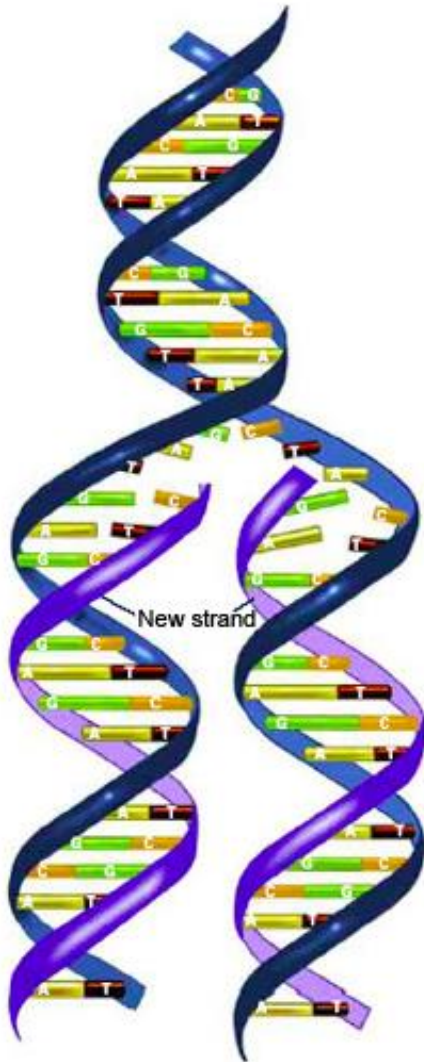


MODULE 3: Human genetic variation — single nucleotide variants

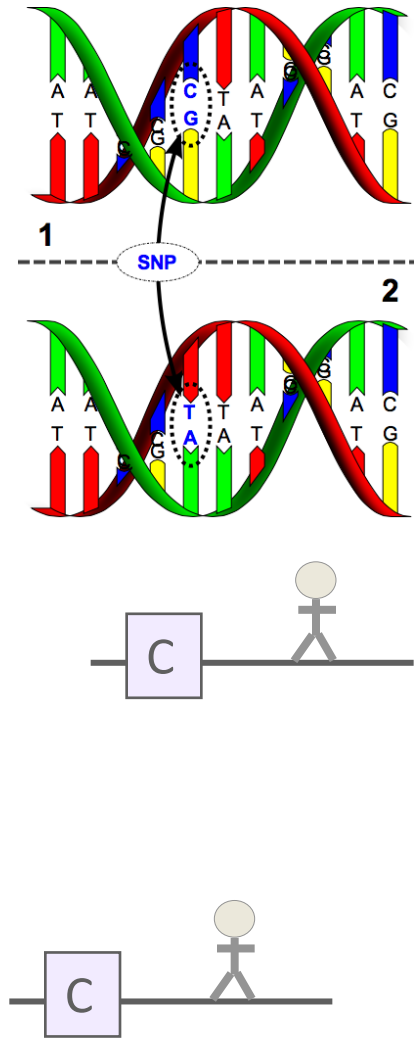
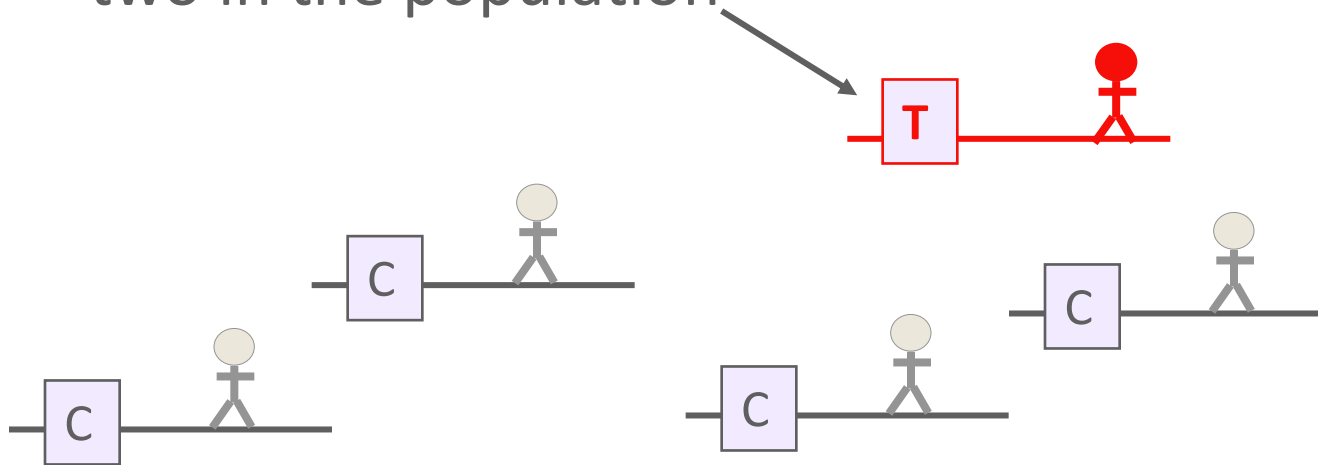
How mutations arise



