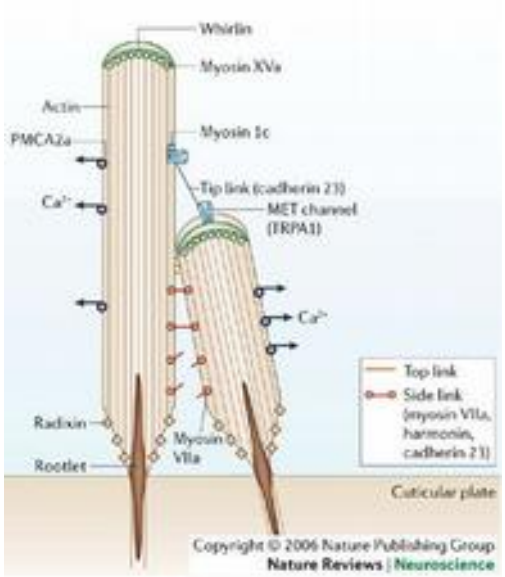
Searching for the“language genes”



Dan Dediu

Language and Genetics
Max Planck Institute for Psycholinguistics
Nijmegen
The Netherlands

LSA2013
Universality and Variability:
New Insights from Genetics
29th of June, 2013

Overview

- Heritability
- Linkage
- Association
- Sequencing
- Examples (hearing loss, dyslexia, SLI, stuttering)
- Conclusions
- Suggested readings

Basic concepts

- Phenotype → observable/measurable properties
  - height

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  - eye color

Basic concepts

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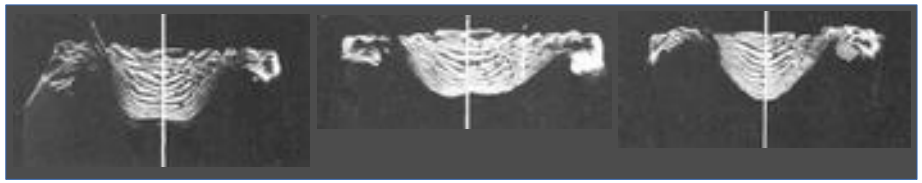
  - hard palate shape



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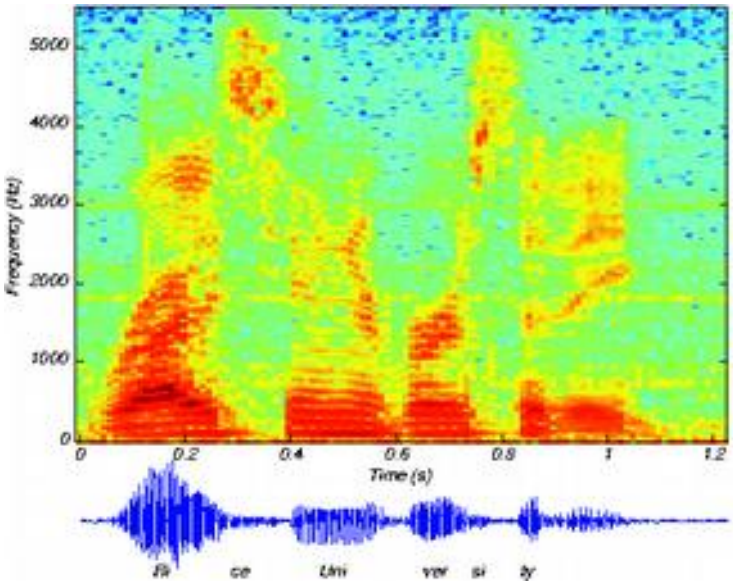



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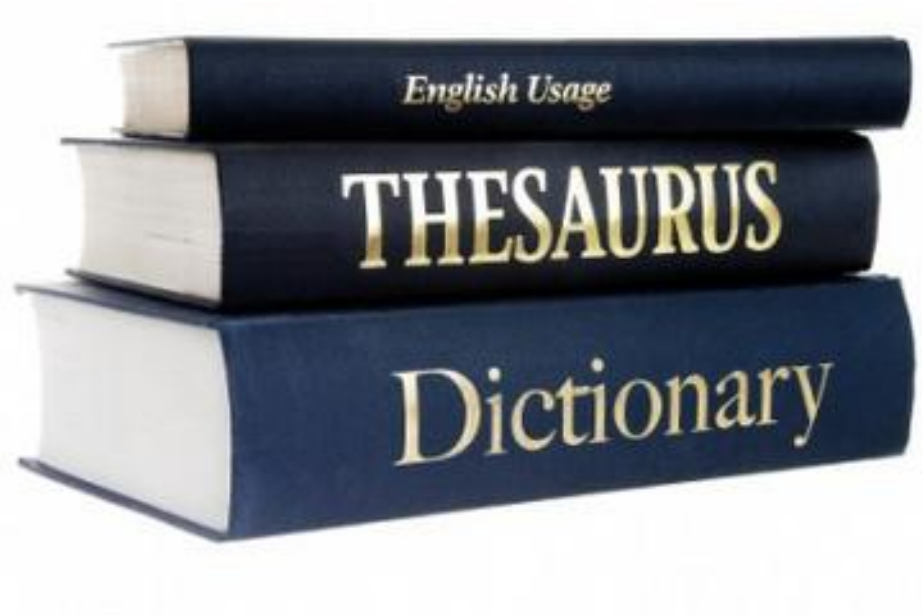




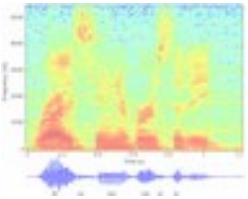

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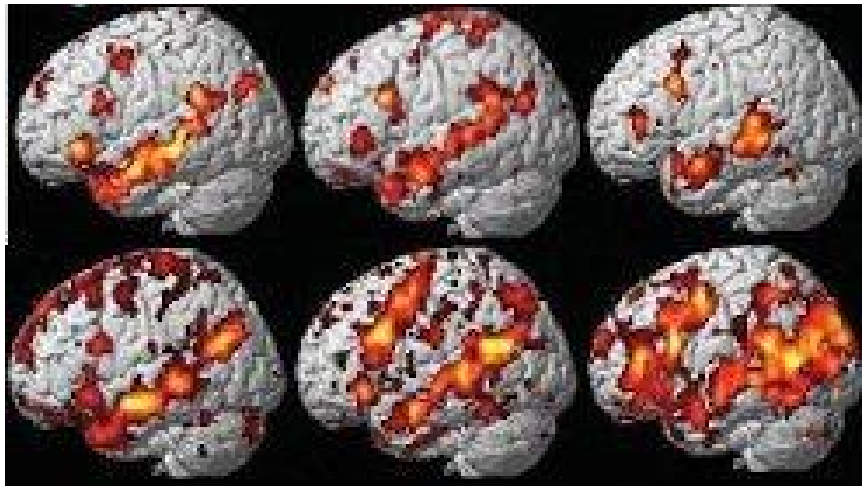




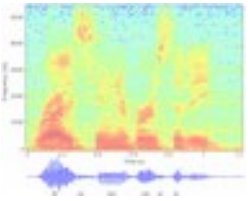
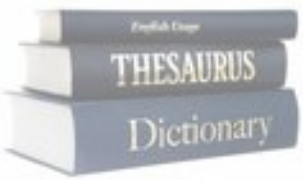

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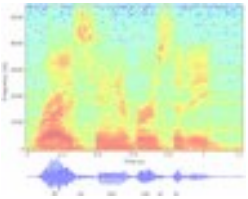
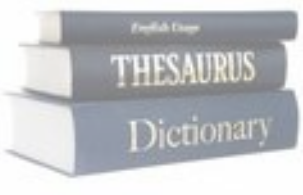

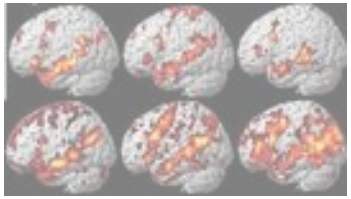

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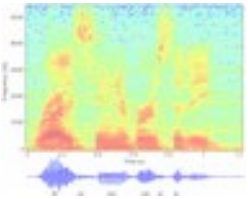
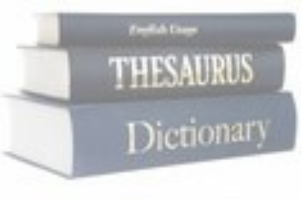

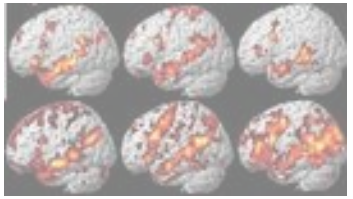


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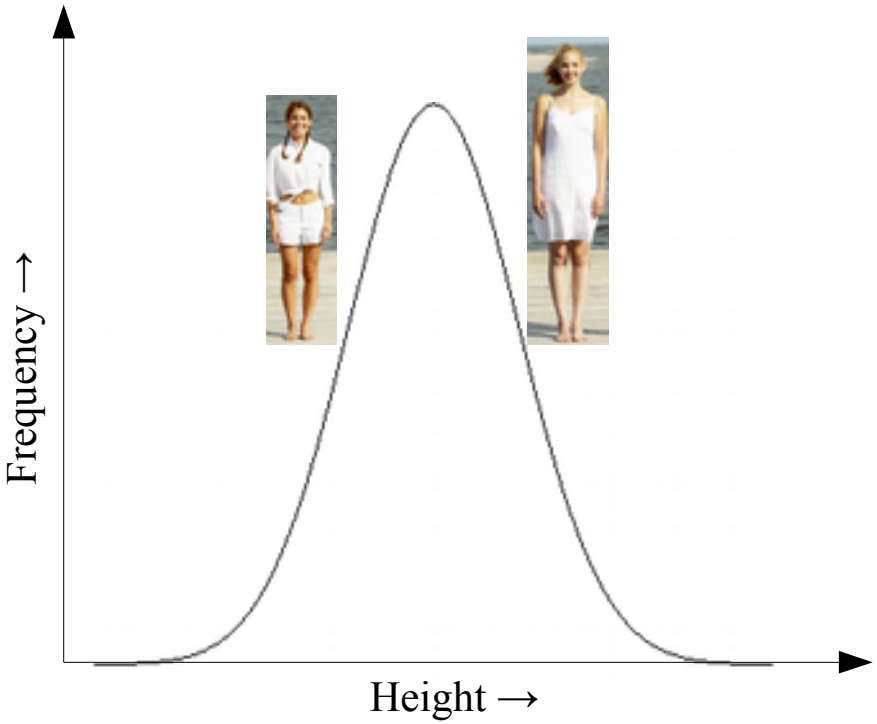

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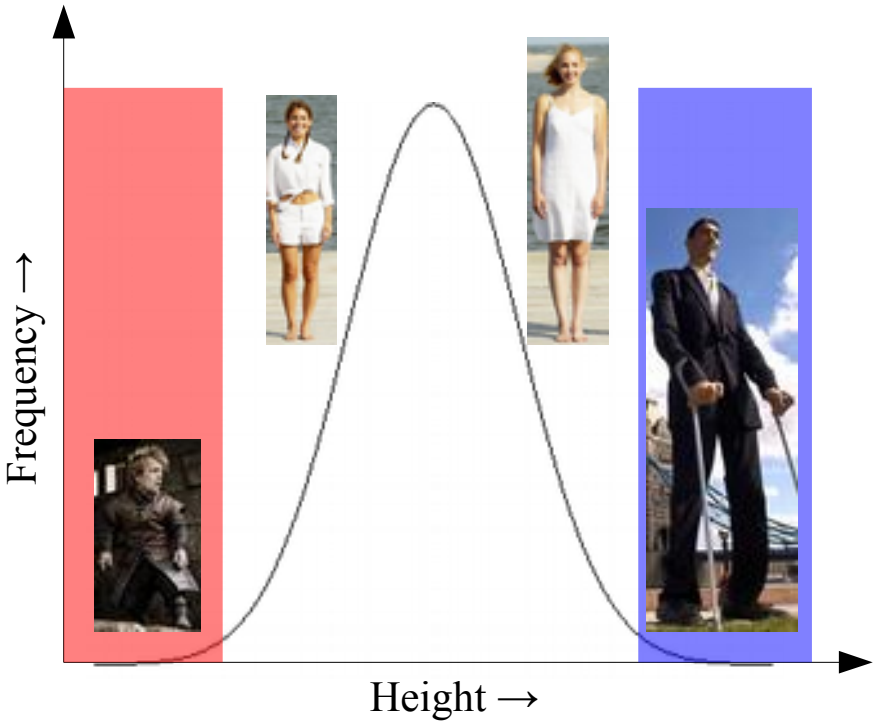

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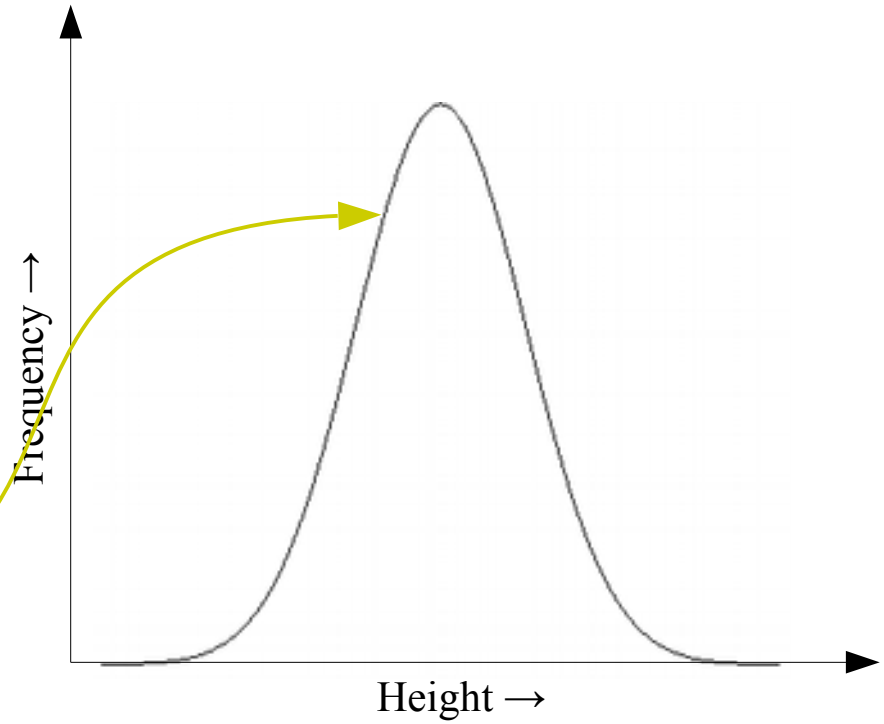

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  - gene → genetic locus
  - alleles/variants

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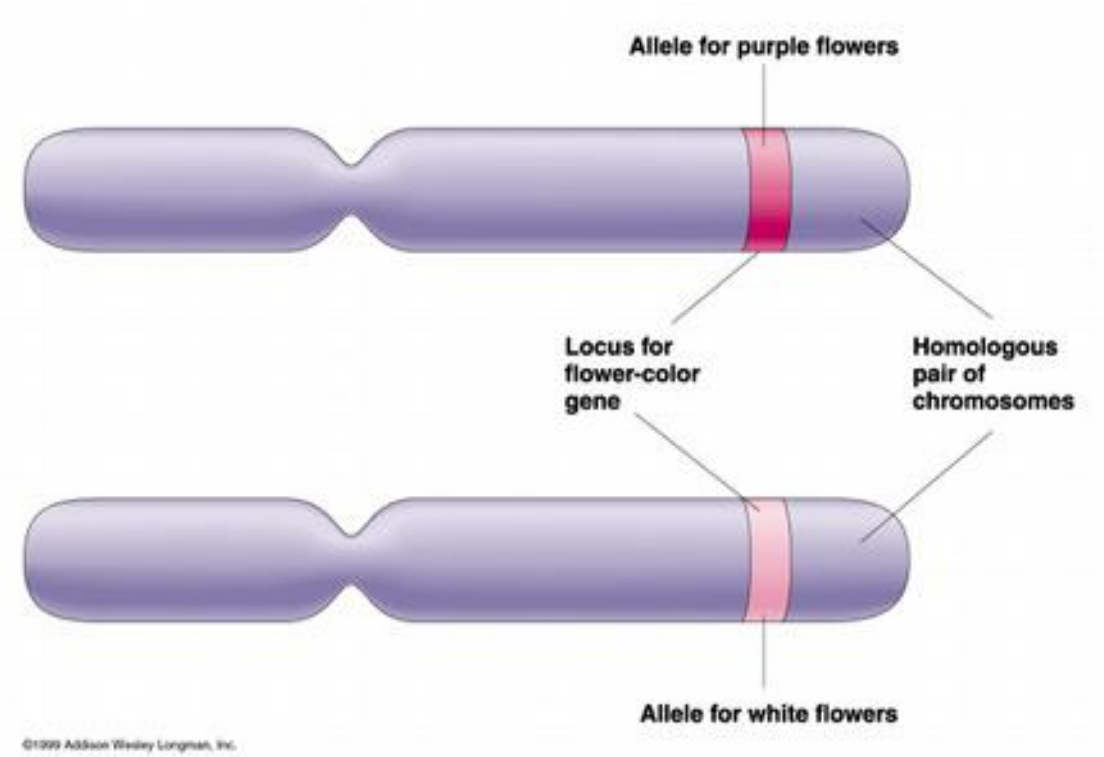

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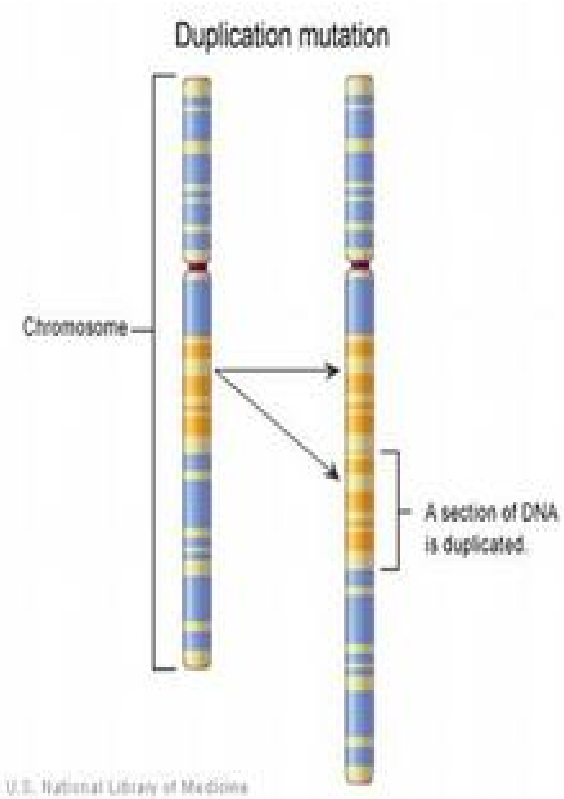

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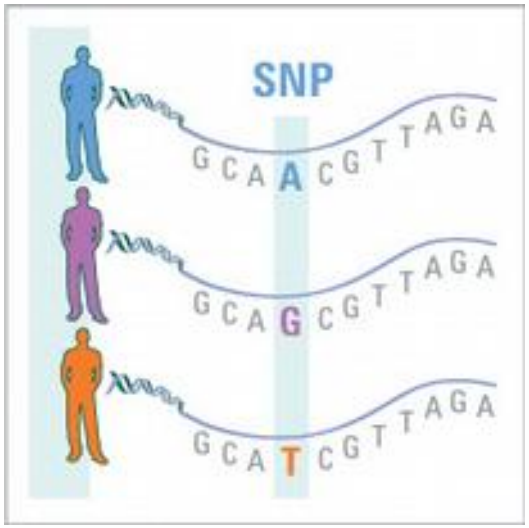

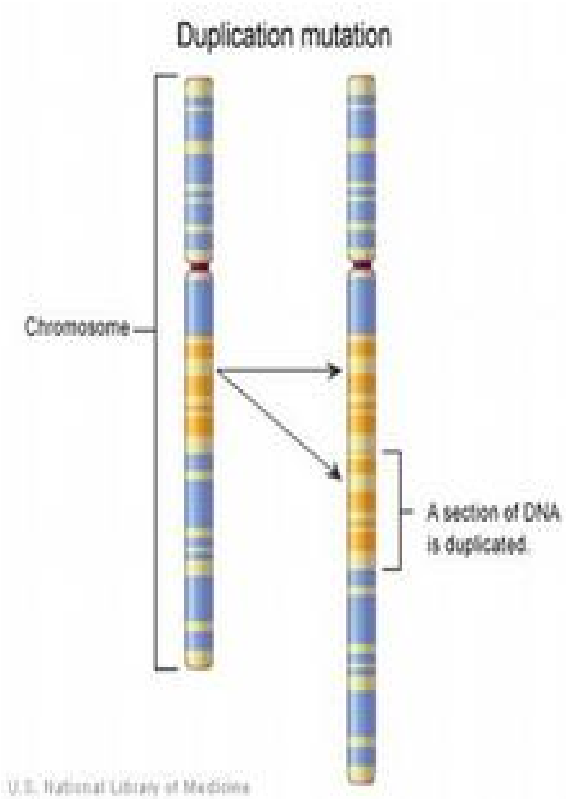

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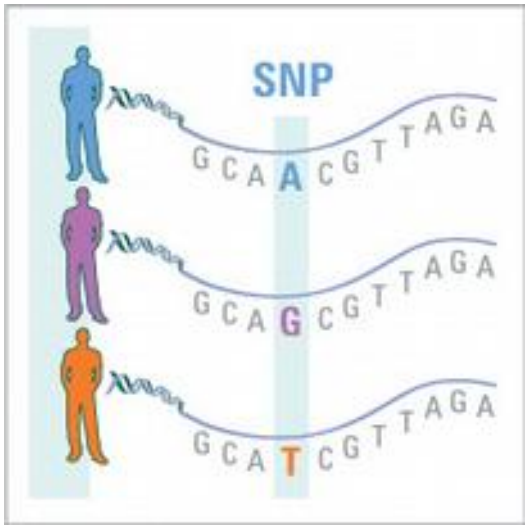

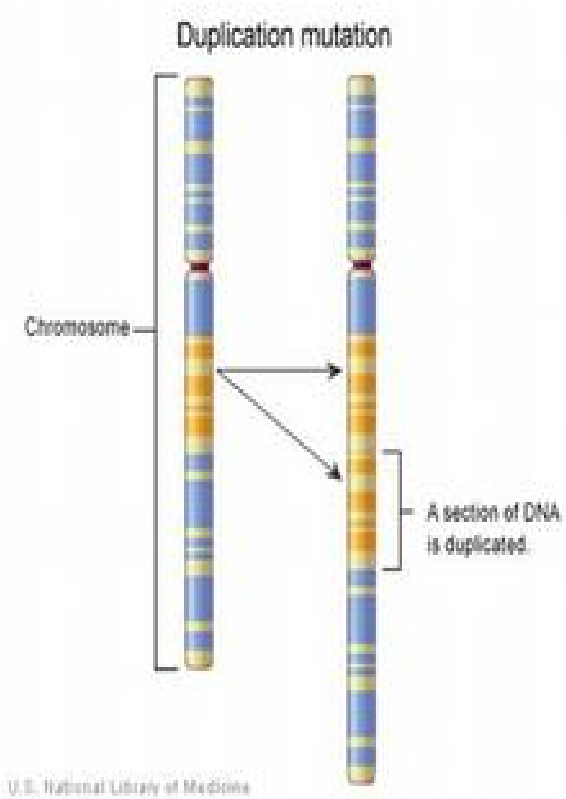

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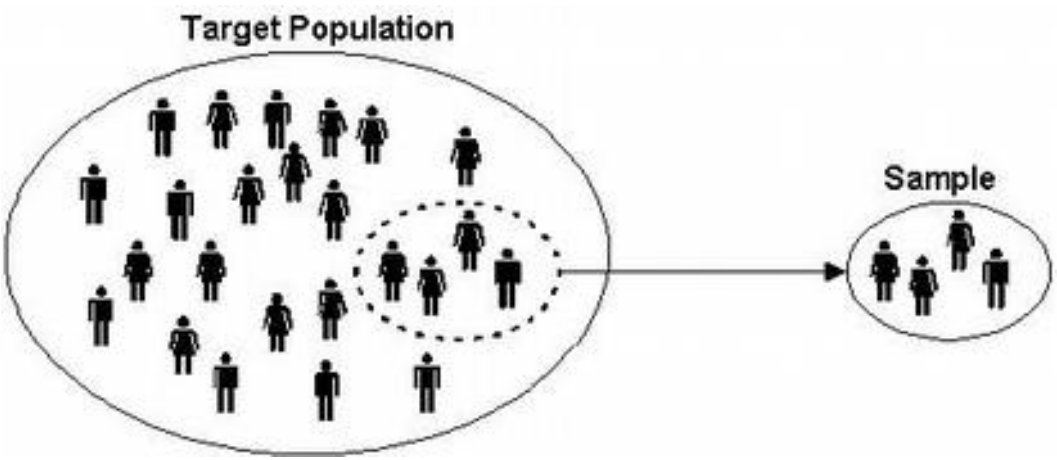

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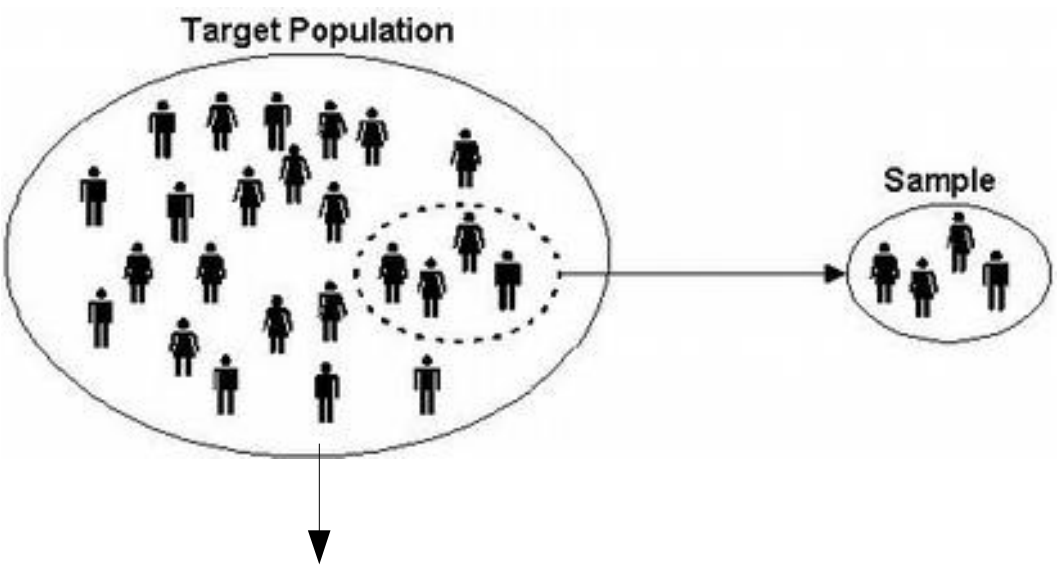

Parameters
(e.g., population mean μ)

