

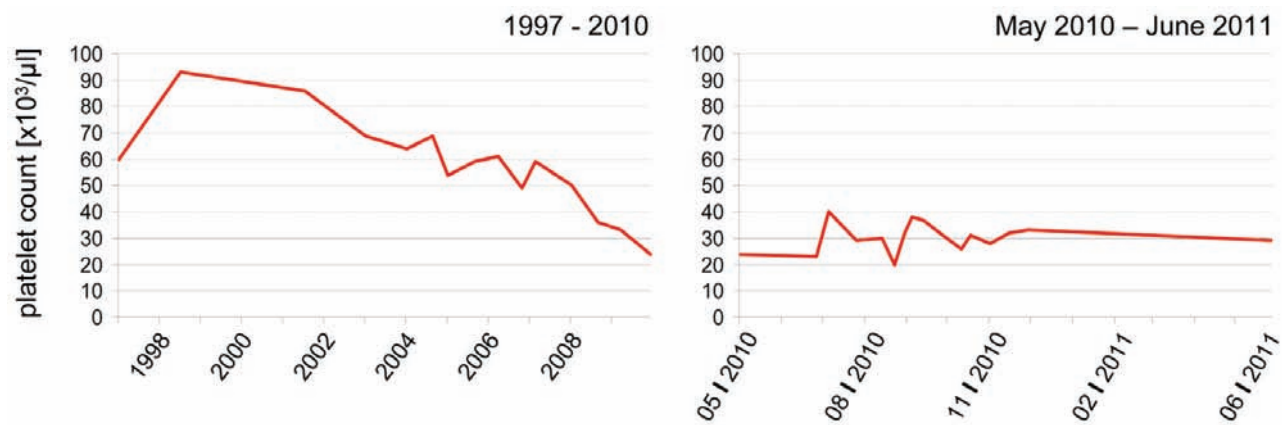
Managing individuals with propensity to myeloid malignancies due to germline *RUNX1* deficiency

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Clinical synopsis

In August 2004, diagnosis of bone marrow failure syndrome due to chronic thrombocytopenia, mild anemia and mild neutropenia; no evidence for myelodysplastic syndrome or overt leukemia; neutrophils $3.2 \times 10^9/L$, hemoglobin 12.9 g/dL, thrombocytes $64 \times 10^9/L$; no detection of platelet antibodies; ongoing decrease of thrombocytes down to approximately $30 \times 10^9/L$, with a minimum of $20 \times 10^9/L$ in autumn 2010; meanwhile stable around $30 \times 10^9/L$.



Histopathological investigation, bone marrow aspirate, July 2010

Mildly elevated cellularity, reduced granulopoiesis, expanded erythropoiesis, no ring sideroblasts, some hypolobulated megakaryocytes, no excess of blasts, no lymphoma infiltration or overt leukemia; most likely toxic etiology with peripheral loss of thrombocytes and erythrocytes; as differential diagnosis, refractory cytopenia with multilineage dysplasia with atypical megakaryocytes and ineffective erythropoiesis was discussed, but finally, no clear evidence for myelodysplasia was seen.

Fluorescence in situ hybridisation, bone marrow aspirate, July 2010

nuc ish 5p15.2(D5S23:D5S721x2),5q31(EGR1x2),cen7(CEP7x2),7q31(D7S522x2),cen8(CEP8x2),17p13.1(TP35x2),20q12(D20S108x2),cenX(CEPXx1),cenY(CEPYx1)[100],[AML1/RUNX1x1][96/100].

Cytogenetic analysis, phytohemagglutinin-stimulated peripheral blood cells, July and September 2010

46,XY[25].
ish 12p13(TELx2),del(21)(q22q22)(AML1/RUNX1-).
nuc ish 12p13(TELx2)[100],[AML1/RUNX1x1][93/100].

Microarray-based comparative genomic hybridization (aCGH), 400k (Agilent), and long-distance PCR, February 2010

arr 21q22.11q22.12(35,304,856-36,864,010)x1 dn; the interstitial deletion was reconfirmed by long-distance PCR in DNA of several blood cell populations and buccal swabs.

DNA-based mutation analyses of *RUNX1*, February 2010

Molecular investigations of ENST00000344691, exon 1-6, ENST00000300305, exon 1, 2, and ENST00000358356, exon 5; no evidence of a mutation in the remaining *RUNX1* allele.