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HST.161 Molecular Biology and Genetics in Modern Medicine
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Lecture 9

Chromosomes

Chromosome is made up of one complete strand of double-stranded DNA, packed up very compactly (10,000-fold).

Karyogram: images of the actual chromosomes in a particular person

Karyotype: chromosomes written out with notation, e.g. 46,XY

In the karyogram, the chromosomes are laid out in a traditional way (which is mostly by size, from largest to smallest), with the sex chromosomes last.

G-banded chromosomes: use trypsin to denature some of the proteins in chromosomes for awhile, and then stain it (e.g. with Giemsa). The stain will get into some places and not others, based on how the proteins are denatured. The dark bands are A-T bands, and have fewer genes. Light bands are G-C rich, and have more genes.

Ideogram: cartoon-type chart of a chromosome drawn out, showing banding patterns.

P-arm: “petite” arm, short arm

Q-arm: long arm (Q comes after P)

Each band is labeled with 2 numbers; the first number labels the region, the second labels the band. So band number is not “thirteen” but “1, 3” and more specifically, “Q/P 1, 3”

If you culture the chromosome with ethidium bromide, you can stretch out the chromosome a bit and resolve bands into even more narrow, specific bands.

(So you can resolve q21 into q21.1, q21.2, q21.3 etc)

Chromosome classification: based on location of the centromere, describes how long the arms are.

- metacentric: all arms are of equal length
- submetacentric: one pair of arms is shorter than the other
- acrocentric: one pair of arms is almost nonexistent

Chromosome testing in a clinical cytogenetics lab:

- 50% of early miscarriages may have a chromosome abnormality; it's not recommended for a first miscarriage to be karyotyped.
- Most chromosome abnormalities are miscarried.
- Most common trisomy is trisomy 16.
- Cancer: leukemias and lymphomas especially. Chromosome abnormalities can be not only diagnostic, but prognostic as well.

Identifying abnormalities:

- On the karyogram, the abnormal chromosome will always be pictured as the right-side one in the pair.

Types of abnormalities: numerical (abnormal number of chromosomes), structural (normal number, but chromosomes themselves are altered)

Nondisjunction events happen most often during maternal meiosis I.

Trisomy 13: (aka Patau syndrome)

- holoprosencephaly: one brain, no hemispheres
- anophthalmia: no eyes, possibly one eye
- cleft lip/palate
- cardiac defects
- low set ears
- clenched hands
- post-axial polydactyly (extra fingers/toes)

Full trisomy 13's can live into their teen years; some are born with only partial +13.

Trisomy 18: (aka Edwards syndrome)

- muscle contractions in limbs
- clubbed feet
- wide-spaced nipples; short sternum
- clenched hands (thumb and pinky clench over the top of the rest of the fingers; very characteristic)
- wide-space eyes, small mouth

Trisomy 21: (aka Down's syndrome) Only really survivable trisomy.

- mental retardation
- low muscle tone at birth
- large mouth
- transpalmar crease: one single crease that runs across their palm
- wide gap between first and second toes ("sandal gap"): characteristic ultrasound finding (not diagnostic, though)
- usually live into 40s-50s; fertile, not necessarily likely to pass on trisomy
- higher than normal incidence of leukemia

Trisomy 21 is the least severe, probably because this chromosome has the fewest number of genes on it.

1 in 500 people has a balanced chromosome rearrangement; so, it's not a universal death sentence. 80% of the time these are phenotypically normal.