Basic concepts

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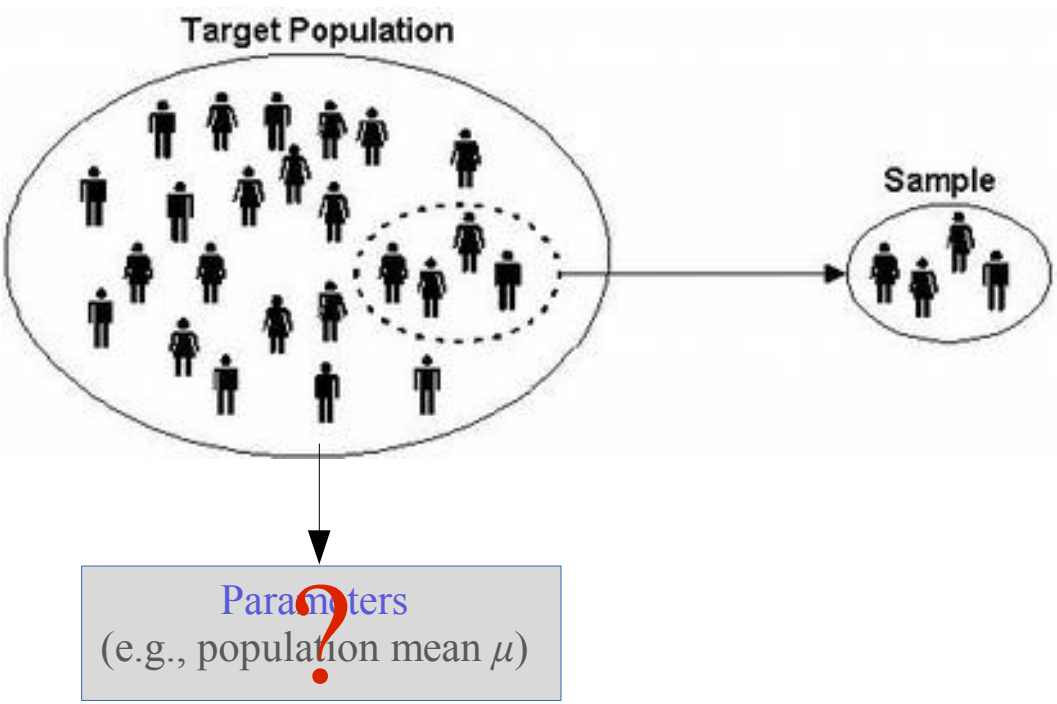

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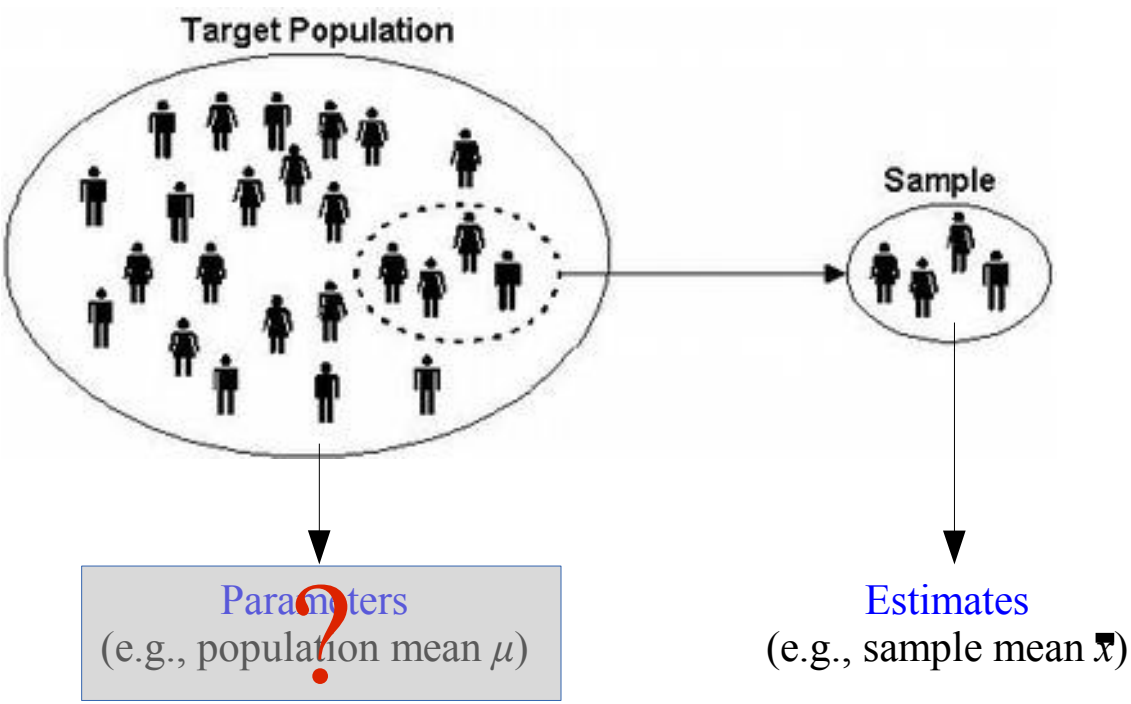

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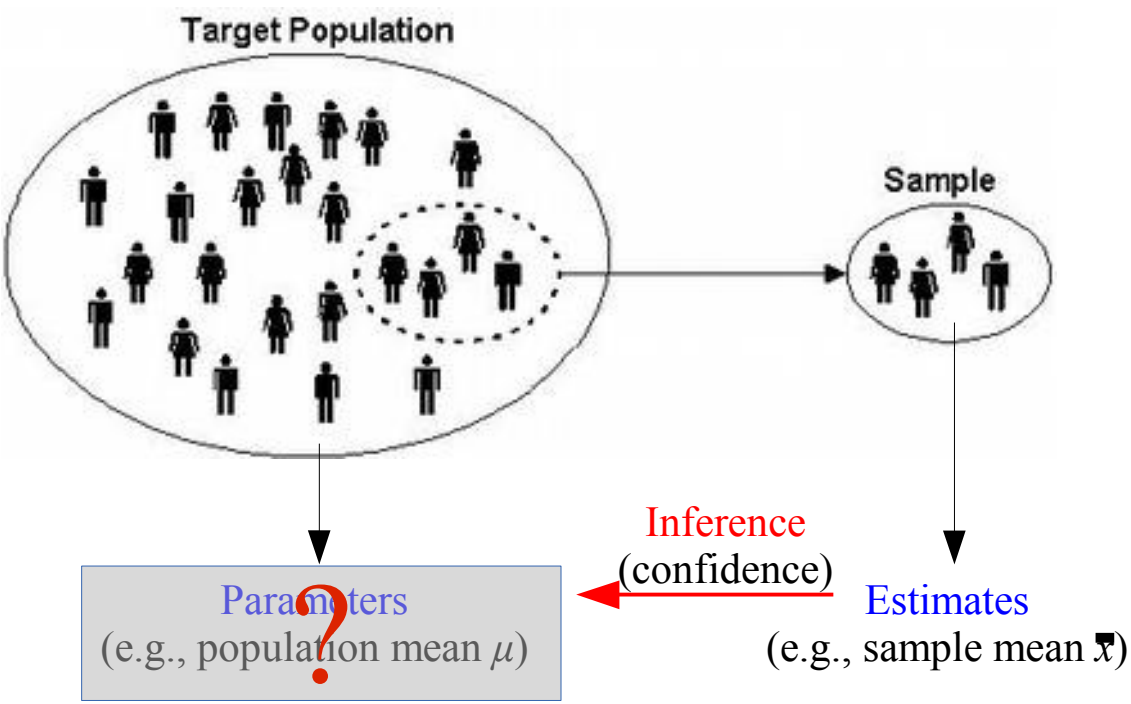

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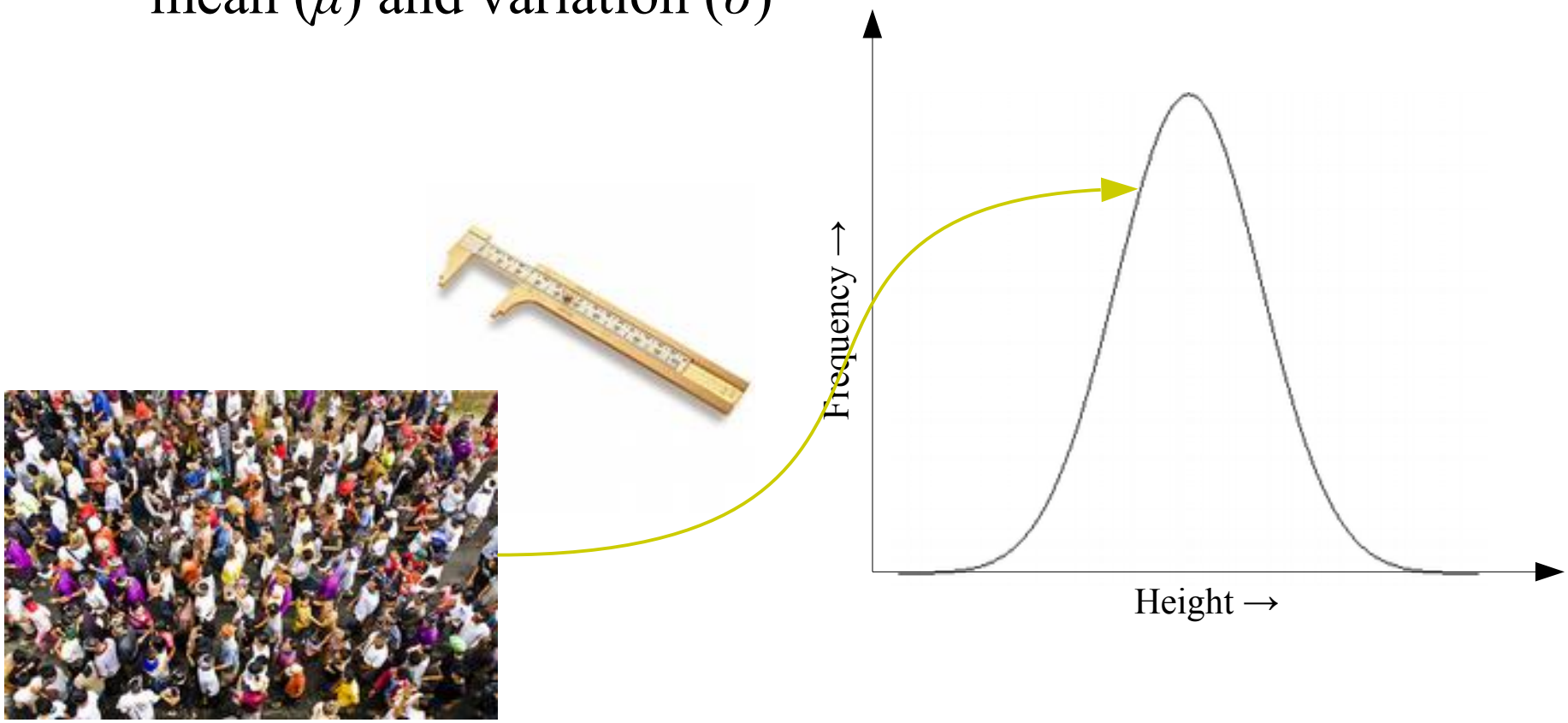

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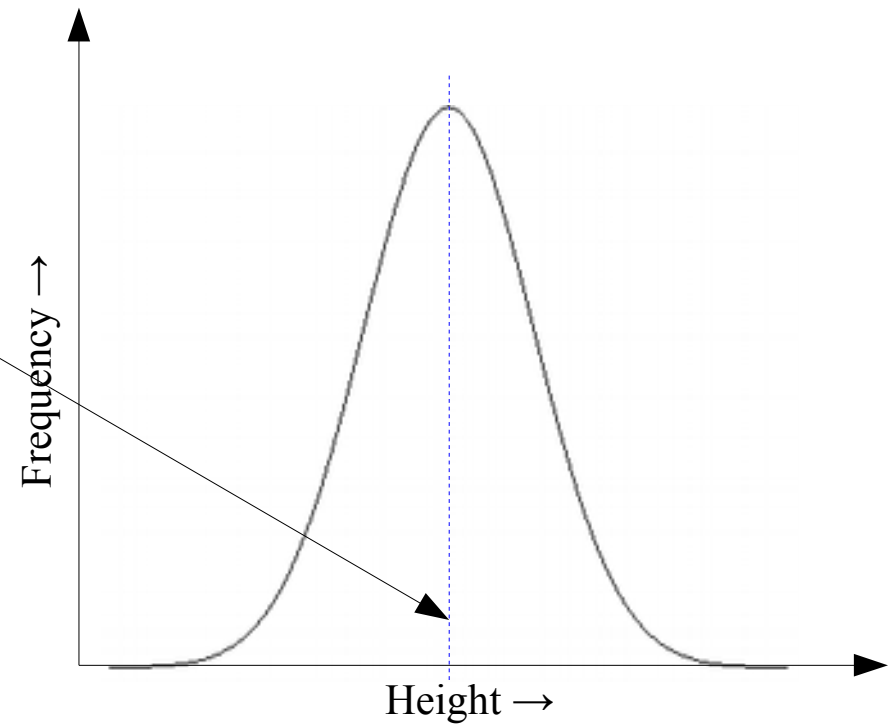

