Identification of a TPM3-PDGFRB fusion transcript and its chromosomal breakpoints by RNA-Seq in a case of Chronic Eosinophilic Leukemia

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Introduction

We received a bone marrow from a 77-year-old patient presenting with hypereosinophilia. FIP1L1-PDGFR fusion was not detected, but cytogenetic analysis revealed a t(1;5)(q21;q33), with locus 5q33 corresponding to PDGFRB. This was in accordance with a diagnosis of Chronic Eosinophilic Leukemia (CEL), a rare subtype of myeloproliferative neoplasm, frequently characterized by rearrangements involving PDGFRB/FIP1L1 genes. As FISH couldn’t identify the fusion partner of PDGFRB, we performed a whole transcriptome sequencing (or RNA-Seq).

Identification of the fusion transcripts

- RNA-Seq was performed using polyA selection. The run was analysed using a cloud version of TopHat alignment in BaseSpace.
- TPM3 was found to be the fusion partner.
- The two fusion transcripts identified have already been described in two cases of childhood CEL (Li et al. 2011, Rosati et al 2006).

Identification of the chromosomal breakpoints by RNA-Seq - Confirmation by PCR

- By looking at the reads in IGV viewer, we could identify « mate-pair » reads aligning to intronic regions of TPM3 and PDGFRB.
- We then performed a PCR with primers annealing upstream of the intronic reads, and we were able to localize the genomic breakpoints more precisely.

The chromosomal breakpoints are located ~6kb (TPM3) and ~1.5kb (PDGFRB) further than those previously published.

Conclusion

We describe here a third case of TPM3-PDGFR fusion
- With the same fusion transcripts previously described but not concerning a childhood CEL.
- With chromosomal breakpoints differing from those previously described.

The patient was treated with imatinib therapy, responded well, and was in hematological remission at his last follow-up.

RNA-Seq allows for a rapid screening of fusion transcripts and can identify the rare ones, for which no diagnostic test is developed for routine work. In addition to the « transcriptome » information, we used the « genome » information present in the data to identify the chromosomal breakpoints. This methodology was more time-efficient than performing a screening by PCR, and more cost-efficient than performing a whole genome sequencing.

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