

Published: 01 July 2012

Structural diversity and African origin of the 17q21.31 inversion polymorphism

Karyn Meltz Steinberg, Francesca Antonacci, Peter H Sudmant, Jeffrey M Kidd, Catarina D Campbell, Laura Vives, Maika Malig, Laura Scheinfeldt, William Beggs, Muntaser Ibrahim, Godfrey Lema, Thomas B Nyambo, Sabah A Omar, Jean-Marie Bodo, Alain Froment, Michael P Donnelly, Kenneth K Kidd, Sarah A Tishkoff & Evan E Eichler

DOI <https://doi.org/10.1038/ng.2335>

Nature Genetics volume 44, pages 872–880 (2012)

Abstract

The 17q21.31 inversion polymorphism exists either as direct (H1) or inverted (H2) haplotypes with differential predispositions to disease and selection. We investigated its genetic diversity in 2,700 individuals, with an emphasis on African populations. We characterize eight structural haplotypes due to complex rearrangements that vary in size from 1.08–1.49 Mb and provide evidence for a 30-kb H1-H2 double recombination event. We show that recurrent partial duplications of the KANSL1 gene have occurred on both the H1 and H2 haplotypes and have risen to high frequency in European populations. We identify a likely ancestral H2 haplotype (H2') lacking these duplications that is enriched among African hunter-gatherer groups yet essentially absent from West African populations. Whereas H1 and H2 segmental duplications arose independently and before human migration out of Africa, they have reached high frequencies recently among Europeans, either because of extraordinary genetic drift or selective sweeps.