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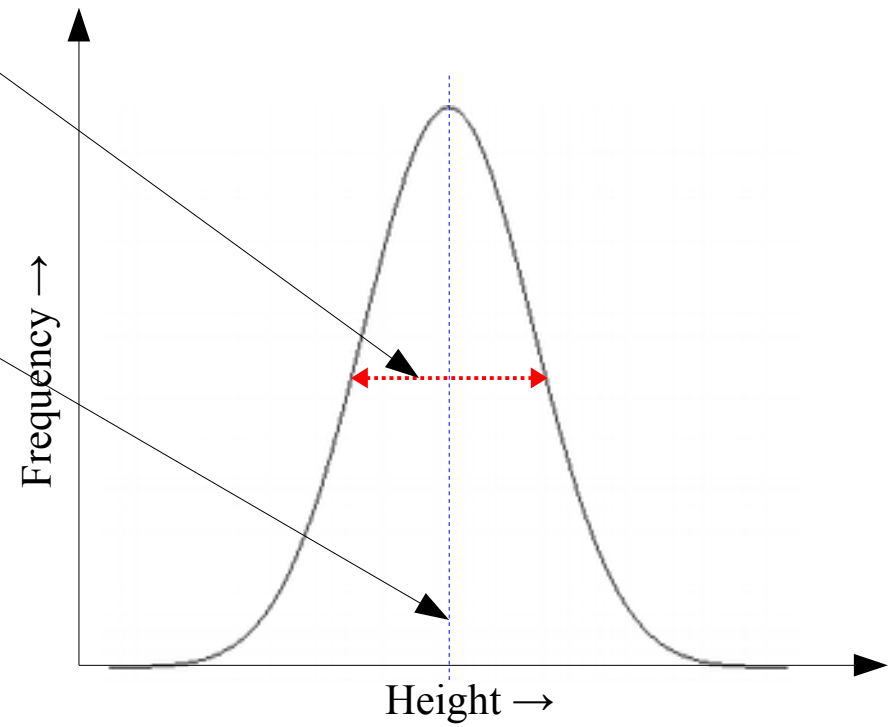

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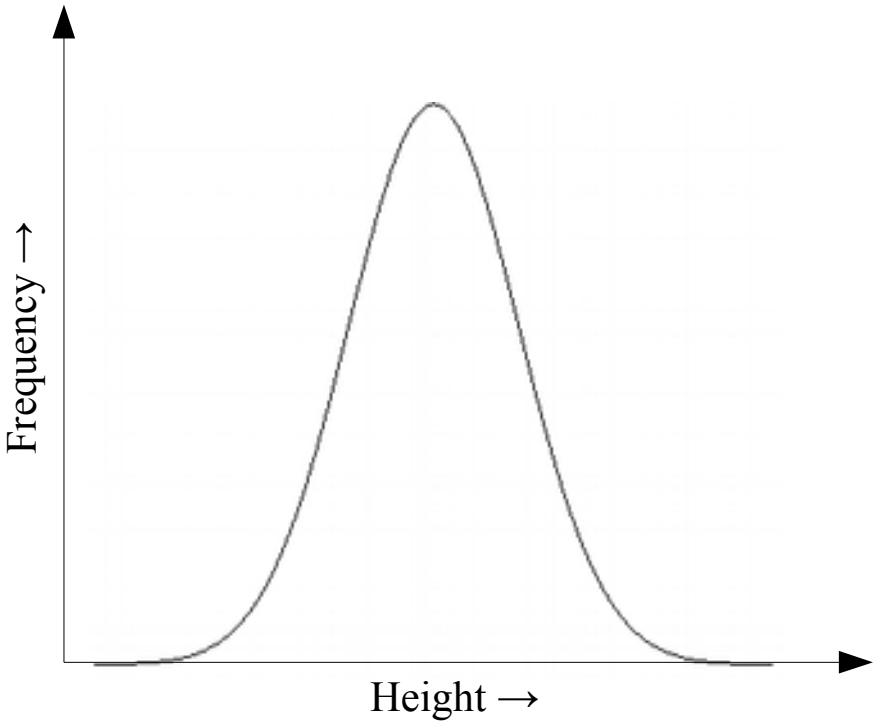

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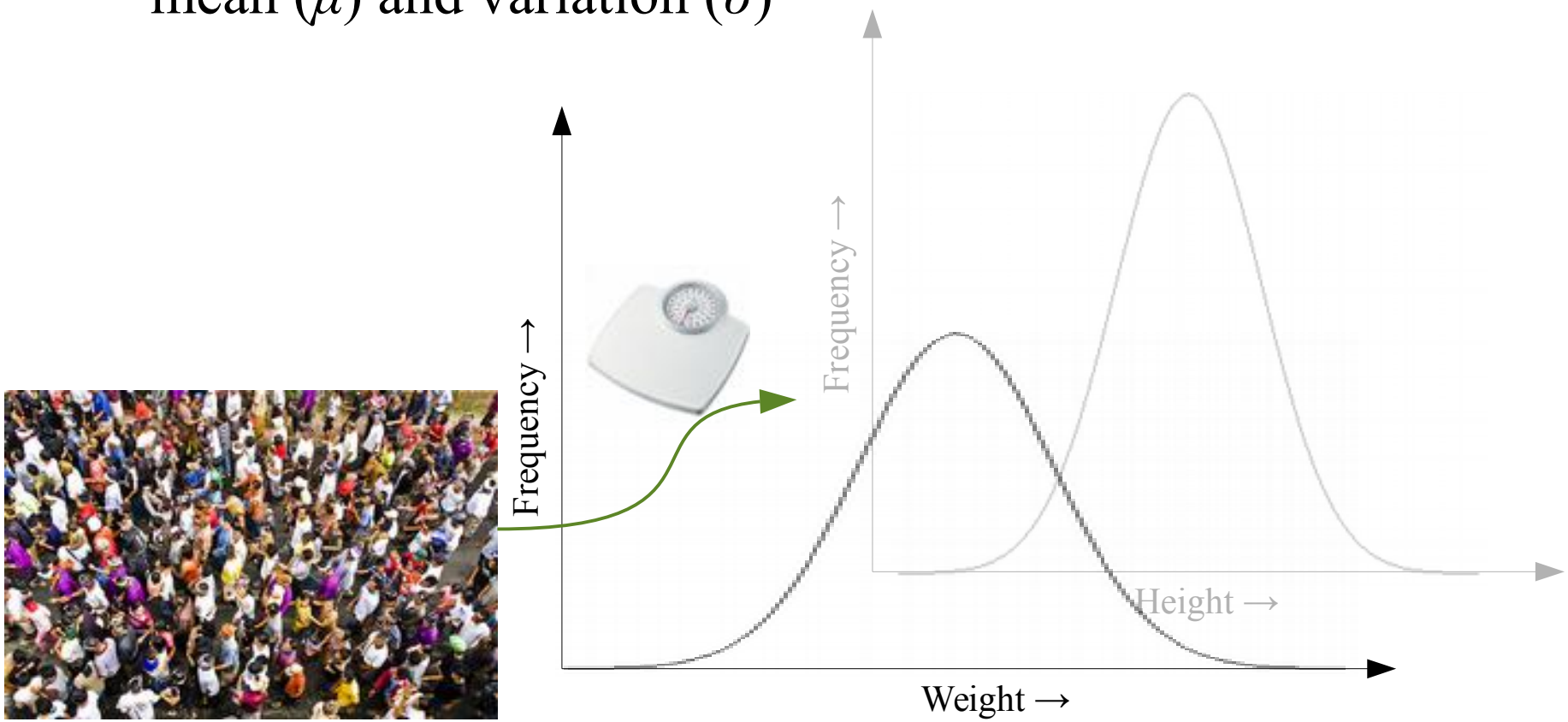

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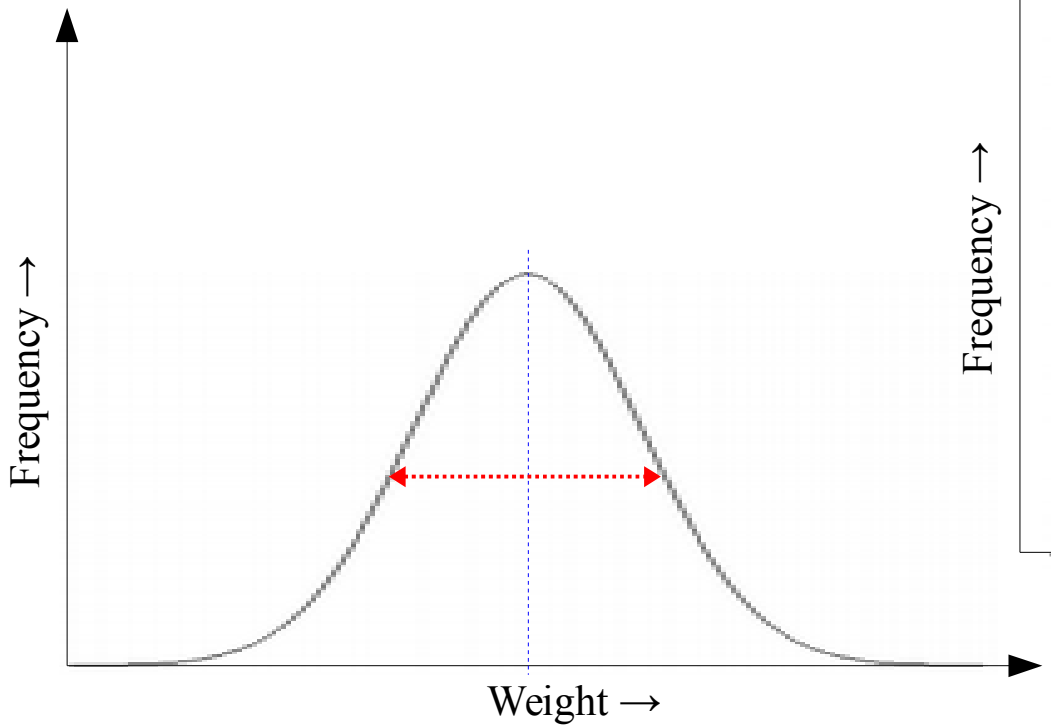

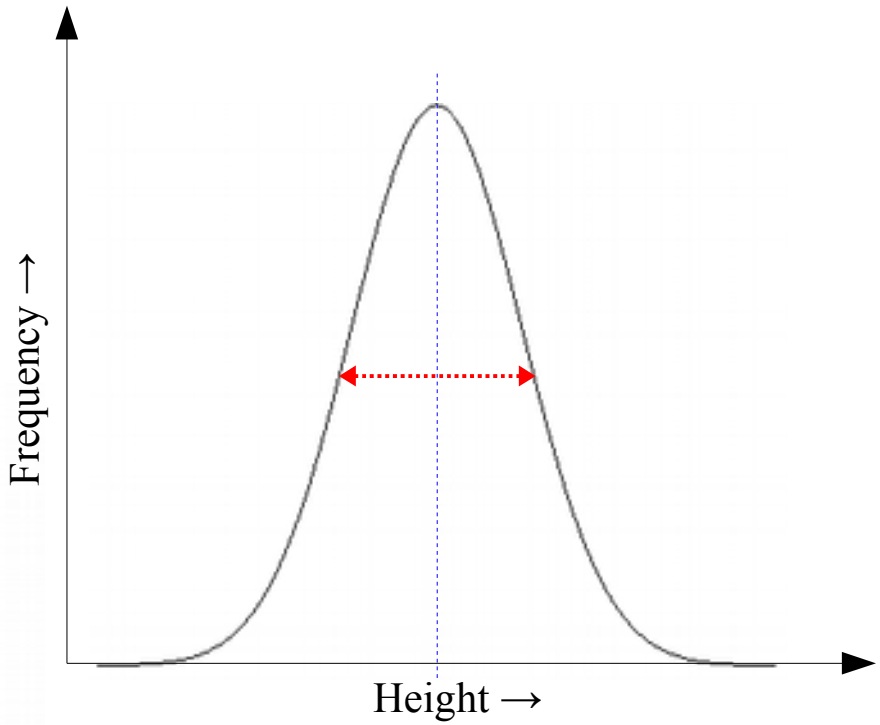

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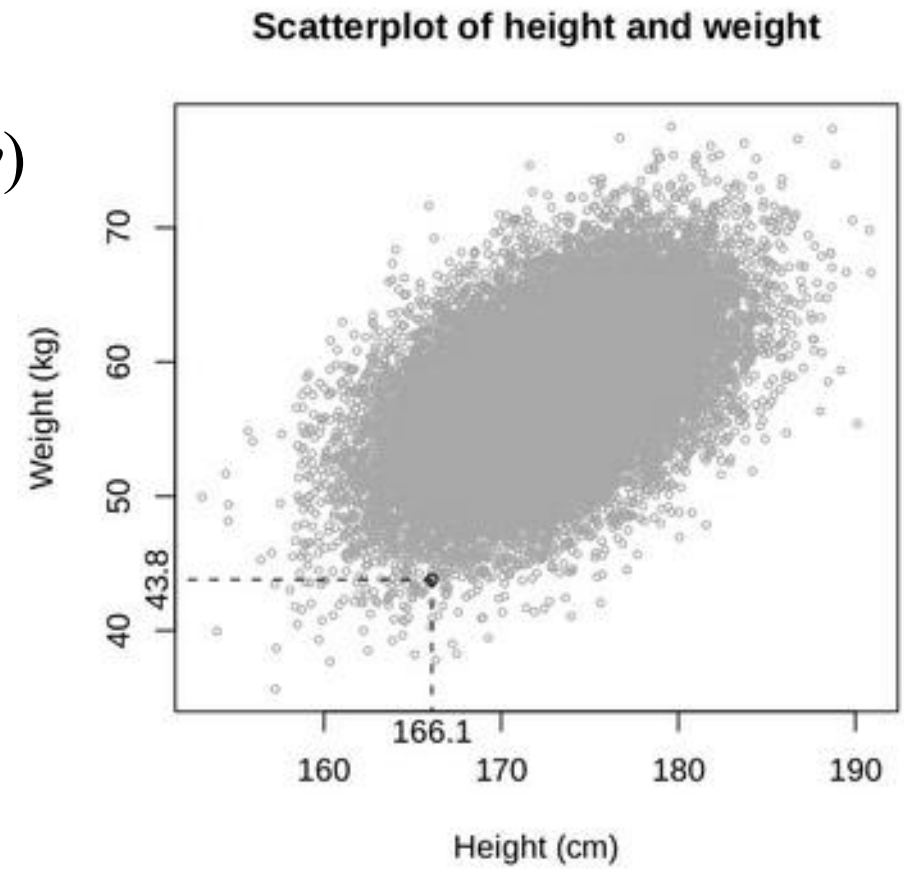

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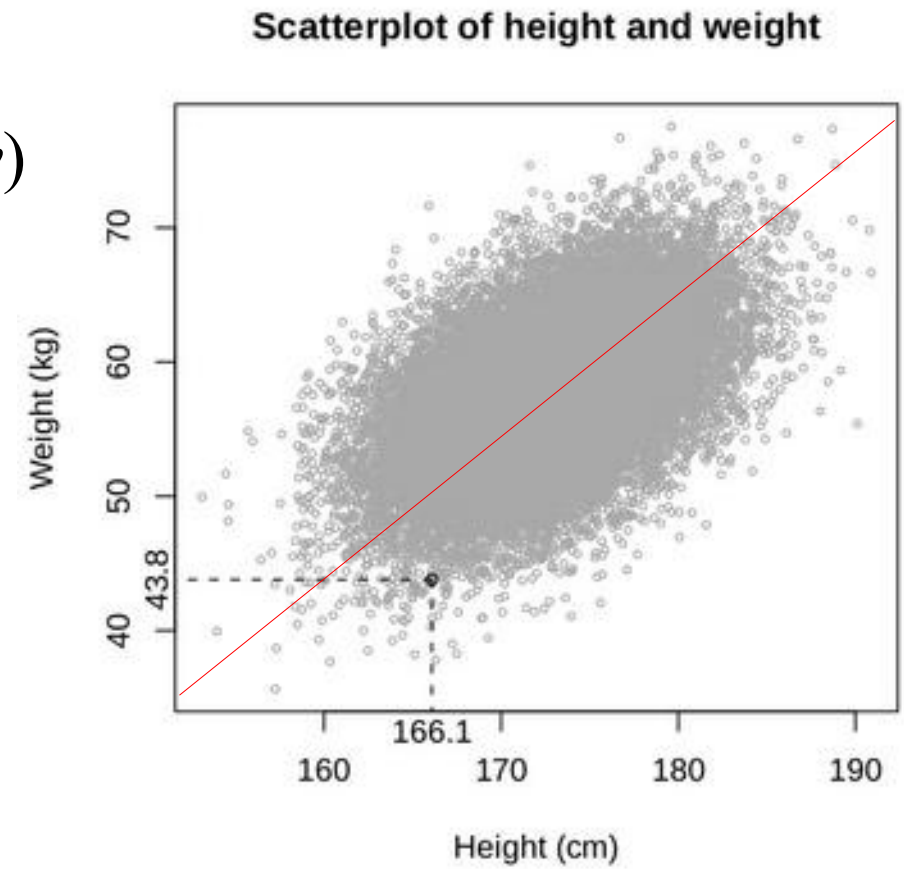

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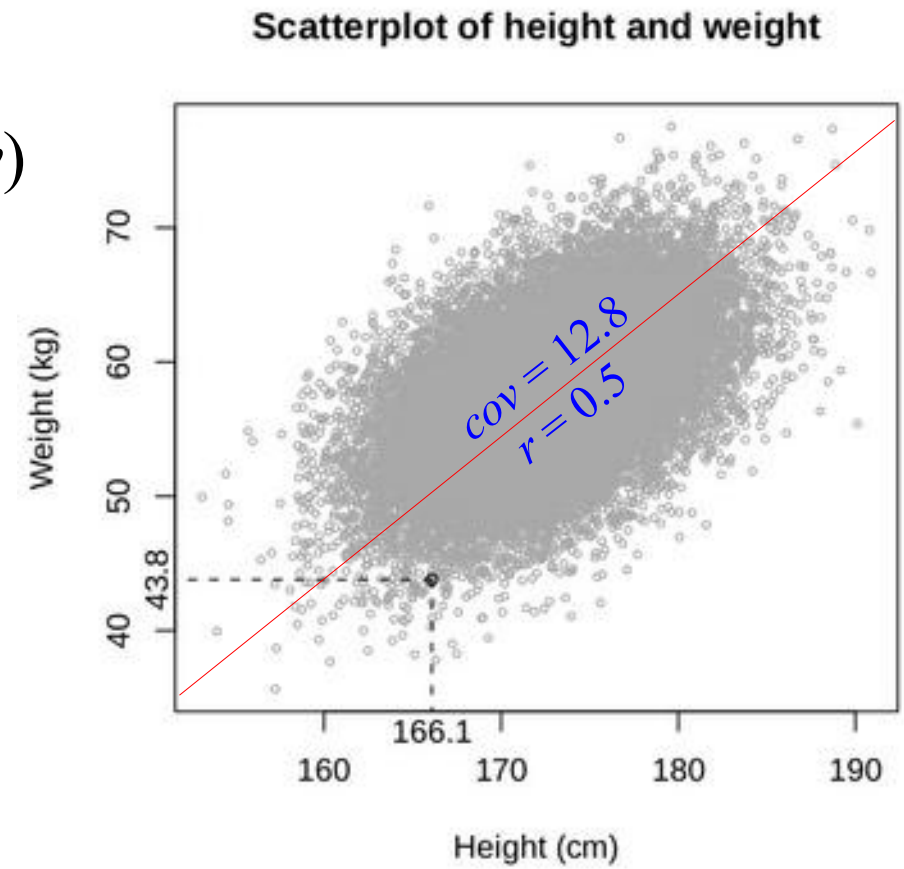

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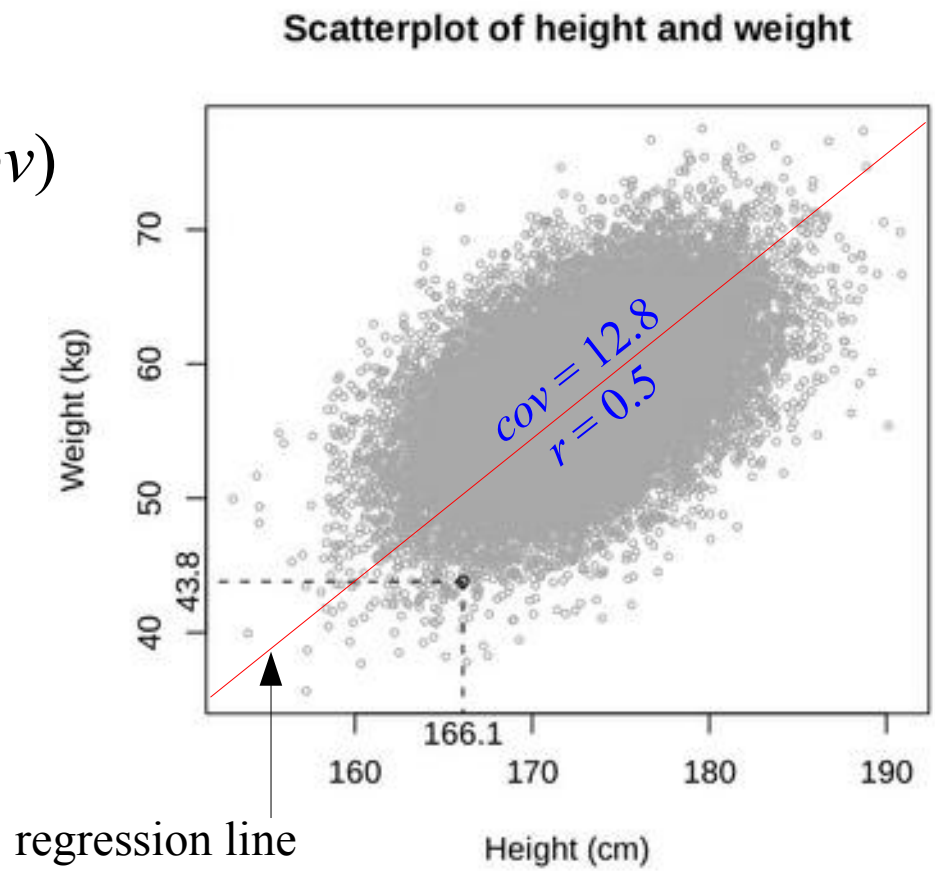

Heritability

$$H^2 =$$

Heritability

= proportion of phenotypic variation due to genotypic variation

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σ_P^2

$H^2 =$

Heritability

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σ_G^2

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Heritability

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Heritability

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$$H^2 = \frac{\text{[DNA]}}{\text{[lips]}} = \frac{\sigma_G^2}{\sigma_P^2}$$

H^2 (broad sense heritability) $\neq h^2$ (narrow sense heritability)

Heritability

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H^2 (broad sense heritability) $\neq h^2$ (narrow sense heritability)

0 (genetic variation has no effect) $\longrightarrow$ 1 (all phenotypic variation is genetic)

Heritability

Caveats in interpretation:

- Uniform traits

Heritability

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- Essential (fixed) genes

Heritability

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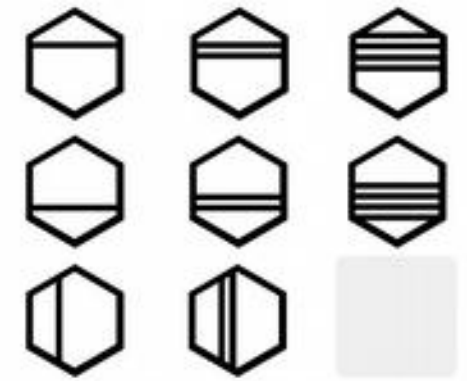

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Heritability

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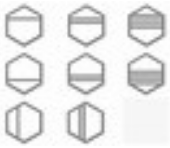
→ high heritability ≠ innateness/“genetic determinism”







Heritability

Estimation:

Twin studies  vs.  $\rightarrow h^2 = 2(r_{MZ} - r_{DZ})$

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Adoption studies  vs.  and 

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Adoption studies  vs.  and 

Non-related samples (genome-wide complex trait analysis; GCTA)

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- Moderate → high heritabilities for:

  - almost all aspects of speech and language

  - normal and pathologic

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  - (I)SLA (0.7), conversational language (0.7), formal language (0.5), vocabulary size (0.7), "phonology & articulation" (0.7) …

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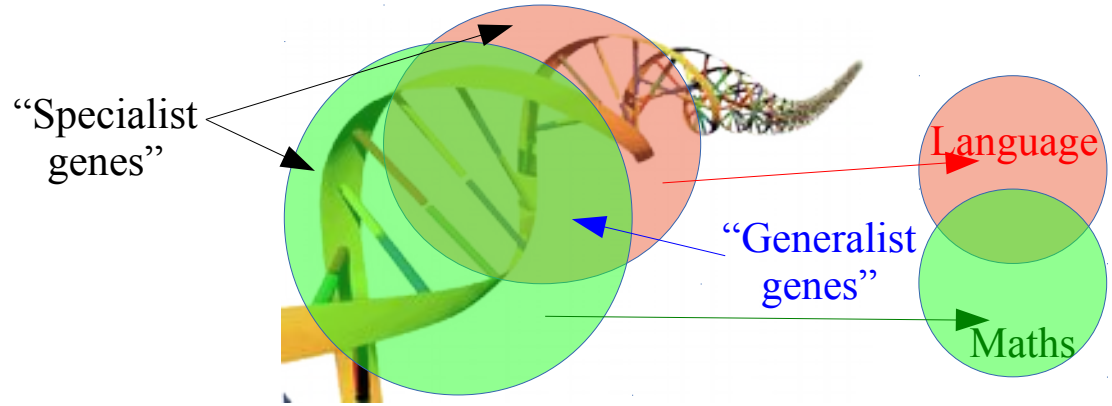
Genetic correlations:



