression profiling was further validated in a prospective second stage in an independent cohort of 1,191 patients. An 88.1% accuracy of classification prediction was observed across all 18 MILE study microarray categories, rising to 91.5% when considering just the 14 acute leukemia subgroups. A high positive prediction accuracy was achieved, particularly for those leukemias with discrete disease-defining fusion genes.

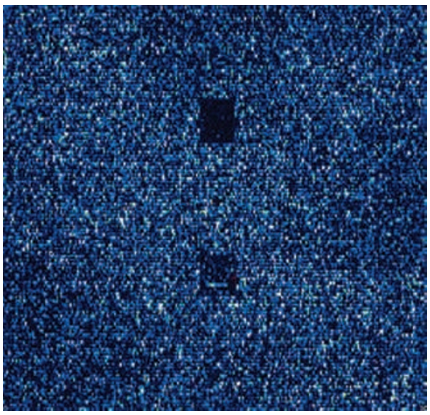

Figure courtesy of T. Haferlach and colleagues

To aid research focusing on the molecular understanding of leukemias, the investigators submitted their comprehensive gene expression data set to the public domain. Haferlach adds that "any researcher interested in the data can access it on the Gene Expression Omnibus website, accession number GSE13204".

Lisa Richards

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