diagnosis of *FGFR3* rearranged PCM was rendered. In contrast, RNASeq data showed overexpression of *NSD2* due to fusion with *IGH*. Patient two is a 15-year-old girl who presented with fever, elevated leukocyte count, B-lineage blasts in peripheral blood (PB) and in cerebrospinal fluid and was diagnosed with B-lymphoblastic leukemia (B-ALL). Chromosome analysis of a PB specimen at diagnosis showed an abnormal karyotype including a t(1;5)(q23;q33). A high risk ALL FISH panel of probes (Cep4/Cep10, *ABL1*/*BCR*, *ETV6*/*RUNX1, ABL1*, *ABL2*, *PDGFRB*, *KMT2A*) detected rearrangement in *PDGFRB* in 69.5% cells and loss of one signal for *ETV6* in 19% cells. Therefore, a chromosomal diagnosis of *PDGFRB* rearranged B-ALL was rendered. Contrary to this, NGS analysis detected fusion between *MEF2D* (1q22) and *CSF1R* (5q33).

Conclusion: *FGFR3* and *NSD2* located 6.25kb apart on 4p16.3 are involved exclusively in the t(4;14) in PCM. Since *FGFR3* involvement is more frequent than *NSD2*, a commercial probe was designed to identify *FGFR3* rearrangement, but design of this probe included *NSD2*. *FGFR3*/*IGH* fusion is routinely interpreted as *FGFR3* positive PCM. Clinically patients positive for *NSD2*/*IGH* fusion have extremely poor prognosis compared to *FGFR3*/*IGH* positive patients. Moreover, the patients with t(4;14) with upregulation of *FGFR3* may be treated with the novel pan-TKI, dovitinib, on a clinical trial. Patients with high-risk B-ALL are routinely screened for rearrangement in *PDGFRB* using a FISH probe, and cases positive for *PDGFRB* are rendered a cytogenetic diagnosis of *PDGFRB* rearranged B-ALL. Another infrequent genetic marker of extreme poor prognosis in Ph-like B-ALL is translocation of *MEF2D* (at 1q22) with several partners including *CSF1R* which is about 500pb apart from *PDGFRB*. Since *PDGFRB* and *CSF1R* are closely linked, *PDGFRB* FISH positive patients can be erroneously classified as *PDGFRB* positive B-ALL. Similar to *FGFR3* positive PCM, some patients with *PDGFRB* rearranged B-ALL may benefit treatment with TKIs.

These two cases highlight the necessity to exercise caution in the interpretation of FISH results, and the necessity for performing fusion screening using RNAseq or NGS methods for prognostication and therapeutic management of patients.

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eP050

Cytogenomic profiling and clinical correlation of 21q22 amplification in acute myeloid leukemia reveal distinct cytogenomic features and poor outcomes

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Background: 21q22 amplification is a rare cytogenetic aberration in acute myeloid leukemia (AML). So far, the cytogenomic and molecular features and clinical correlation of 21q22 amplification in AML have not been well-characterized.

Case presentation: Here, we describe a case series of three AML patients with amplified 21q22 identified by fluorescence in situ hybridization (FISH) using a *RUNX1* probe. Two of these patients presented with therapy-related AML (t-AML) secondary to chemotherapy, while the third had de novo AML. There was one case each of FAB M0, M1 and M4. Morphologic evidence of dysplasia was identified in both t-AML cases. Phenotypic abnormalities of the myeloblasts were frequently observed. Extra copies of 21q22 were present on chromosome 21 and at least one other chromosome in two cases. Two showed a highly complex karyotype. Microarray analysis of 21q22 amplification in one case demonstrated alternating levels of high copy number gain split within the *RUNX1* locus at 21q22, a pattern distinct from the iAMP21 profile reported in B-cell precursor acute lymphoblastic leukemia (B-ALL). The same patient also had mutated *TP53*. Two patients died at 1.5 and 11 months post-treatment, while the third elected palliative care and died within 2 weeks.

Conclusion: Our results provide further evidence that 21q22 amplification in AML is associated with complex karyotypes, *TP53* aberrations, and poor outcomes. Furthermore, we demonstrate that 21q22 amplification is not always intrachromosomally localized to chromosome 21 and could be a result of structural aberrations involving 21q22 and other chromosomes.

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eP052

Coding defects in chromosomal segregation and protein targeting are central to TGCT predisposition

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Introduction: Testicular germ cell tumor (TGCT) is the most common cancer of young men of genetic European ancestry. Although rare, TGCT results in the most years of life lost of all adult cancers. Genome-wide association studies (GWAS) of TGCT have been highly successful, with over 66 independent hits, the highest OR = ~3.5 (*KITLG*). This reflects the high heritability of the disease. We and others identified the tumor-suppressor *CHEK2* as the first Mendelian gene associated with TGCT predisposition. Earlier exome studies yielded a variety of results, including association with *DNAAF1, PLEC*, *DNAH7*, *EXO5,* and ciliary genes. Follow-up studies indicated that the high heritable (HR) component is multigenic.

Methods: We performed exome sequencing and gene burden analysis on 293 individuals with HR-TGCT, representing 228 unique families, and 3157 cancer-free controls.