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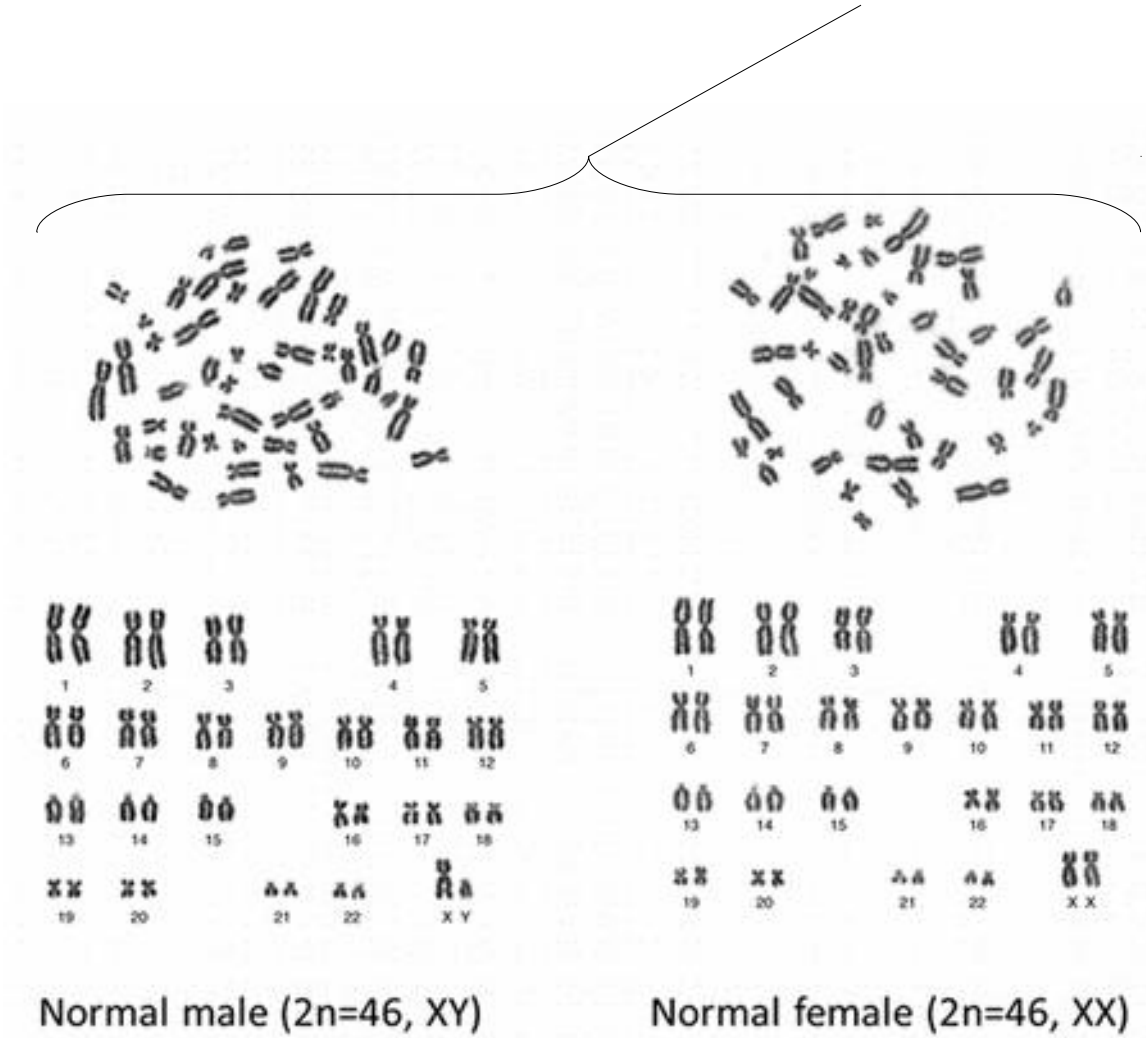

Linkage

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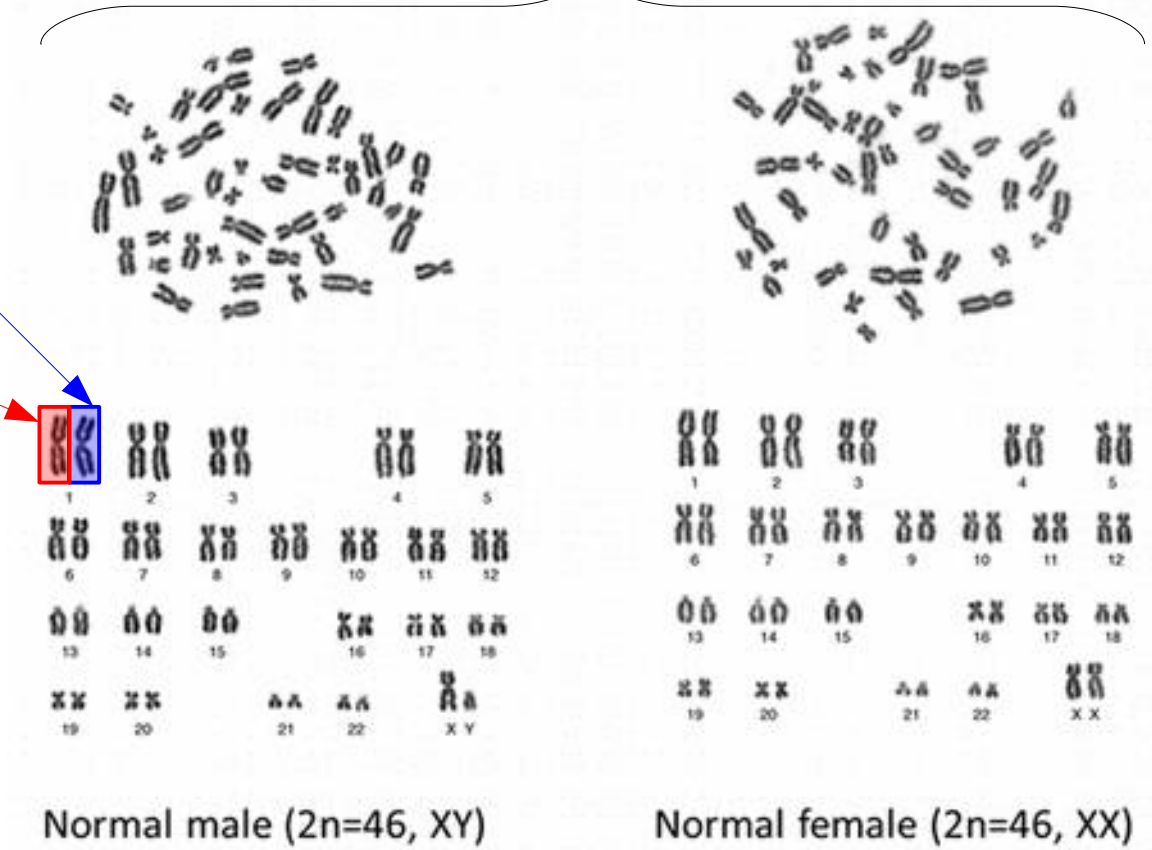
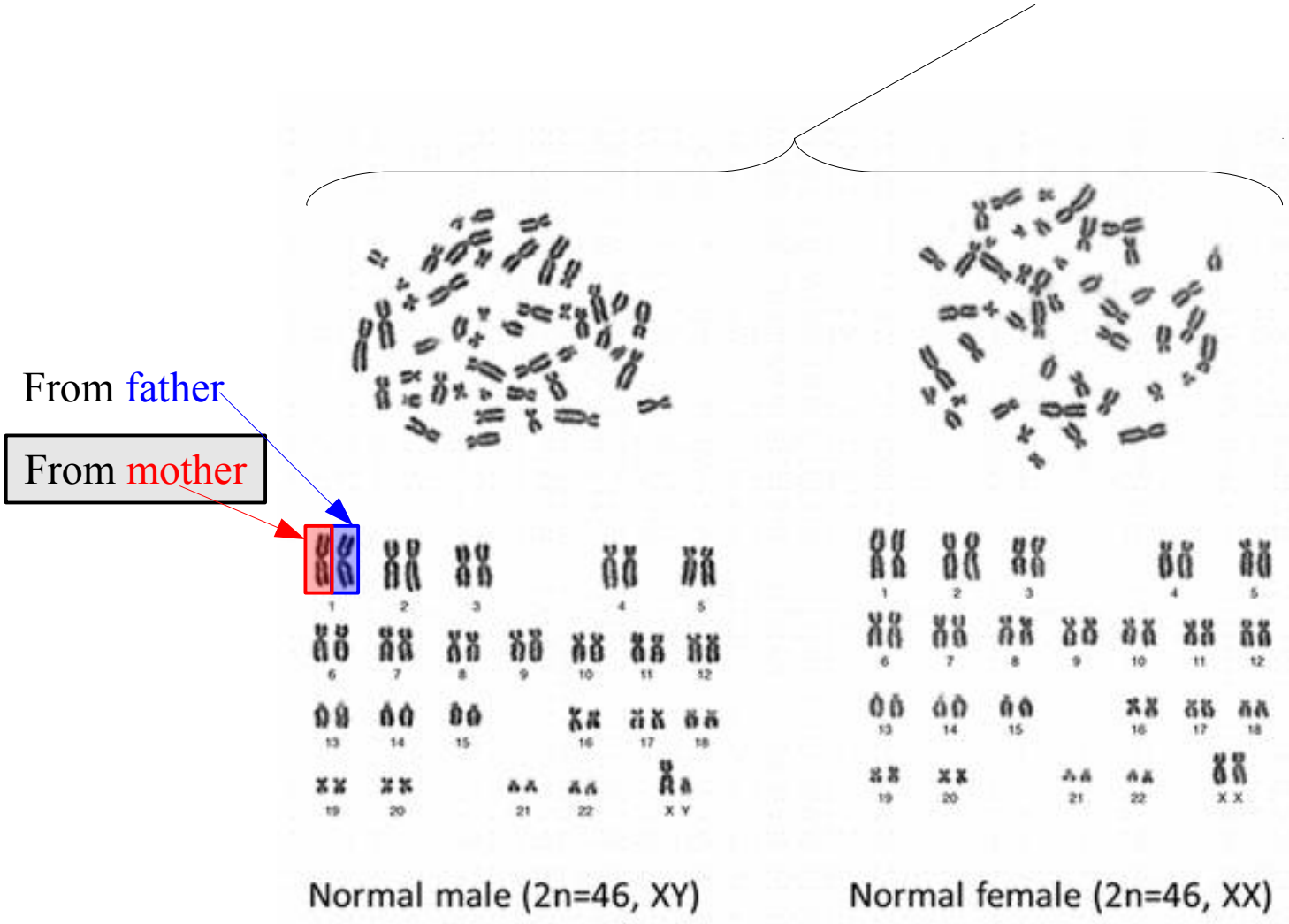
From father

From mother



Linkage

- Genome: discrete linear molecules (chromosomes + mtDNA)



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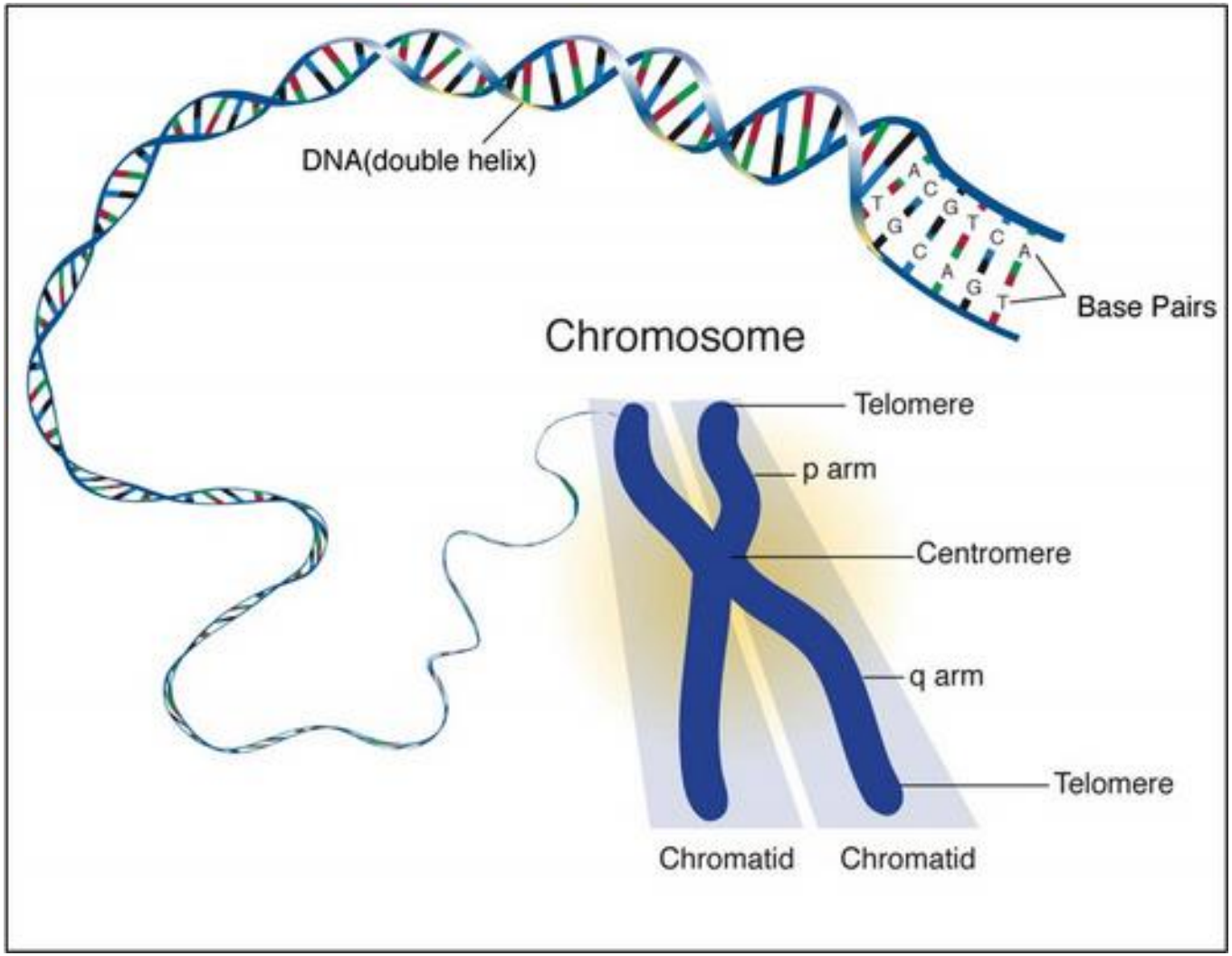

Linkage

- Genome: discrete linear molecules

  → independent loci (genes):

