Familial transmission of chromoanagenesis leads to unpredictable unbalanced rearrangements through meiotic recombination

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Abstract

Chromoanagenesis are complex chromosomal rearrangements that are supposed to occur during a single catastrophic event. They may result in loss or gain of genetic material and may be responsible for various phenotypes. These rearrangements are usually sporadic. However, some familial cases have been reported. Here, we studied six families in which a healthy parent carrying a chromoanagenesis transmitted its rearrangement in an unbalanced manner to its descent. The rearrangements were characterized by karyotype, fluorescent *in situ* hybridization, chromosomal microarray and whole genome sequencing (WGS) in the parents and their offspring. We then hypothesized meiosis-pairing figures of parental chromosomes that may have led to meiotic recombination between normal and abnormal homologous chromosomes, resulting in the formation of new unbalanced rearrangements. This work underlines that chromoanagenesis can be associated with a normal phenotype and a normal fertility, even in males, and that WGS may be the unique way to identify these rearrangements in some cases. Chromoanagenesis can be transmitted in an unbalanced and unpredictable way because of meiotic recombination. Thus, genetic counseling and technical choice for prenatal diagnosis are complex. Finally this work questions the meiotic pairing mechanisms of complex rearrangements, still poorly understood.

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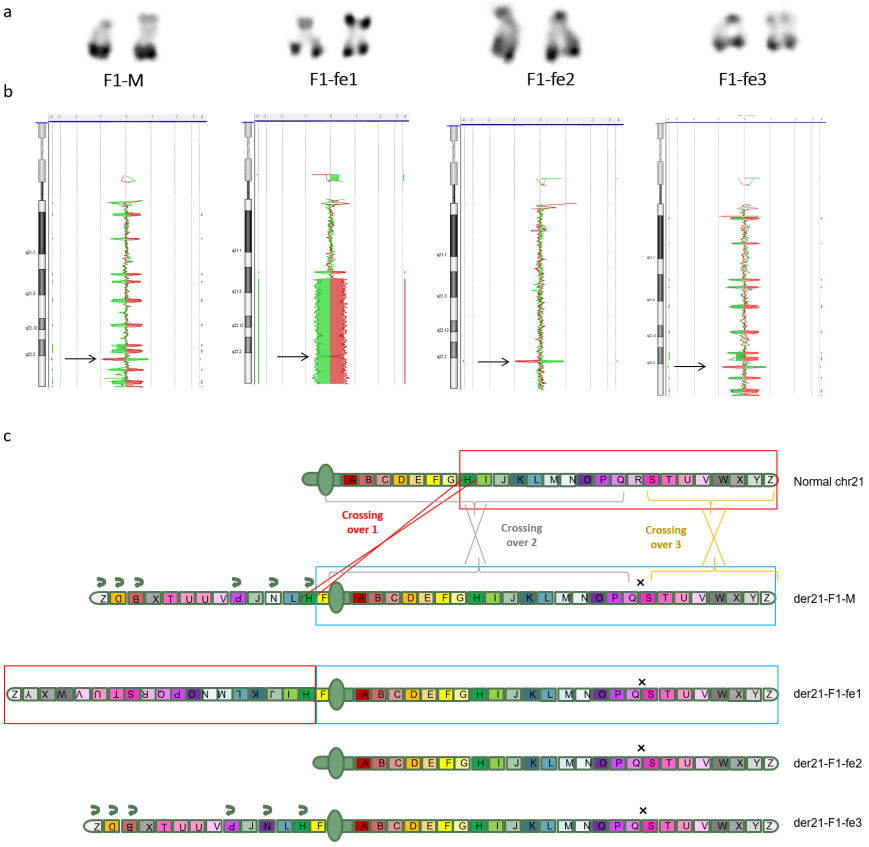

