

Dosage compensation

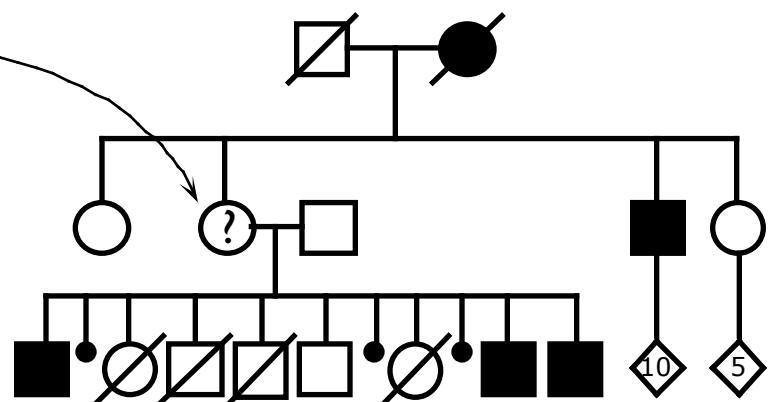
Genetics 371B Lecture 18

29 Oct. 1999

Puzzling behavior of X-linked traits

- ◆ Dosage: Viability is extremely sensitive to gene dosage...so how to explain **XX** vs. **XY**?
- ◆ **“Exceptional females”**: X-linked traits not showing the phenotype expected for the genotype – e.g., Becker-type muscular dystrophy, X-linked recessive

Genotype of II-2?



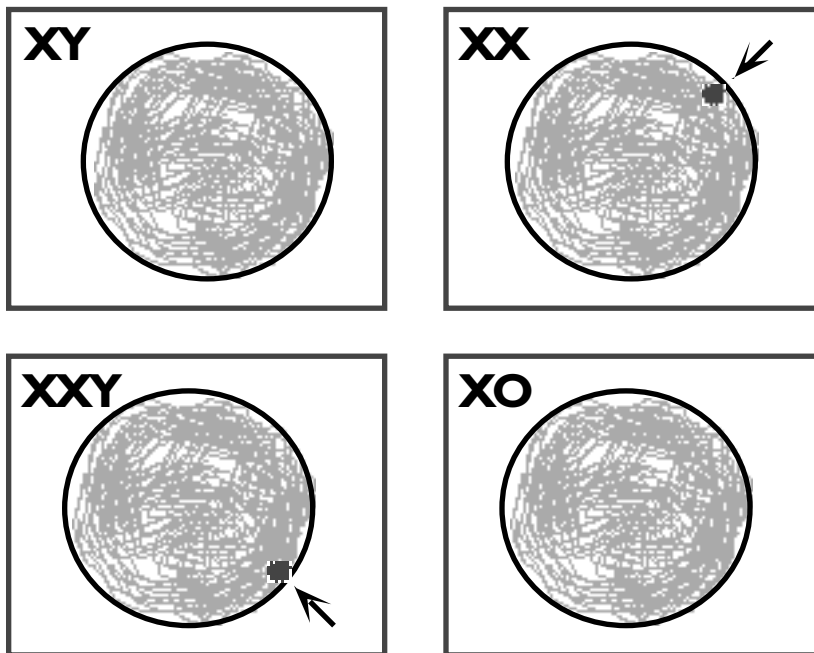
Predicted

phenotype:

Actual phenotype:

The Lyon hypothesis

- ◆ 1949 – Murray Barr: “sex chromatin” in cells from female mammals
- ◆ 1959 – sex chromatin **present** in XXY males, **absent** in XO females



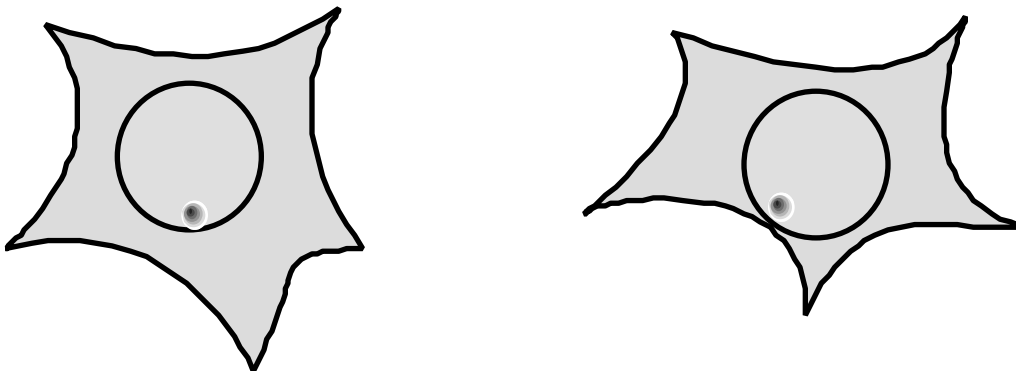
- ◆ 1961 – Mary Lyon: **inactive-X hypothesis**
 - ◇ condensed X is genetically **inactive**
 - ◇ inactivation early in development
 - ◇ inactivation **independent** and **random** in each embryonic cell

Evidence supporting the hypothesis: correlating late-replicating X with inactive allele

Fibroblast cells from female **mule**; look at expression of G6PD gene...

