Centromere structure, function & evolution
**Centromere function**

- chromosomes can be **monocentric** or **holocentric** (*Luzula, Eleocharis, some insects*)
- **dicentric** chromosomes usually unstable (anaphase bridges >> breakage), one centromere has to be inactivated epigenetically (cf. dicentric Robertsonian fusions)
- **acentric** chromosome fragments are unstable at mitosis/meiosis and lost
- **sister chromatid cohesion** throughout cell cycle until sister chromatid segregation at mitosis/meiosis II (centromeres enriched with cohesin)
- **sites of kinetochore** formation ensuring correct chromosome position on mitotic/meiotic spindle (chromosome congression) and subsequent migration
Centromere function: mitotic chromatid segregation

Accurate chromosome segregation requires that kinetochores from each sister chromatid bind microtubules that emanate from opposing spindle poles (amphitelic attachment). This is achieved by a process called chromosome bi-orientation. Incorrect attachments can lead to improper chromosome segregation and aneuploidy.
The overall chromatin structure of the centromere is conserved among different species.
The CENH3-binding domain contains active genes (red bars), but with a lower density than the flanking domains.

in rice (Oryza sativa), centromeres contain satellite repeats (CentO repeat) and centromere-specific retrotransposons

[several wild rice species do not contain the CentO repeat >> CentO repeat have either diverged significantly or been replaced by unrelated sequences]
Centromere FAQs

➢ What is determining the centromere identity? (only one site on a monocentric chromosome is functioning as centromere)

➢ How the centromere identity is transmitted from one cell or generation to the next?

‼ centromeric sequences are not conserved between closely related species, or even among chromosomes in a single species,

‼ centromeric DNA is not sufficient for kinetochore formation,

‼ centromere position along a chromosome displays dramatic plasticity during evolution (centromere inactivation and neocentromere formation)

X chromosomes in mammals retain conserved genetic synteny, but have centromeres in different positions & contain different satellite repeats >>> explained by centromere repositioning via neocentromere activation & the loss or inactivation of the original centromere
A model of neocentromere-mediated centromere evolution in plants (rice)
Neocentromeres

In mammals, centromere movement along a chromosome (including gains and losses) without a change in linear gene order (colinearity) is best explained by neocentromere formation. Such centromere plasticity is best explained if centromere identity is determined epigenetically.

**neocentromerization** - abnormalities within an individual karyotype

**centromere repositioning** - abnormalities in an evolutionary context; not rare event in karyotypic evolution
The result of an asymmetric reciprocal translocation are acentric and dicentric chromosomes, both of which are normally unstable and lost.

Epigenetic regulation allows the neocentromere formation on the acentric chromosome and the centromere inactivation on the dicentric.

Evolutionary significance
(chromosome rearrangements can be fixed)
Neocentromere formation in Drosophila

Fragment of euchromatin and telomeric chromatin can be separated from the rest of a Drosophila chromosome by irradiation. Such acentric fragments can acquire a functional centromere, but only after a pericentric inversion has occurred. **The neocentromere is activated only in a region adjacent to the endogenous centromere** (epigenetic mechanism: spreading of centromeric proteins onto adjacent, non-centromeric regions). Neocentromere formation is inhibited when heterochromatin is present between the endogenous centromere and the neocentromere-forming region (no “spreading” possible).
Neocentromere formation in humans

- Centromeric sequences are not necessary or sufficient for kinetochore formation and function.
- Neocentromeres do not contain satellite DNAs. However, they are epigenetically modified (H3K9 methylation and HP1 binding), in the same way as endogenous centromeres.
Stable barley chromosomes without centromeric repeats

- gametocidal system induces a translocation between a barley and wheat chromosome in a wheat line with added barley chromosomes

- an isochromosome for the short arm of barley chromosome 7H (7HS) that lacked the barley-specific centromeric satellite sequence (AGGGAG)n was obtained

- two telocentric derivatives of the isochromosome arose in the progeny: 7HS* with and 7HS**; both telosomes lacked not only the barley-specific centromeric (AGGGAG)n repeats and Ty3gypsy-like retrotransposons but also any of the known wheat centromeric tandem repeats

- although they lacked the centromeric repeats, 7HS* and 7HS** both showed normal mitotic and meiotic transmission >> the barley centromeric repeats are neither sufficient nor obligatory to assemble kinetochores at novel centromeres