

**P008** Sequence variation reveals an hotspot for non-allelic homologous recombination in the CMT1A-REPs

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The identification of allelic recombination hotspots has been greatly advanced by the inference of hotspot locations throughout the human genome from population genetic data. The number of inferred AHR hotspots exceeds the number of experimentally identified hotspots by at least three orders of magnitude. There has been no such revolution in the identification of hotspots of non-allelic homologous recombination (NAHR). The handful of known NAHR hotspots have all been identified from the painstaking mapping of rearrangement breakpoints in patients suffering from genomic disorders. We have explored the sequence variation in phenotypically-normal humans and hominoid species in the 24kb CMT1A-REPs that contain perhaps the best characterised NAHR hotspot. We have identified signature patterns of sequence variation within humans that reveal the existence of a single predominant gene conversion hotspot within the CMT1A-REPs. This gene conversion hotspot precisely corresponds with the known hotspot for deletions and duplications. There is also circumstantial evidence to suggest that the NAHR hotspot within the CMT1A-REPs is also an allelic homologous recombination hotspot. The extension of our methods to other potential substrates for NAHR should reveal the existence of novel NAHR hotspots that drive both gene conversion and chromosomal rearrangements.