Which X late-replicating?

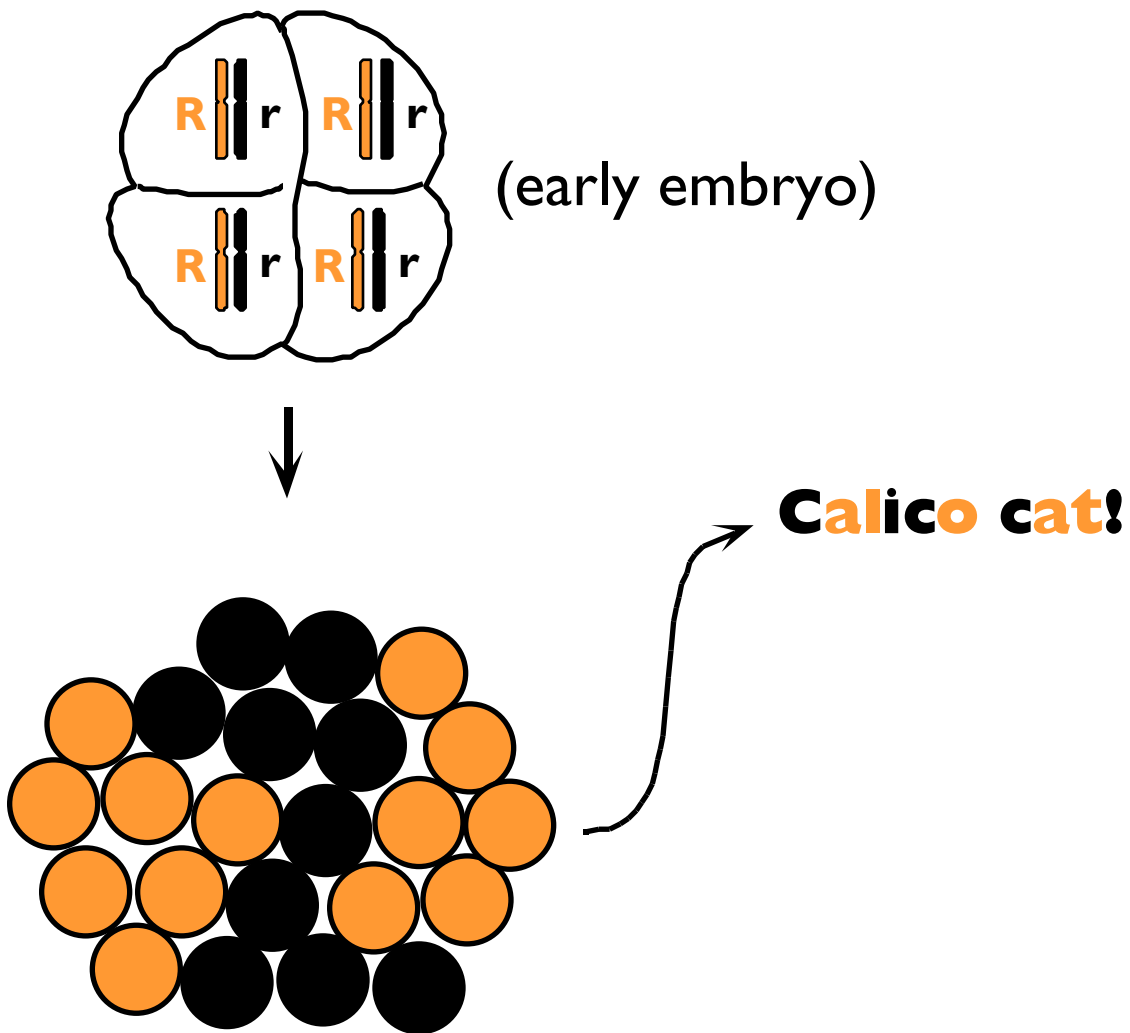
Which form of G6PD present?



Consequences of X chromosome inactivation (explaining the puzzles):

- ♦ **Dosage compensation** – Only one X chromosome genetically active
- ♦ **Mosaic** expression pattern
 - ♦ **Example I:** the unexpected pedigree (Becker dystrophy)

- ◇ **Example 2:** Making a calico cat
X-linked coat color gene



Mechanism of X chromosome inactivation?

- ◆ **Selection** of one X...
- ◆ ...**inactivation** of the others
- ◆ **Propagation/maintenance** of inactive state

Dosage compensation in other species

- ◆ *Drosophila*: up-regulation of X-linked genes
- ◆ *Caenorhabditis elegans*: down-regulation of X-linked genes