Peas plant

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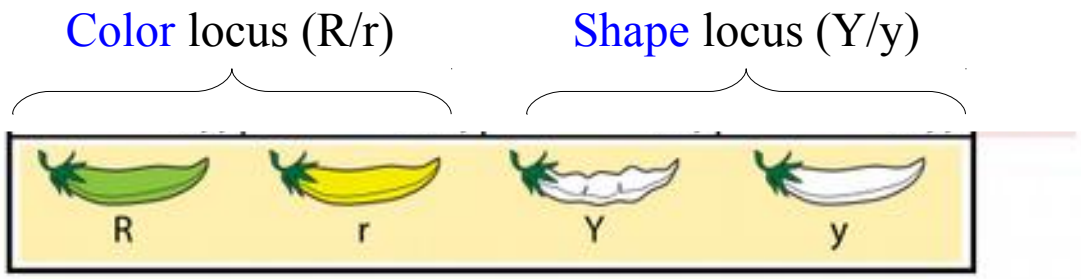

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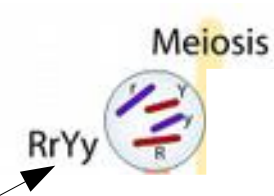

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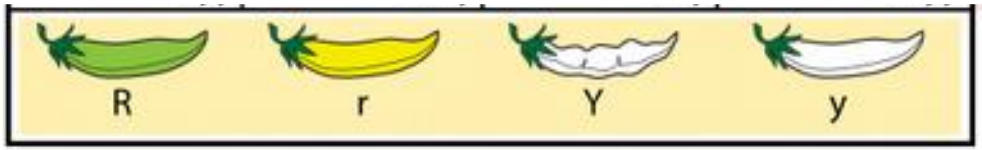

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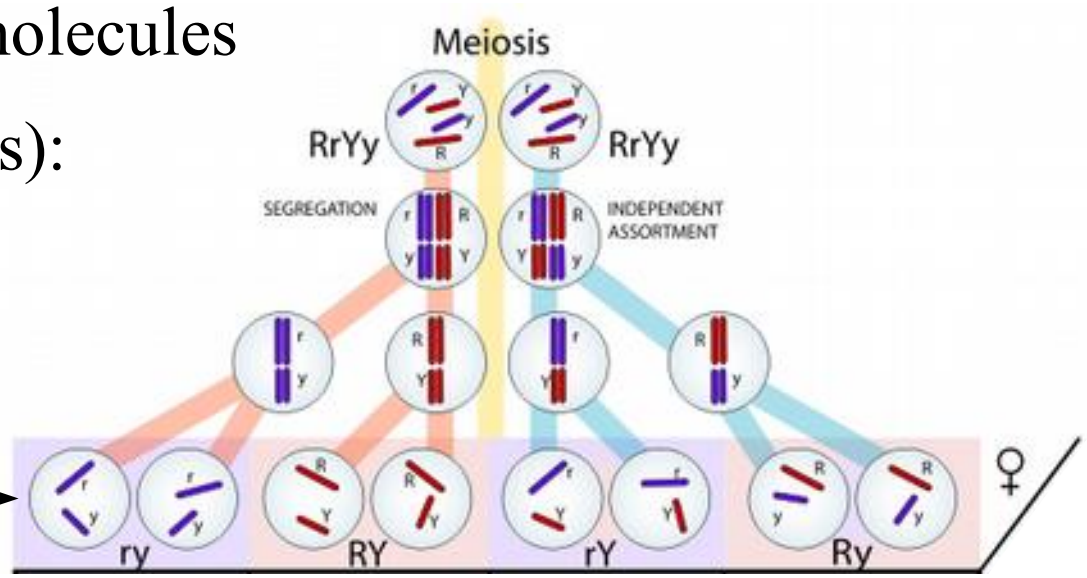

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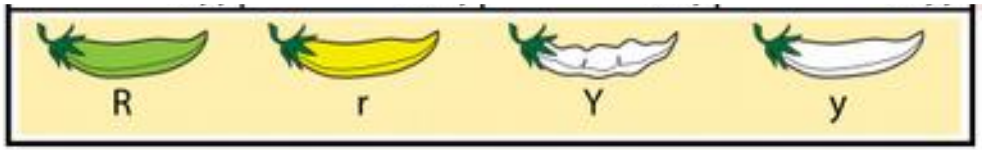

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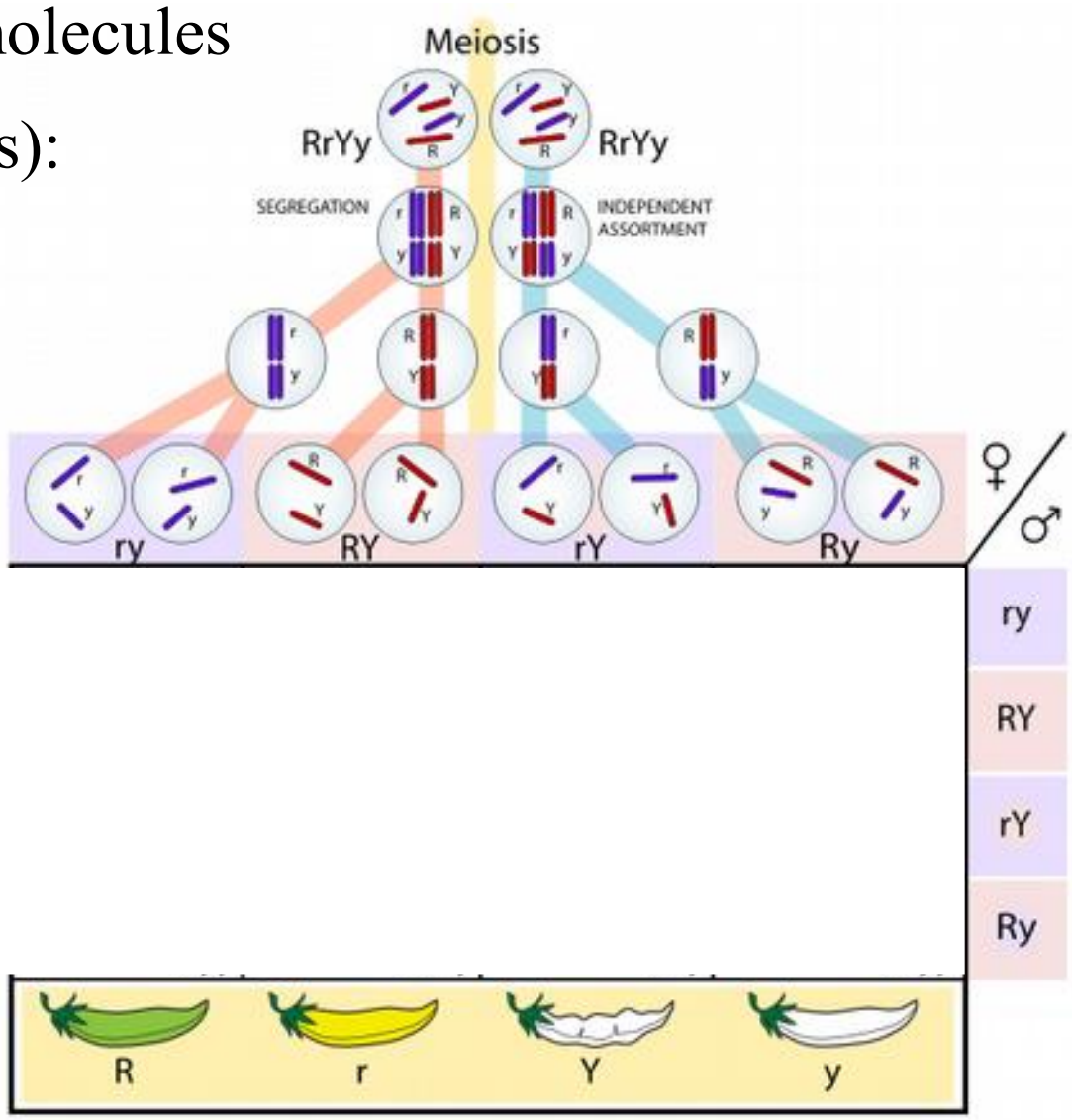

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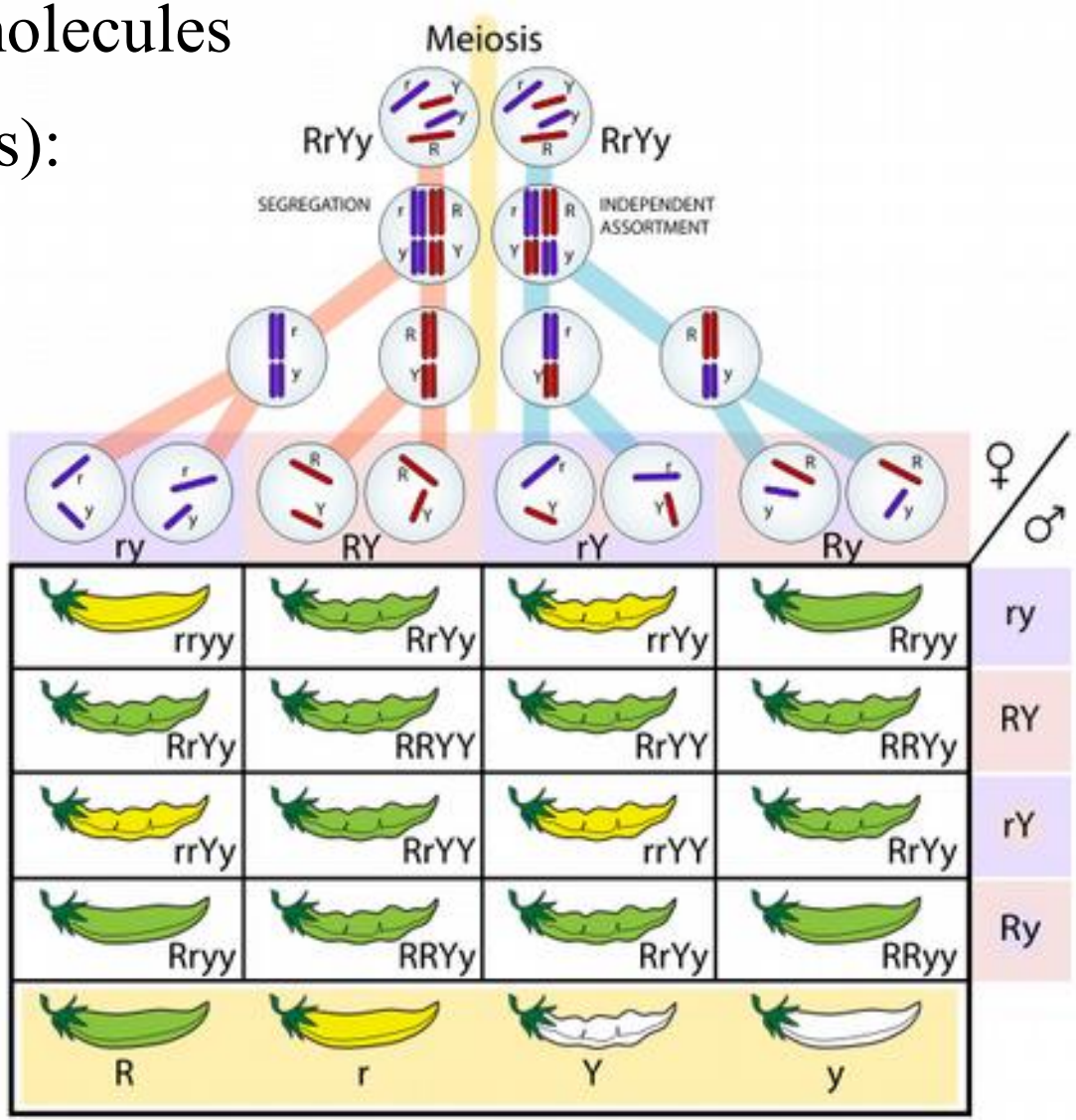

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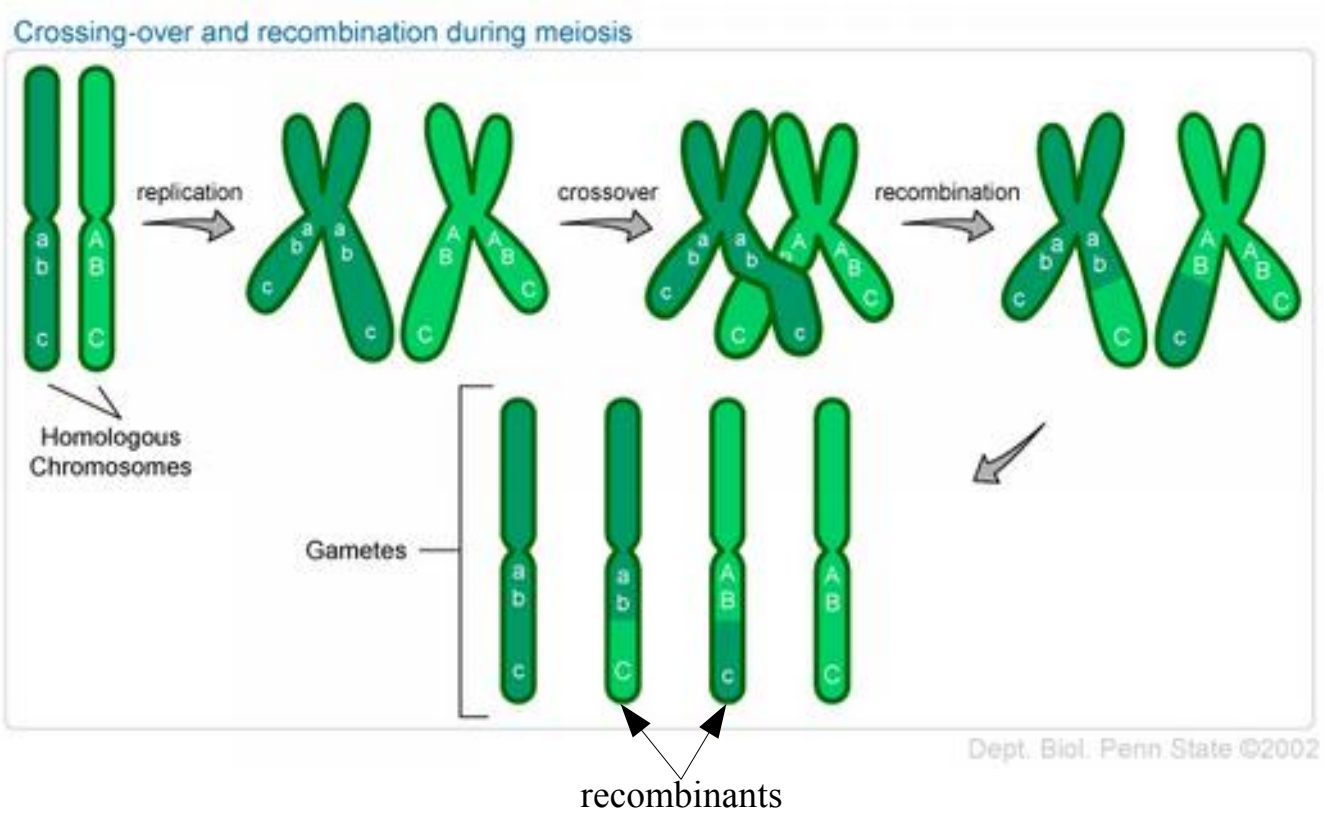
  → independent loci (genes)

