Human Genome Variation

If you compare the genomes of two randomly chosen people, the sequences are roughly 99.9% the same. Compared to other animals this is very similar; for instance randomly chosen fruit flies from Malawi show 10-fold more variation. These differences divide into polymorphisms+mutations and other places in the genome where the genomes compared simple don't have the same content. Altogether, those differences are responsible for much of what makes us individuals and strongly influence what health issues we may each face. They are also therefore the stuff of evolution.
In this module we categorize human sequence variation, look at their frequency and distributions and consider, a bit, their evolutionary history, and their medical and evolutionary consequences.

Reading:

MBoC(6th) Ch4: HOW GENOMES EVOLVE, pgs 216-226. **Ch8**: *STUDYING GENE EXPRESSION AND FUNCTION, pgs. 492-494.*

*Wall and Pritchard (2003) **Haplotype blocks and linkage disequilibrium in the human genome**

Conrad et al (2006) **A worldwide survey of haplotype variation and linkage disequilibrium in the human genome**

Vittori et at (1014) **Copy-number variation of the neuronal glucose transporter gene SLC2A3 and age of onset in Huntington's disease.**

Prüfer et al (2017) **A high-coverage Neandertal genome from Vindija Cave in Croatia**
(Just because sequencing the genome of something that's been dead for so long is really, really cool.)

Hu et al (2023) **Genomic inference of a severe human bottleneck during the Early to Middle Pleistocene transition**

Dutta et al (2017) **Intricacies in arrangement of SNP haplotypes suggest "Great Admixture" that created modern humans**

Need to know and understand

Variations

- single nucleotide polymorphisms (**SNPs**)
- insertions/deletions (**Indels**)
- degree of variation (heterozygosity) approximately 0.1% in humans
- copy number variation (**CNV**) and structural variation (**SV**)
- polymorphism vs mutation
- allele
- variation and race
- linkage disequilibrium and haplotypes and haplotype maps
- Contribution of Neanderthal genome

Evolutionary forces

- Positive selection (aka 'selective sweep'), negative selection (aka 'purifying' aka 'background sweep'), and neutral selection
- hitchhiking

Association with health

- copy number variation
- trinucleotide repeat expansion in coding regions
- alleles and fitness to the environment
- Genome Wide Association (GWA) studies: associating difference with pathology.