- Random mutations arise naturally during cell division
- Mutations in gametes (**germline**) have the potential to be transmitted to offspring, but **somatic** mutations do not
- Human mutation rate: 10^{-8} per bp per generation
 - 50 to 100 **de novo** (new) mutations in average newborn
- Mutation, variant, polymorphism

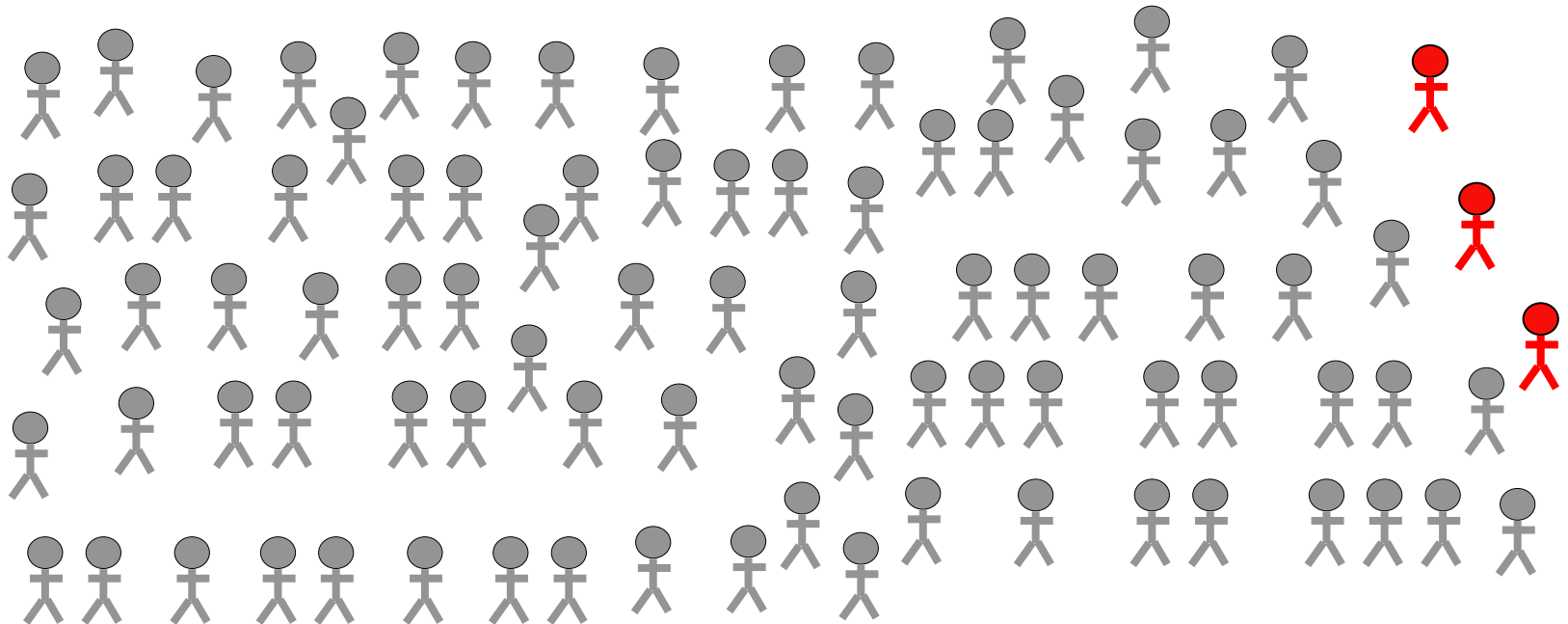
Single nucleotide variants (SNVs)

- Mutations arise in one individual (the **founder**)
- In this example, C is the **ancestral** allele, T is the new allele
- The **minor allele** is the less common of the two in the population

