Terry's Corner

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New prognostic marker

The prognostic factors of CLL are well established and include clinical stage, IgVH mutational status, CD38 expression, ZAP-70 expression (when it is done properly and well), and fluorescent in-situ hybridisation (FISH) for detecting deletions at 17p and 11q (recognising loss of either the *TP53* or the *ATM* genes). Although FISH has proved a useful substitute for chromosomal metaphase analysis (which is difficult in CLL and only successful in the very best laboratories), it is limited in its ability to detect every possible chromosomal abnormality or indeed to detect malfunctions of individual genes which might contribute to inflicting a poor prognosis on the patient. To ameliorate this deficiency the Liverpool group have developed a test to examine the function of a particularly vulnerable cellular pathway, malfunction of which leads to drug resistance and poor prognosis [1]. Although variations of this test have been exported to other expert laboratories, it has not yet enjoyed widespread adoption.

Single nucleotide polymorphism (SNP) array analysis has proved to be a sensitive and highly specific method for determining sub-chromosomal copy number losses and gains, and this techniques has been employed by workers at the University of Michigan to perform a genome-wide copy number analysis in an attempt to risk-stratify CLL patients into low- and high-risk cohorts based on their degree of genomic complexity [2]. Using a cut off of three or more genomic losses they found that genomic complexity determined by this method was an independent poor prognostic risk factor both for time to first treatment and time to subsequent treatment.

The importance of this finding is that the test can be automated and will not depend on observer competence. This disadvantage is that at present SNP arrays are very expensive, and currently most patients are not even getting the very much cheaper IgVH gene mutational analysis.

1. Lin K, Sherrington PD, Dennis M, Matrai Z, Cawley JC, Pettitt AR. Relationship between p53 dysfunction, CD38 expression, and IgV(H) mutation in chronic lymphocytic leukemia. **Blood**. 200215;100:1404-9.

2. Lisa Kujawski, Peter Ouillette, Harry Erba, Chris Saddler, Andrzej Jakubowiak, Mark Kaminski, Kerby Shedden, and Sami N Malek. Genomic complexity identifies patients with aggressive chronic lymphocytic leukemia **Blood** First Edition Paper, prepublished online April 24, 2008; DOI 10.1182/blood-2007-07-099432