Mechanisms of 22q11.2 Deletions and Duplications

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Low copy repeats (LCRs) have been recognized as drivers of human evolution as well as a cause for genomic disorders. The 22q11 deletion syndrome is the most frequent genomic disorder. The deletions and duplications are mediated by non-allelic homologous recombination (NAHR) between low copy repeats (LCRs). Chromosome 22q11.21 contains four LCRs (LCR22A - D) which lead to different sized 22q11 deletions and duplications. Why 22q11 is the most frequent genomic disorder remains an enigma. Also, the exact mechanism and sequences driving the NAHR remain unresolved. This is because the 22q11 LCRs are amongst the most polymorphic and complex regions in the genome. As a consequence, the traditional massive parallel sequencing approaches do not resolve the structures and the reference genome still contains gaps. Novel technological approaches are now resolving the LCR structures and providing novel insigths on the mechanisms underlying the rearrangements.