with acute promyelocytic leukemia (APL) were treated with standard chemotherapy, all-trans-retinoic acid. The patients experienced remission. Assays for fusion protein transcript were conducted on bone marrow samples at regular intervals following remission. Where levels of mRNA increased, after remission, and where the remission triggered a finding of MRD, patients were further treated with pre-emptive chemotherapy to prevent subsequent clinical remission. Evidence from this study suggested that use of MRD assays, coupled with pre-emptive therapy, can reduce subsequent relapse. The data indicated that this approach to treating APL can cut in half the rate of relapse.

IX. CONFLUENCE OF CYTOGENETICS AND GENE EXPRESSION

Diagnostic, prognostic, and predictive information acquired from cytogenetics and from gene expression may or may not agree with each other. Fortunately, the confluence of these two fields, the ancient field of cytogenetics and the modern field of gene expression, has provided consistent results. The following concerns pediatric acute lymphoblastic leukemia (ALL). This disease can be classified according to whether the leukemic cell is in the B cell lineage (B-ALL) or in the T cell lineage (T-ALL) (278). Within these two classes, the ALL can be further classified according to cytogenetics, that is, abnormalities such as translocation, hyperploidy, and hypoploidy. Alternatively, or in addition, within these two classes of ALL, the disease can be classified according to gene expression. One goal of gene expression studies is to identify which genes are expressed in association with each chromosomal abnormality. Yeoh et al. (279) discovered that distinct groups of genes distinguish cases of leukemia that are B cell lineage cases of ALL, such as t(1;19)E2A-PBX1, t(9;22)BCR-ABL, and t(12;21)TEL-AML1, and MLL. The term "MLL" refers to the B cell lineage ALL where there are rearrangements in the MLL gene on chromosome 11. To provide examples of these correlations, t(1;19)E2A-PBX1 leukemias were characterized by high expression of the MERTK gene, while MLL arrangement leukemias were characterized by high expression of the HOXA9 gene and MEIS1 gene.

Gene expression data have an advantage over cytogenetics, in that they can identify ALL patients where there are no chromosomal translocations. For example, only 30% of all cases of T cell lineage ALL (T-ALL) have chromosomal translocations. Gene expression profiling of T-ALL provided an explanation for this, namely, that the oncogenes HOX11, TAL1, and LYL1 that are involved in T-ALL translocations can also be overexpressed by other mechanisms, in patients where the leukemic cells lack translocations (280).

[278] Staudt LM. It's ALL in the diagnosis. *Cancer Cell*. 2002;1:109–110.

[279] Yeoh EJ, Ross ME, Shurtleff SA, et al. Classification, subtype discovery, and prediction of outcome in pediatric acute lymphoblastic leukemia by gene expression profiling. *Cancer Cell*. 2002;1:133–143.

[280] Staudt LM. It's ALL in the diagnosis. *Cancer Cell*. 2002;1:109–110.