

7q22 deletion in myeloid malignancies: be attentive to the design of the FISH probe

Délétion 7q22 dans les pathologies myéloïdes : attention au design des sondes FISH

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Partial deletion of the long arm of chromosome 7 [del(7q),7q-] is a highly recurrent chromosomal aberration in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) [1, 2]. In AML, isolated 7q- is assigned to the intermediate genetic prognostic risk group (ELN classification) or the high risk prognostic group (revised MRC classification). In MDS, isolated 7q- is classified into the intermediate cytogenetic prognostic risk group or into the poor risk group if associated with another abnormality according to the revised IPSS (International prognostic scoring system). The deleted regions are distributed along the long arm of chromosome 7 but studies have indicated the existence of at least three commonly deleted regions, at bands 7q21-22, 7q34 and 7q35-q36 [3, 4]. Our study focused on small 7q22 deletions, suspected on karyotype analysis and requiring confirmation by FISH. We explored the region using commercial and home-made probes.

17 patients with myeloid malignancies (4 AML, 10 MDS, 1 MPN – myeloproliferative neoplasm, 2 MDS/MPN) were selected because a small 7q22 deletion was observed on the karyotype.

The deletion was isolated in 15/17 cases and associated with trisomy 8 or 12p deletion each in one case. According to the manufacturer's specifications, commercial 7q22 locus specific probes offer different coverage areas targeting *CUX1*, *RELN* or *KMT2E* genes. In our series 15/17 patients showed a deletion of the *CUX1* probe and 2/17 patients had deletion of the three loci (*CUX1*, *RELN* and

KMT2E probes). No patient had an isolated deletion of *RELN* and/or *KMT2E*. Thus 15 patients would not have been detected with commercial probes not targeting the *CUX1* gene. We then explored the size of this deletion centered on the *CUX1* gene using different home-made probes. We studied the region between the *MUC17* and *KMT2E* genes in band 7q22 according to Jerez *et al.* [3] and Honda *et al.* [5] (figure 1 figure 1).

The following BACs were used : RP11-1108K10 / RP11-151L12 / RP5-1059M17 (covering the *MUC17*, *TRIM56*, *SERPINE1*, *AP1S1*, *VGF*, *NAT16*, *MOGAT3*, *PLOD3*, *ZNHIT1*, *CLDN15*, *FIS1*, *IFT22*, *COL26A1* genes), RP11-333G13 (*CUX1* gene), RP4-672O11 / RP11-188E1 (*RELN* gene), RP11-148A10 / RP11-708P17 (BACs flanking the *KMT2E* gene). The 7q22 deletion including the *CUX1* gene extended to the *MUC17* gene in 13/17 patients. For the 4 other patients the deletion was limited to RP5-1059M17 and RP11-333G13 BACs (figure 1). We therefore advice to limit FISH exploration of the 7q22 region with probes targeting the *CUX1* gene.

In most cases 7q22 deletion is identified on karyotype analysis. However, in some cases, the deletion can only be suspected and for certainty additional FISH is essential. The design of commercial FISH probes is consensual for the majority of chromosome rearrangements but in the case of the -7/7q- syndrome, many target genes have been suggested and this has generated probes targeting the same chromosomal region but not the same genes. Target gene identification is becoming more efficient and more accurate and the design of commercial probes should be updated regularly in order to remain appropriate.

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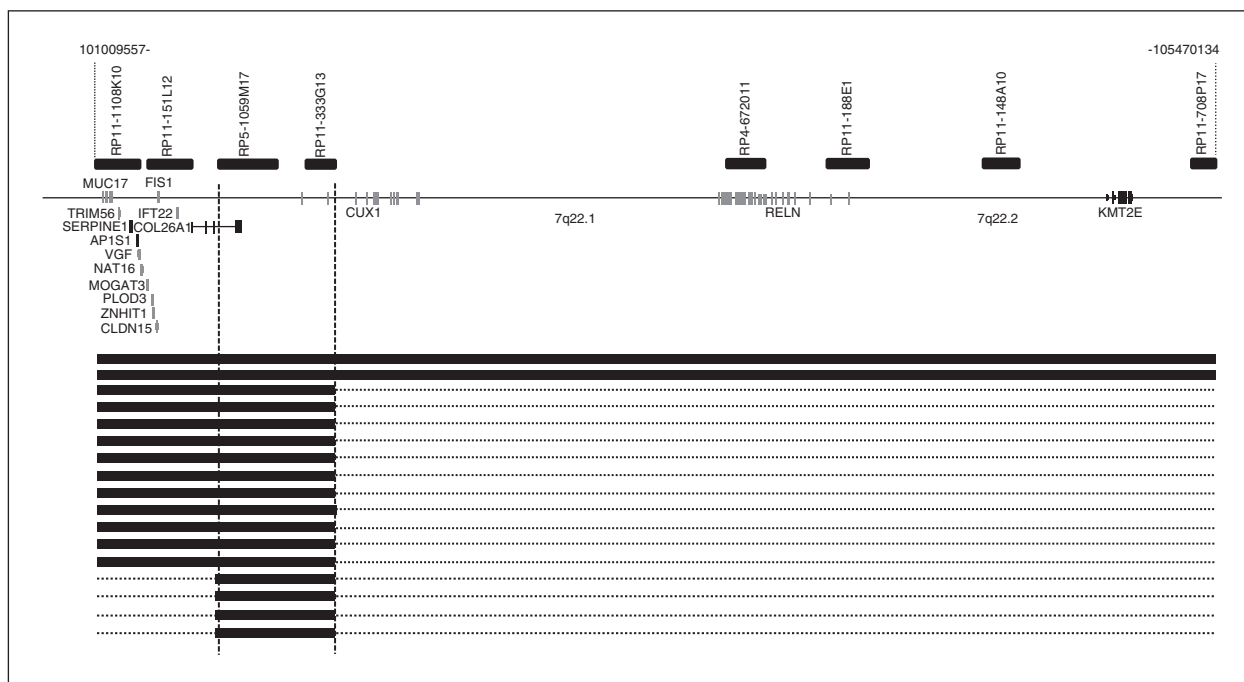


Figure 1. Identification of the common minimal deleted region. Representation of the 7q22.1 to 7q22.2 region with the BACs used. The deleted region for each of the 17 patients is indicated by a black box, the dotted line represents the conserved area. The minimal region common to these patients covers BACs RP5-1059M17 and RP11-333G13 (372 kb).

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