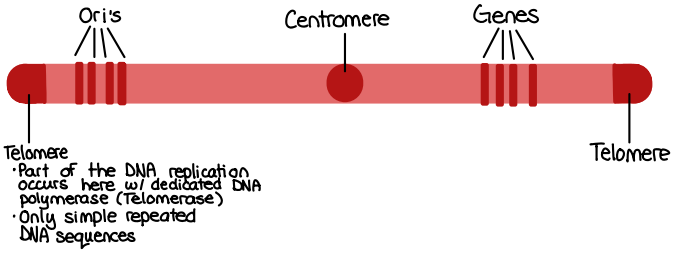
Chapter 12 ~ Physical Mapping of Chromosomes & Genomes

Introductions

- We will look at the larger picture of chromosomes & whole genomes & the various methods used to visualize them.
- Many types of mapping technique available to identify single genes responsible for disorders such as ankylosing spondylitis & cystic fibrosis, as well as the multiple genes responsible for common conditions, such as cardiovascular disease & diabetes mellitus.
- Gene & chromosome mapping tools used to develop detection, monitoring diagnosis & treatment regimens for persons suffering from genetic diseases.
- Chromosomes
  - Long molecule of double-stranded DNA
  - Carry genetic information
- Chromosome 1 = largest chromosome
  - 4778 genes (Most genes)
    - ↳ Many are transcribed into mRNA's which encod proteins
    - ↳ Other are transcribed into tRNA's, rRNA, & other non coding RNA molecules
- Centromere = middle part
  - Place where proteins attach to the chromosomes as required during cell cycle
  - Cohesin proteins hold the sister chromatids together begining in the S phases.
  - Kinetochore protein from attachment point for microtubules during mitosis
  - Not necessarily in the middle of the chromosome
    - ↳ @ center = metacentric
    - ↳ Offset = submetacentric
    - ↳ Towards one end = Acrocentric

ex: Chromosome 1, 5, 21



- Part of the DNA replication occurs here w/ dedicated DNA polymerase (Telomerase)
- Only simple repeated DNA sequences

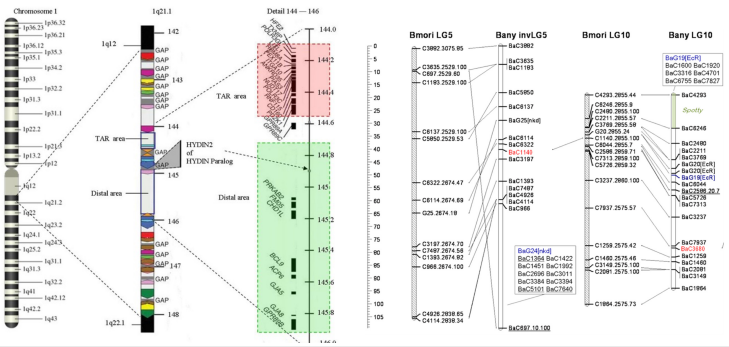
- Humans do NOT have any telomettic chromosomes
  - when centromere is are at one end
  - Mice & other mammal do have telometric chromosomes
- At the beginning of S phase, DNA polymerases begin the process of chromosome replication
  - Begins at origins of replication (ORI)
  - Distributed along the chromosome ~40 Kb apart
  - S phase begins at each ori as two replication forks leave, travelling in opposite directions.
  - Replication continues, & replication forks travelling from one ori will collide w/ forks travelling towards it from the neighboring ori
  - Forks meet = DNA replication is complete
- Chromosomes are long duplex molecules of DNA that are either linear or circular & composed of relatively consequence of nucleotides
  - 3 Discriptions for linear contents of a chromosome:
    1. Genetic map
    2. Cytogenetic map
    3. Physical map

Genetic Maps

- We can use genetic distances (cM/mu) to produce a genetic map which shows the locations of genes along a linear chromosome

NOTE: Map distances are always calculated for one pair of loci at a time, however, by combining the result of multiple pair wise calculation a genetic map of many loci on a chromosome can be produced

- Shows the map distance (in cM) that separate any two loci & the position of these loci relative to all other mapped loci
- Genetic map distance ~proportional to the physical distance
  - Ex: Amount of DNA b/w two loci
  - Ex: Arabidopsis 1.0 cM correlates to approximately 150,000 bp & contains approximately 50 genes



Examples of Genes in Humans

- LCT - An autosomal Gene
- F8 - An x Chromosomal Gene
- SRY - A y Chromosomal Gene
- MT-CO1 - A Mitochondrial Gene

Location of a gene	Number of alleles of this gene in males	Number of alleles of this gene in females
Autosomal chromosome	2	2
X chromosome	1	2
Y chromosome	1	0
Mitochondrial chromosome	1	1

- Novel gene & previously mapped genes show complete or partial linkage the recombination frequency will indicate the approximate position of the novel gene within the genetic map.
  - Useful in isolating specific fragments of DNA via mapped based cloning
  - Useful to track genes/alleles in breeding crops & animals in studying evolutionary relationships b/w species & in determining the causes & individual susceptibility of some human diseases

Cytogenetic Map

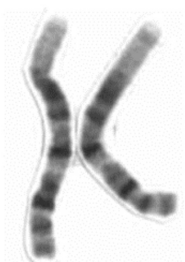
Cytogenetics deals w/ how chromosomes relate to cell behaviour particularly during meiosis & mitosis

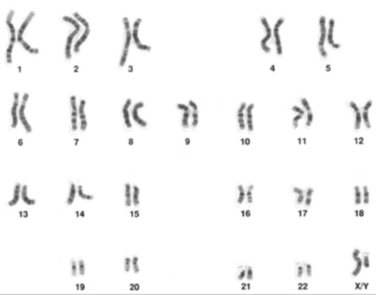
Produced after staining metaphase chromosomes w/ a particular dye mixture & visualizing the dark / ligh colour bands under microscope

Each chromosome pair stains w/ its own characteristics banding pattern

Correlates approximately w/ DNA sequence underlying it AT-rich areas stain dark GG areas stain lightly

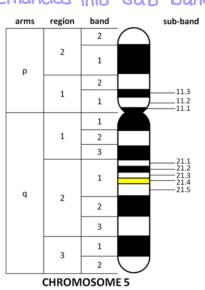
Cytogenic description of chromosome:
length centromere position banding pattern after staining





Karyograms:

- When cytogenetisits sort the photo to put the chromosomes in a standard pattern
- Karyogram assembly is usually reviewed by a qualified cytogenetisits
  - Ex: Haploid human nucleus (sperm or egg) normally has 23 chromosomes ($n = 23$)
    Diploid human nucleus has 23 pairs of chromosomes ($2n = 46$)
  - In each Karyogram there are:
    - ↳ Material chromosomes from the mother
    - ↳ Paternal chromosomes from the father
- Stains & fluorescent dyes like Trypsin + Giesma & Quinacrine are used to produce characteristic banding patterns to distinguish all 23 chromosomes
  - Bands are first grouped into regions, sectioned into bands and are further demanded into sub-bands



Centromere location	Name	Shape
Middle	Metacentric	
Around middle	Submetacentric	
Towards one end	Acrocentric	
At one end	Telocentric	

Physical Maps Example: