Identifying NAHR mechanism between two distinct Alu elements through breakpoint junction mapping by NGS

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Abstract
Background: Genomic rearrangements encompass deletions, duplications, inversions, insertions and translocations and may be the cause of several genetic diseases. One of the most frequent mechanisms that generates these rearrangements is the Non-Allelic Homologous Recombination (NAHR). They are caused by a misalignment between regions of high level of similarity, like Low Copy Repeats (LCRs) and Alu sequences. We aimed to sequence the breakpoint of a patient with a single deletion on chromosome 22q13.2 in order to understand the genomic structure of the region involved as well as elucidate the mechanism behind this rearrangement. Investigating breakpoints are of the utmost importance in the understanding the influence of the genomic architecture in clinical assays.
Results: We flanked the breakpoint detected by array and then we captured the regions using Illumina Nextera Rapid Capture Custom to sequence with Illumina MiSeq. We found a chimeric read on Chr22:41,026,090, setting a 624,688 bp deletion on Chr22:41,026,112-41,650,780 (hg19). This deletion merges the intronic region of MKL1 and RANGAP1 genes, on two different Alu sequences (AluSx and AluY, respectively). Conclusions: The sequence of the breakpoint reveals that Alu elements are an important characteristic of the human genome on generating rearrangements.

Full Text
Due to technical limitations, full-text HTML conversion of this manuscript could not be completed.
However, the manuscript can be downloaded and accessed as a PDF.

Figures

Sequence of the breakpoint: on the first and last lines are the hg19 reference sequence of the designated regions. On the second line is the sequence of the patient found by breakpoint sequencing. Highlighted in yellow the breakpoint.