## Changing the human genome

Changing the genome leads to variation in the information manual, which may, or may not lead to variation in phenotype, which can be bad ... or good ... or perhaps even necessary; after all, the single most dramatic change in human genomes are a result of recombination during meiosis and sexual reproduction, a reshuffling of the information manual that occurs by design. Other times, the change is accidental. Finally, sometimes the change hits the pieces of the information manual that make the machinery that takes care of the integrity of information manual - bad news indeed. Here we consider some of the mechanisms that lead to changes in the manual and their consequences.

## Reading:

MBoC: Ch20. Cancer as a microevolutionary Process. Pgs. 1097, 1111-1116, 1124-1125, 1133-1134

Madan (2020) Natural human chimeras: A review

Martincorena et al (2018) Somatic mutant clones colonize the human esophagus with age

Bonnivard and Higuet, 2009: Fluidity of eukaryotic genomes

Graham (2021) Horizontal Gene Transfer in Vertebrates: A Fishy Tale

Aguilera and Garcia-Muse, 2013: Causes of Genome Instability

Negrini, 2010: Genomic instability - an evolving hallmark of cancer

## Need to know and understand

Chimerism, Mosaicism

Mechanisms of changing the genome

recombination

gene conversion, Loss of heterozygosity (LOH)

Unequal crossover

Chromosome assortment

Whole genome duplication - tetraploidy

Non-disjunction

translocation

gene amplification, multidrug resistance (MDR)

imperfect repair

errors during DNA replication

transposition

L1 retrotransposition, processed pseudogenes

horizontal transfer

Genome instability

Repair machinery failure and checkpoint failures associated with cancerMINmicrosatellite instability - MMR errors (triplet repeat expansion - TRE), HNPCCNINNER associated instability - Xeroderma PigmentosumCINchromosomal instability