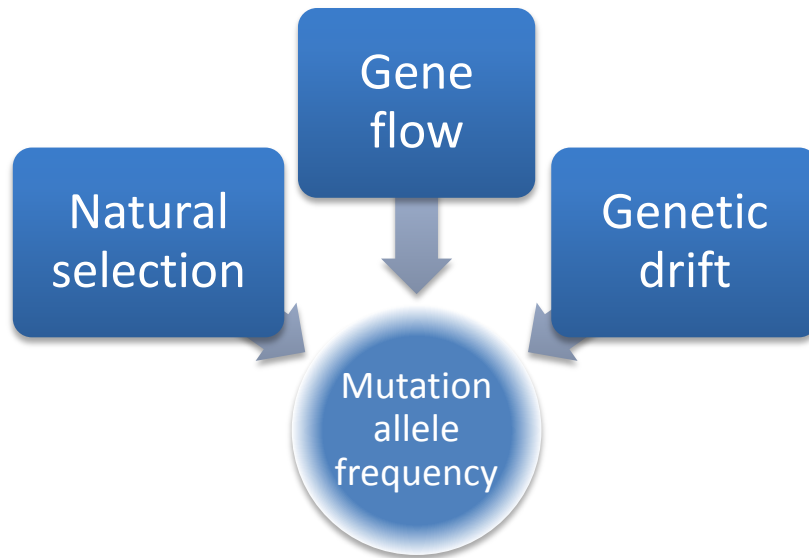


Ancestral nature of alleles

- After many generations, offspring of the founder contribute to an increasing **allele frequency** (prevalence) of the new allele, T
- All alleles are shared among individuals in the population by descent, *not* by recurrent mutations at the same location

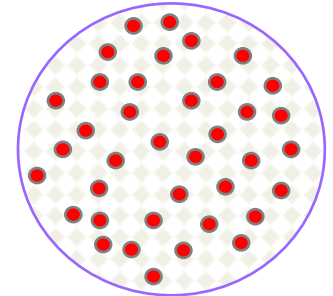
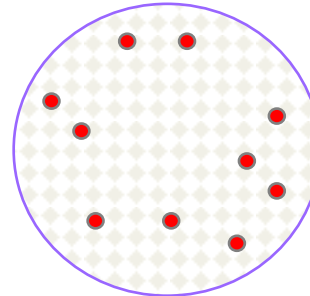
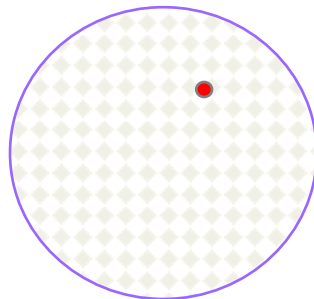


Allele frequencies of single nucleotide variants (SNVs/SNPs) in the population



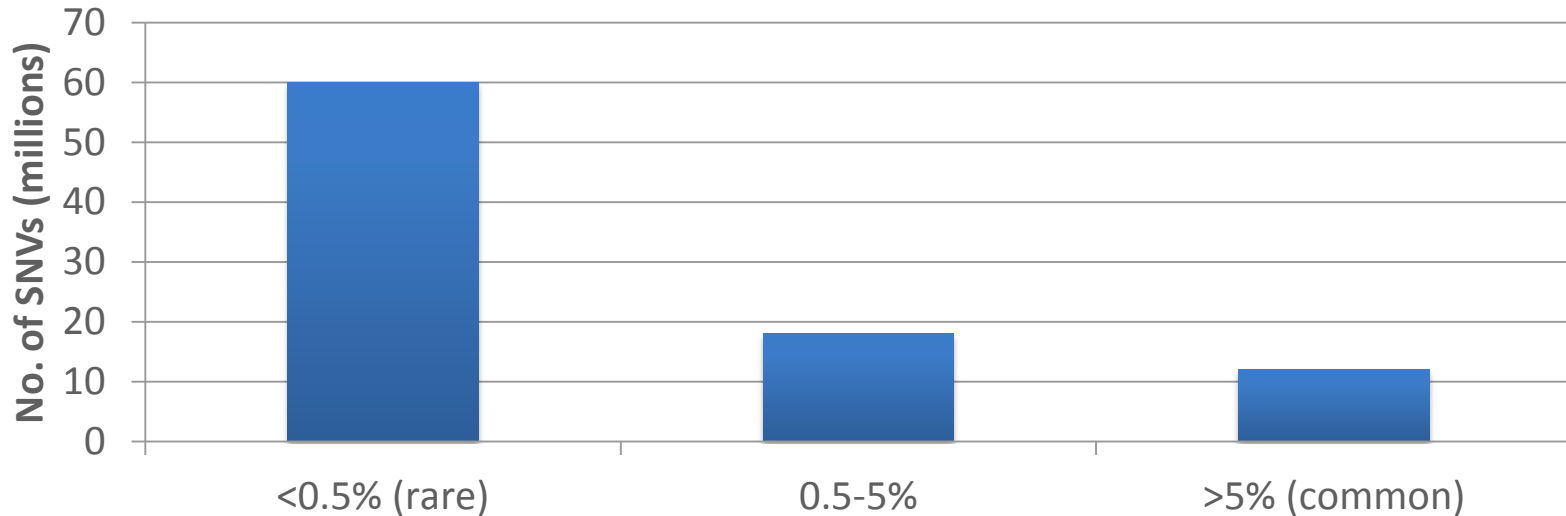
Polymorphisms are mutations with allele freq $>1\%$

Classification:	Rare variants	Low freq variants	Common variants
Minor allele freq.:	$<0.5\%$	$0.5-5\%$	$>5\%$



How many SNVs in the population?

Expected number of SNVs in human population



Rare variants are collectively abundant in the population



Rare variants

1/50 bp

Minor allele frequency

SNPs

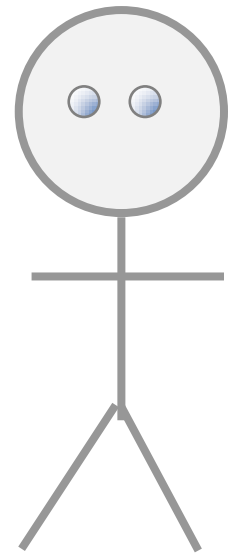
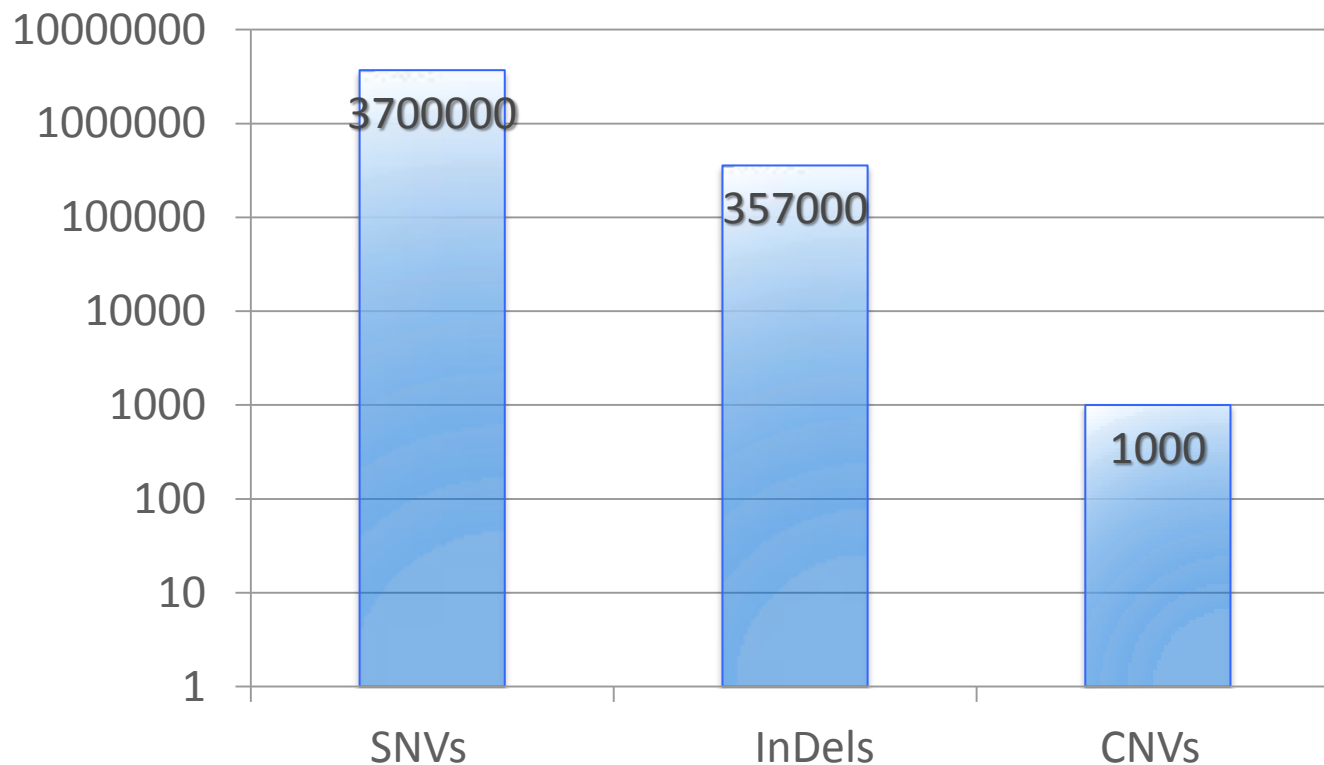


