Genomic instability is a frequently occurring feature of cancer that involves large-scale structural alterations. These somatic changes in chromosome structure include duplication of entire chromosome arms and aneuploidy where chromosomes are duplicated beyond normal diploid content. However, the accurate determination of aneuploidy events in cancer genomes is a challenge. Advances in sequencing technology allow the characterization of haplotypes that extend megabases along the human genome using high molecular weight (HMW) DNA.

Bell et al. employed a library preparation method in which sequence reads have barcodes linked to single HMW DNA molecules. Barcode-linked reads are used to generate extended haplotypes on the order of megabases. We developed a method that leverages haplotypes to identify chromosomal segmental alterations in cancer and uses this information to join haplotypes together, thus extending the range of phased variants. With this approach, we identified mega-haplotypes that encompass entire chromosome arms. We characterized the chromosomal arm changes and aneuploidy events in a manner that offers similar information as a traditional karyotype but with the benefit of DNA sequence resolution [1].

Meningiomas with mutant NF2 and/or chromosome 22 loss were more likely to be atypical, showing genomic instability, and localizing to the cerebral and cerebellar hemispheres [2].

1)
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2)
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