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Introduction to Medical Genetics: Human Chromosome

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At the end of this resource, you should be able to

- Describe the chromosome structure and organization
- Distinguish chromosome, chromatin and chromatid

Topics

- Human DNA organization and content
- The equation
- Chromosome, Chromatin and Chromatid
- Heterochromatin and Euchromatin
- Centromere and Telomere
- Gross anatomy of Chromosome

Human DNA organization

- **Why do we need this organization?**

  $\rightarrow$ 6 billion base of DNA (2 meters long)
- **How to fit this inside a nucleus?**
- **How to get access for enzymatic and regulatory proteins reactions?**
- **How to ensure no entanglement?**

  $\rightarrow$ DNA is organized and packaged into 46 chormosome.

Human Chromosome- The equation

- Chromosome = **DNA** + **Protein** + **Nuclear Scaffold Matrix**
- **DNA** = nucleic acid
- **Protein** = histone
- **NSM** = non histone proteins
- Nucleosome = 146 bp of DNA + 8 Histones
- Histone octamer = Dimers of H2A, H2B, H3 and H4
- Nucleosomes are joined by linker DNA (50-60 bases)

Human Chromosome – The content

- H1 Histones interact with linker DNA
- → Coil **nucleosome filaments** with 6-8 nucleosome per turn which will form a **Solenoid**
- → 10 nm of nucleosome filament into **30 nm chromatin fibre**
- **30 nm chromatin fibre** folds into series of large supercoiled loops
- AT rich regions of chromatin loops attach to **non histone proteins** in the **nuclear scaffold matrix** (NSM)
- **NSM** → regulate the degree of coiling and transcription in a loop

Chromatid

- **Chromatin** loops are found within the nucleus
- Normally difficult to visualize
- Some chromatin loops are highly compacted and some are not
- During metaphase (cell division), chromatin loops are condensed and packed tightly to form **metaphase chromosome**
- The dividing metaphase chromosome appears as two **chromatids**

Heterochromatin

- Condensed form of chromatin organization
- Lines the nuclear envelope except the nuclear pore
- Not actively transcribed
- Stays condensed during interphase
- Contains regions of Chromosome that harbour inactive genes
- **Heterochromatin = inactive chromatin**
- Permanently inactive compacted chromatin = **Constitutive heterochromatin** – centromere and telemore
- Transiently inactive compacted chromatin = **Facultative Heterochromatin** – depends on cell's activities

Euchromatin

- Not condensed chromatin organization
- Actively being transcribed
- Found throughout the nucleus
- **Euchromatin = active chromatin**

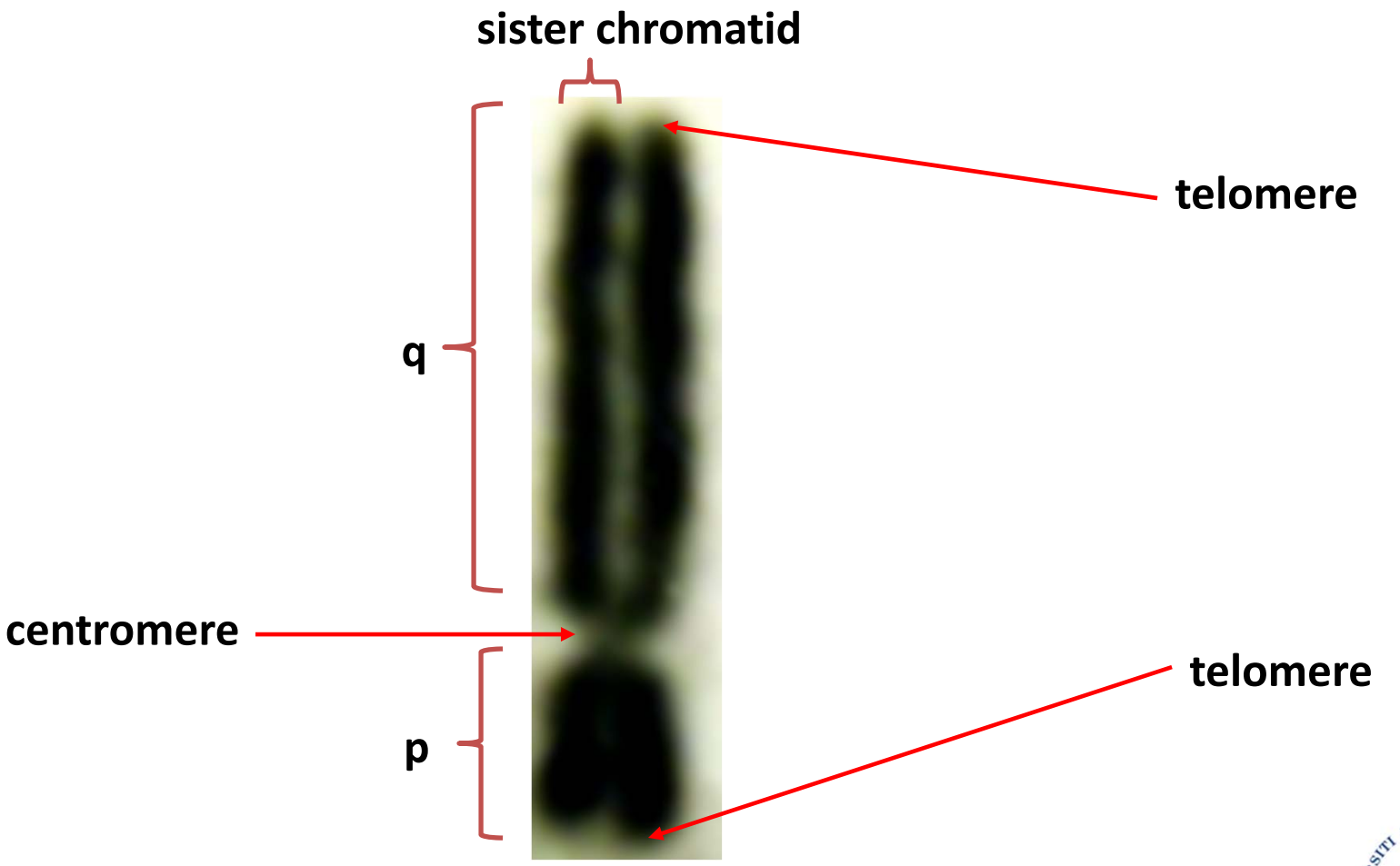
Centromere

- **Site of chromosome constriction**
- Constitutive heterochromatin
- Divides chromosome into **p and q** arms
- Contains short AT rich sequence tandemly repeated
- Contains kinetochore, attachment site for microtubules during cell division

Telomere

- **Tandem repeated DNA sequence**
- Tip of the chromosome
- Required for complete **replication** of chromosome
- Protection against **nucleases**
- Maintain chromosome **integrity**
- Protect against **fusing**
- Facilitate **interaction** between the ends and the nuclear envelope

Gross anatomy of Chromosome



Summary

- Chromosome = **DNA** + **Protein** + **Nuclear Scaffold Matrix**
- **Chromosome** contains histones and non histone proteins
- **Nucleosome** = 146 bp of DNA + 8 Histones
- Nucleosomes form **chromatins**
- **Condensed chromatins** forms sister **chromatids** during S phase

Summary

- **Heterochromatin** = inactive chromatin
- **Euchromatin** = active chromatin
- **Centromere = Constriction** that divides chromosome into p and q arms
- **Telomere =** Tandem repeated DNA sequence at the tip of the chromosome