Common variants

1/1000 bp

How many genetic variants in the average person?

- The average person has ~4 million DNA sequence variants



Human migration and genetic diversity

Historical migration of people has shaped the global distribution of alleles

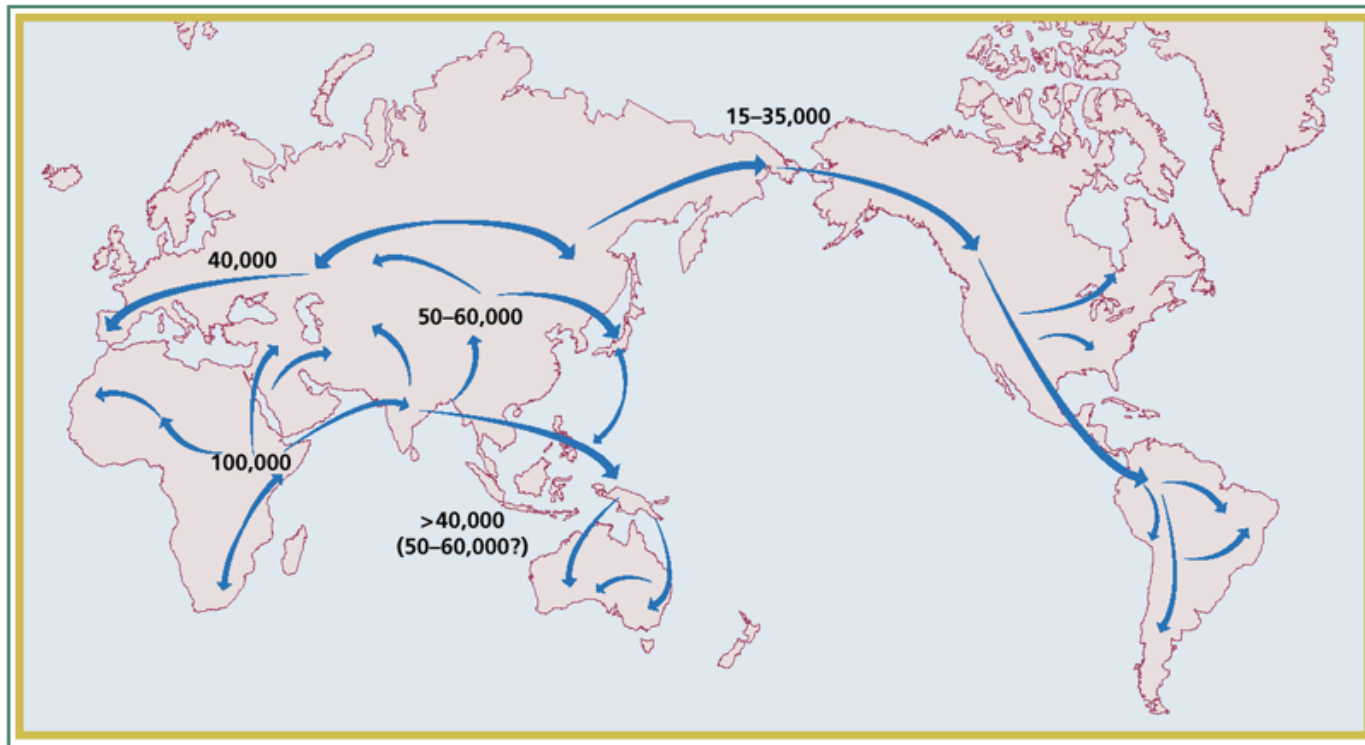
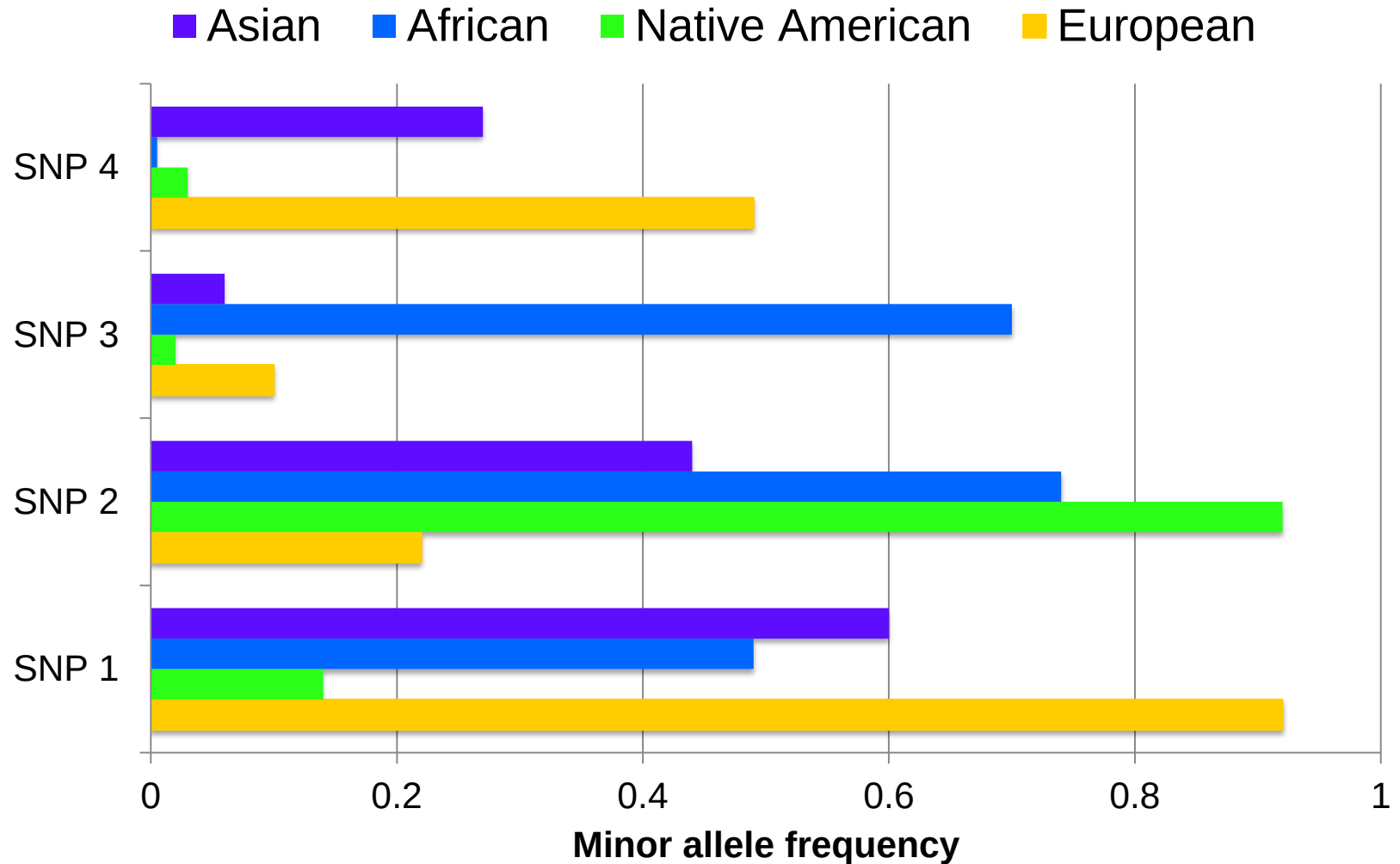


Figure 3. The migration of modern *Homo sapiens*.

The scheme outlined above begins with a radiation from East Africa to the rest of Africa about 100 kya and is followed by an expansion from the same area to Asia, probably by two routes, southern and northern between 60 and 40 kya. Oceania, Europe and America were settled from Asia in that order.

Racial/ethnic variation in allele frequencies



Question

TRUE or FALSE

Common variants are called so because they are the most prevalent type of variation in the human genome.

Answer

FALSE

Common variants are called so because the minor allele frequency is high in the population. Common variants are actually not as prevalent as rare variants are in the population.