## 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. This concerns pediatric acute lymphoblastic leukemia (ALL). ALL can be classified according to whether the leukemic cell is in the B-cell lineage (B-ALL) or the T-cell lineage (T-ALL) (319). 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. (320) 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-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 (321).

## X. CONCLUDING REMARKS

When designing a clinical study on hematological malignancies, the investigator needs to identify methods of diagnosis, endpoints, prognostic markers that indicate risk for outcome of the disease, and predictive markers that mandate use of specific drugs. Methods of diagnosis include clinical methods, as well as blood counts, cytogenetics (chromosomal abnormalities), and genetic mutations. Prognostic aids include age of the patient, microscopic appearance of blood cells, cytogenetics, genetic mutations, and minimal residual disease. Endpoints include EFS, PFS, and overall survival.

Each of the above parameters can be separately evaluated where the patients are children versus adults, where the patients are treatment-naive versus patients having failed an earlier treatment, and where the patient has no coexisting genetic abnormalities

[319]Staudt LM. It's ALL in the diagnosis. Cancer Cell 2002;1:109–10.

[320]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;1:133–43.

[321]Staudt LM. It's ALL in the diagnosis. Cancer Cell 2002;1:109–10.