I velmi malé fragmenty DNA mohou být detekovány a zpracovány reparačními mechanismy během opětovného sestavení chromozomu při chromotripsi

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Abstract

Analyses at nucleotide resolution reveal unexpected complexity of seemingly simple and balanced chromosomal rearrangements. Chromothripsis is a rare complex aberration involving local shattering of one or more chromosomes and reassembly of the resulting DNA segments. This can influence gene expression and cause abnormal phenotypes. We studied the structure and mechanism of a seemingly balanced de novo complex rearrangement of four chromosomes in a boy with developmental and growth delay. Microarray analysis revealed two paternal de novo deletions of 0.7 and 2.5Mb at two of the breakpoints in 1q24.3 and 6q24.1-q24.2, respectively, which could explain most symptoms of the patient. Subsequent whole-genome mate-pair sequencing confirmed the chromothriptic nature of the rearrangement. The four participating chromosomes were broken into 29 segments longer than 1kb.

Sanger sequencing of all breakpoint junctions revealed additional complexity compatible with the involvement of different repair pathways. We observed translocation of a 33bp long DNA fragment, which may have implications for the definition of the lower size limit of structural variants. Our observations and literature review indicate that even very small fragments from shattered chromosomes can be detected and handled by the repair machinery during germline chromothriptic chromosome reassembly.

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