We have recently studied an autosomal dominant macrothrombocytopenia characterized by mild or no clinical symptoms, normal platelet function activity, and normal megakaryocyte count. In an attempt to identify the molecular basis of the disease, linkage analysis in two large families localized the gene to chromosome 17p, in an interval containing the GPIb/α gene, which is altered in Bernard-Soulier syndrome (BSS). A heterozygous Ala156Val missense substitution (Bolzano variant) was identified in all patients of the two families and in another six additional macrothrombocytopenic pedigrees. BBS is an autosomal recessive disorder characterized by prolonged bleeding time, thrombocytopenia characterized by mild or no clinical symptoms, nor-

We speculate that there might be patients, affected by the same severe symptoms as in the recessive BSS, carrying mutations in both the allele of this putative gene. A positional cloning strategy based on linkage analysis and mutation screening in candidates is in progress to identify the gene.

To see if chromosome 11q22.3-23.1 deletion involving the ataxia-telangiectasia mutated (ATM) locus may appear during the course of B-cell chronic lymphocytic leukemia (CLL) and related disorders, i.e. CLL/PL and prolymphocytic leukemia (PLL), 82 patients without 11q- at diagnosis were sequentially ascertained at 1-2 year intervals by conventional cytogenetic analysis (CCA) and fluorescence in situ hybridization (FISH), using an ATM-specific probe. Eight patients acquired a submicroscopic 11q deletion 13-43 months after diagnosis; the diagnosis at presentation was CLL in 3 cases, PLL/PL in 3 cases and PLL in 2 cases. A 13q14 deletion preceded the development of 11q- in four patients; additional aberrations included +12 (three cases), 17p13 deletion and 6q21 deletion (one case each). The acquisition of the 11q deletion was more frequently found in those patients presenting with CLL/PL and PLL than typical CLL (p=0.0016) and with splenomegaly (p=0.003). Follow-up data showed that karyotype evolution (p=0.009) and cytological transformation (p<0.001) were associated with the acquisition of this cytogenetic lesion. The variables predicting for a shorter survival in this series included the 11q deletion (p=0.003), along with other classical clinicobiological parameters (performance status, advanced stage, splenomegaly, elevated serum p2 microglobulin and LDH levels). We arrived at the following conclusions: i) submicroscopic 11q deletion involving the ATM locus may represent in some instances a secondary change in CLL, PLL/P and PLL, suggesting that sequential FISH analysis is necessary to detect this chromosome anomaly in some patients; ii) the acquisition of 11q- /ATM deletion may play a role in determining cytological transformation and disease progression of CLL and related disorders.