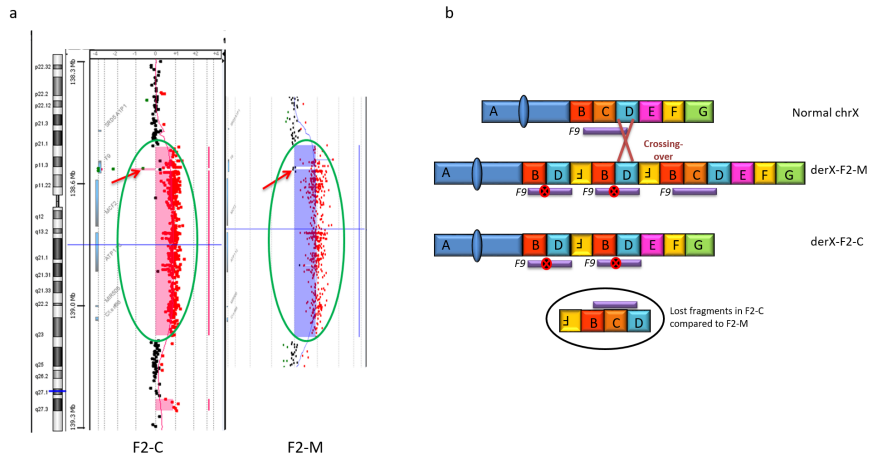

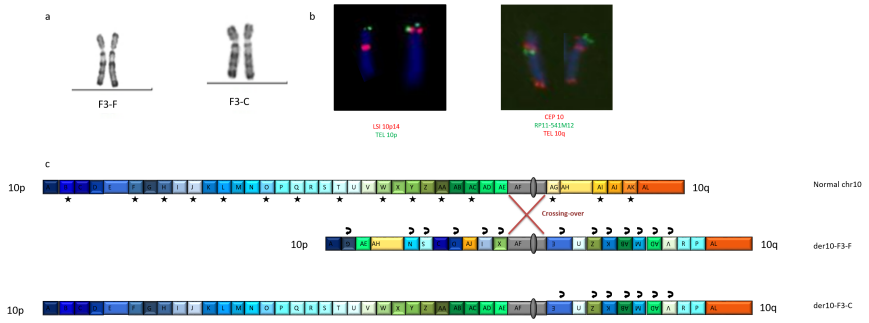

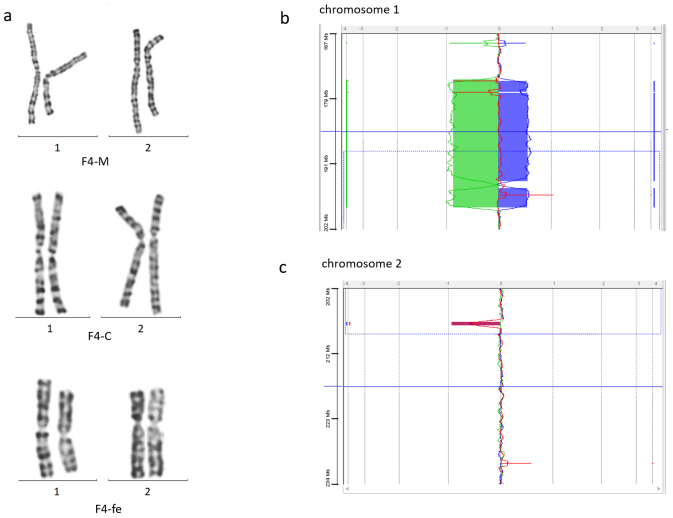

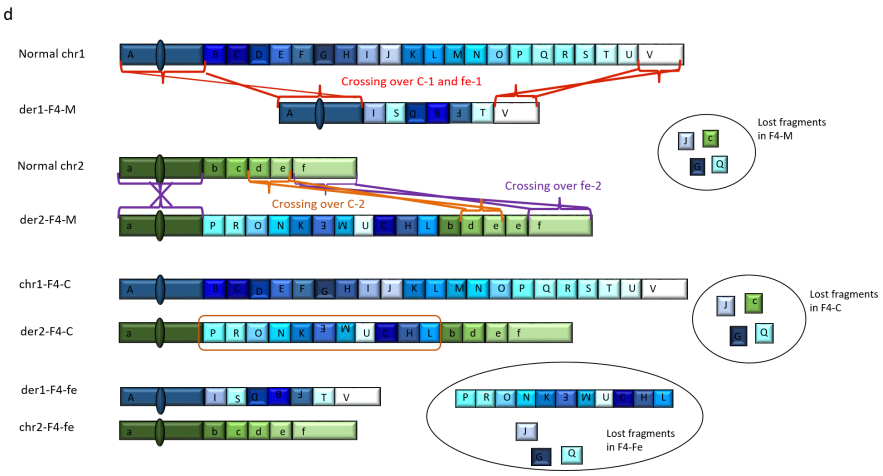

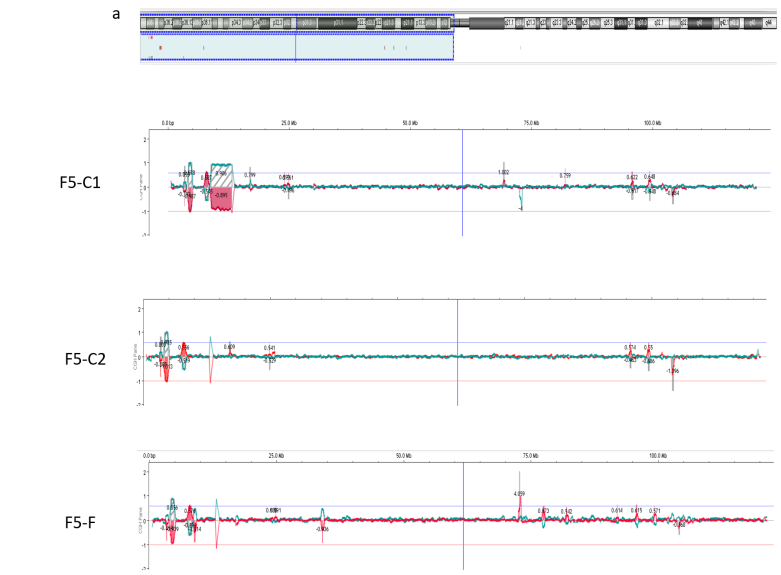

