Nature Reviews Genetics | AOP, published online 2 August 2011; doi:10.1038/nrg3056

HUMAN GENETICS

Recombination diversified

Studies of genome-wide patterns of human recombination have so far been limited to a small number of populations. Two new studies — one in African Americans and the other in African Americans and African Caribbeans — highlight recombination differences between human populations and hint at their molecular genetic basis.

African American and African Caribbean populations are characterized by the recent mixing of genomic regions from European and African ancestries. This 'admixture' can be detected at the level of genetic variation in the form of switching between regions of European and African ancestry in the genome. The positions of these switches in ancestry can, in turn, be used to infer recombination events that have involved shuffling between African and European genomes.

> "The maps generated by these studies provide an important resource for future studies of human genetic variation and evolution"

PHOTODISC

The authors of both the new papers took this approach to generate genome-wide recombination maps. They used genome-wide SNP genotypes from individuals in their study populations and applied computational approaches to identify the switch points between ancestries. Hinch and colleagues did this for 29,589 unrelated African Americans and inferred more than 2.1 million recombination events, whereas Wegmann and colleagues identified hundreds of thousands of crossovers in 2,565 African Americans and 299 African Caribbeans.

The authors compared their findings to recombination maps that have been previously generated for populations of European ancestry. For example, both admixture-based maps were compared with the map of recombination in the Icelandic population, which was generated by deCODE using data from families to identify meiotic crossovers. For both new studies, recombination patterns at large genomic scales (at megabase intervals) were highly similar to those in the European maps. However, at finer scales, both sets of authors identified differences between the maps. Hinch and colleagues went on to identify hotspots of recombination — areas with increased recombination activity in multiple individuals — that are used at significant frequency in African Americans, but not in Europeans, and that therefore correspond to regions of African ancestry.

What is the basis of this difference between populations in recombination hotspots? Using association testing across the genome, Hinch and colleagues identified a SNP that correlates with high levels of use of 'African-enriched' hotspots. This SNP lies close to the gene PR domain-containing 9 (*PRDM9*), which encodes a histone H3 lysine 4 (H3K4) methyltransferase and has previously been identified as a regulator of recombination hotspots. The authors went on to characterize alleles of *PRDM9* that differ in frequency in West Africans and Europeans. They identified a sequence motif of 17 bp that is more prevalent in African-enriched hotspots and that is predicted to be bound by versions of PRDM9 that are encoded by the variants that are common in West Africans and rare in Europeans.

Wegmann and colleagues also provided new insights into the basis of differentiation in recombination rates among populations. Their data implicated structural variants, particularly inversions, as modifiers of recombination.

The maps generated by these studies provide an important resource for future studies of human genetic variation and evolution. The identification of genetic factors that determine differences in recombination between populations also has implications for understanding human diseases that have been linked to recombination events.

Louisa Flintoft

ORIGINAL RESEARCH PAPERS Hinch, A. G. *et al.* The landscape of recombination in African Americans. *Nature* 20 Jul 2011 (doi: 10.1038/nature10336) | Wegmann, D. *et al.* Recombination rates in admixed individuals identified by ancestry-based inference. *Nature Genet.* 20 Jul 2011 (doi:10.1038/ng.894)

FURTHER READING Paigen, K. & Petkov, P. Mammalian recombination hot spots: properties, control and evolution. *Nature Rev. Genet.* **11**, 221–233 (2010) | Seldin, M. F., Pasaniuc, B. & Price, A. L. New approaches to disease mapping in admixed populations. *Nature Rev. Genet.* **12**, 523–528 (2011)