Leveraging long range phasing to detect mosaicism in blood at ultra-low allelic fractions

Most genotyping methods lose information about maternal vs. paternal inheritance of alleles, producing only diploid total allele counts at each genomic position. However, the relative parental inheritance of heterozygous sites can be recovered at high accuracy using statistical techniques. This estimation problem -- termed "phasing" -- is a fundamental challenge in human genetics. In this talk, I will first describe recent advances in phasing methodology that enable efficient phase estimation with chromosome-scale accuracy in the 500,000-sample UK Biobank data set. I will further describe how phase information can be harnessed to detect subtle imbalances between maternal and paternal allelic fractions in blood DNA -- the hallmark of mosaic chromosomal alterations -- revealing new insights into the causes and consequences of clonal hematopoiesis.

List of relevant papers:

[1] http://dx.doi.org/10.1038/ng.2270
[2] http://dx.doi.org/10.1038/ng.2271
[3] http://dx.doi.org/10.1038/ng.3571
[4] http://dx.doi.org/10.1038/ng.3679