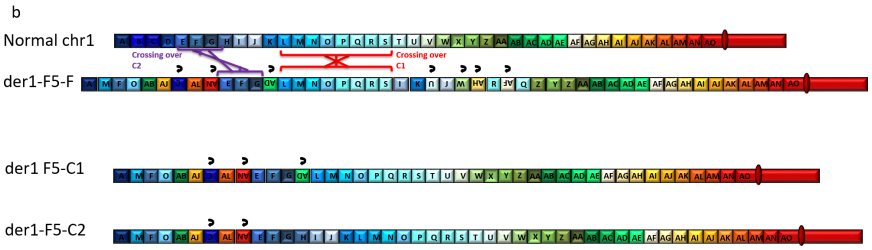

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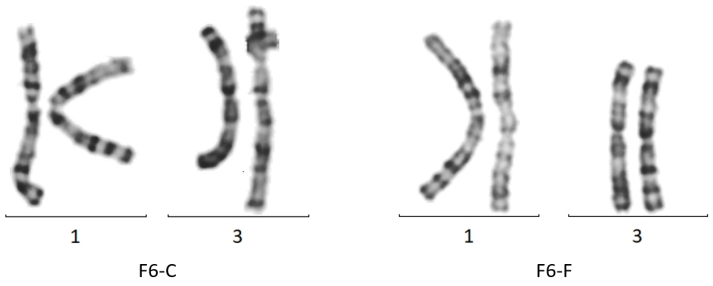

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