  → non-independent loci → linkage + crossing over



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- recombination probability ~ physical distance
- 1 centiMorgan (cM) = 1% recombinants/generation

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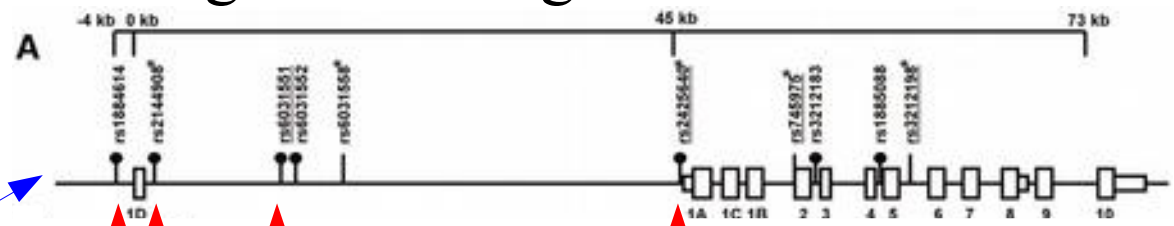
  - LD map:



Gene structure

SNPs (landmarks)

Linkage

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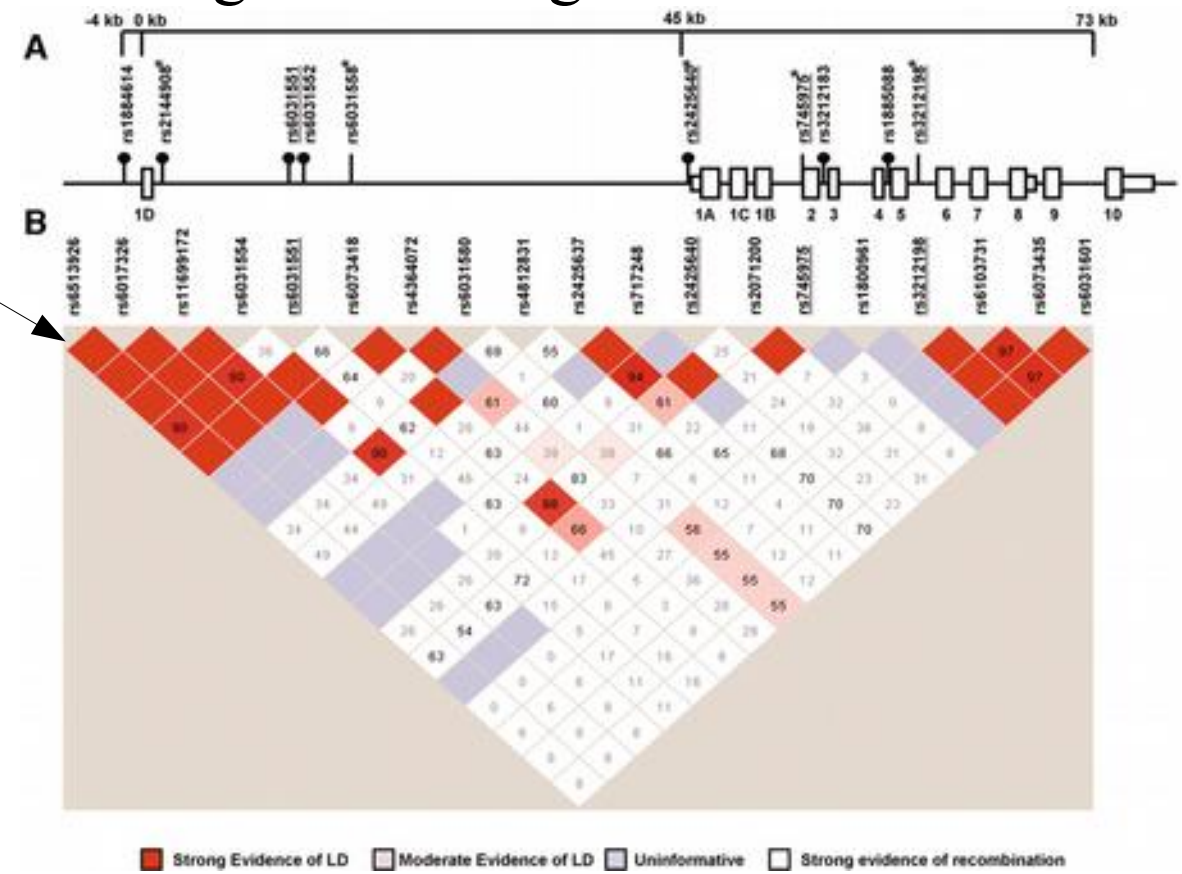
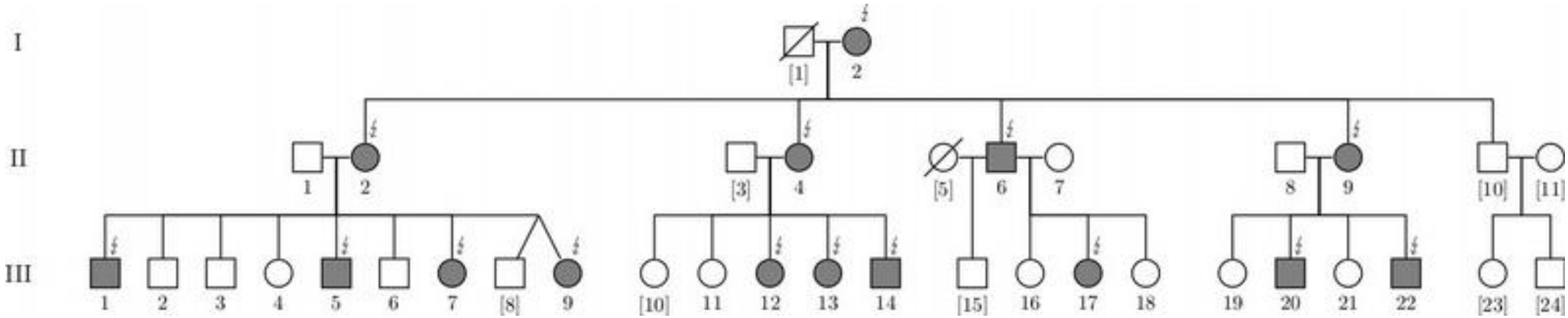


Linkage

- Large pedigrees segregating the phenotype

The “KE” family



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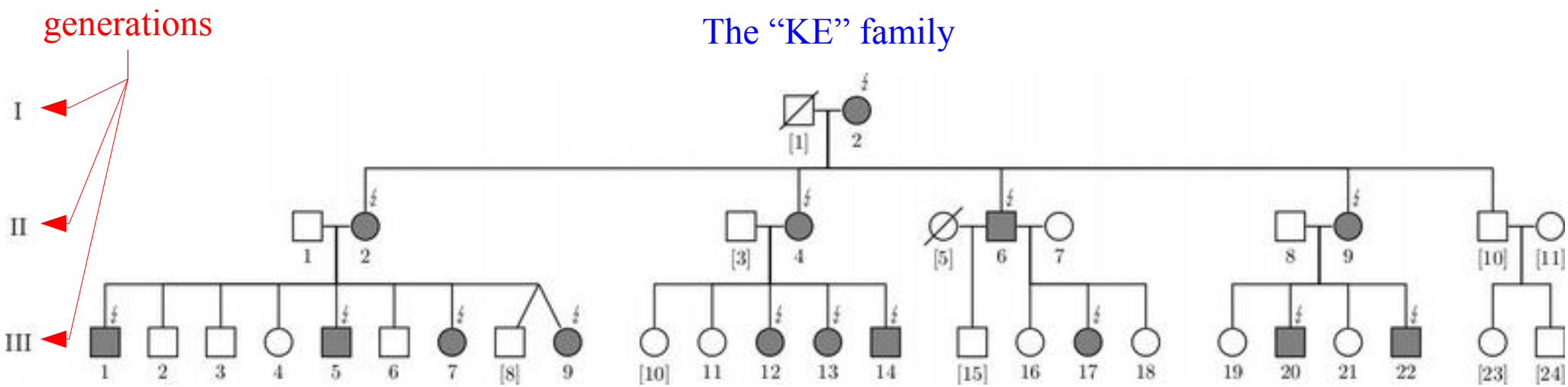

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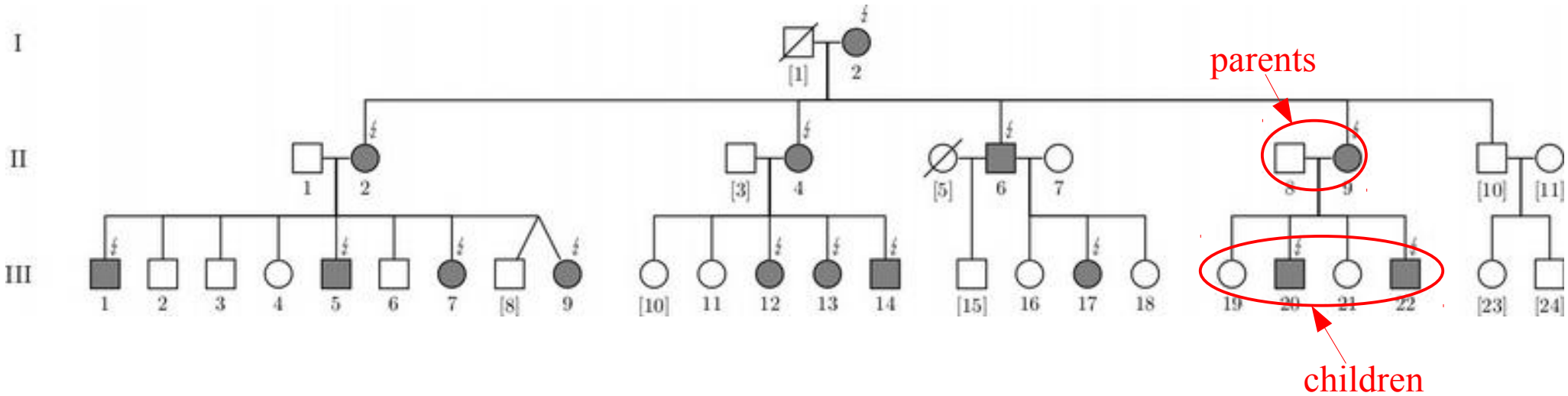

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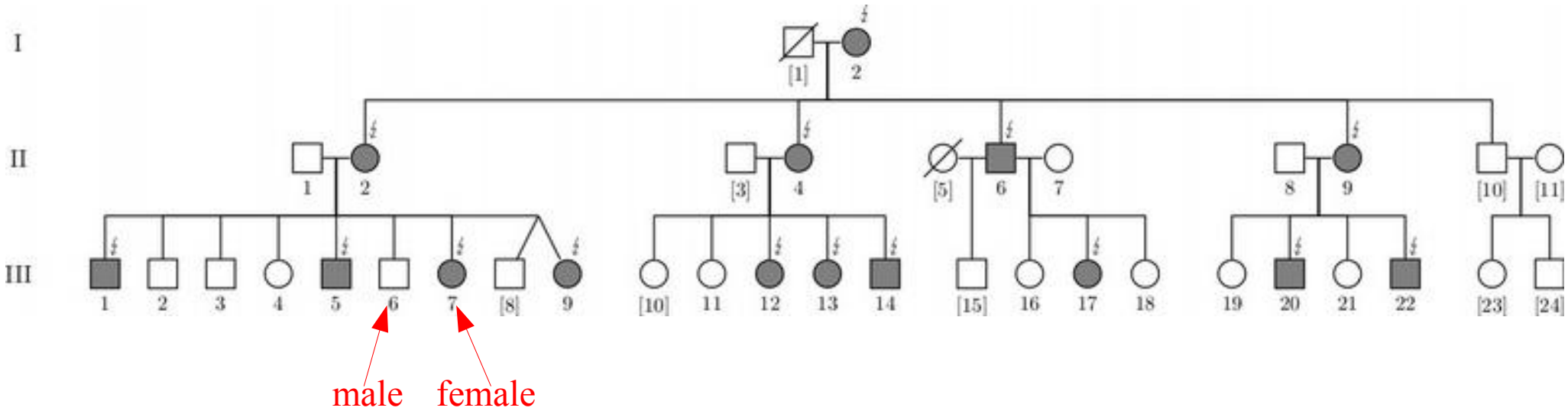

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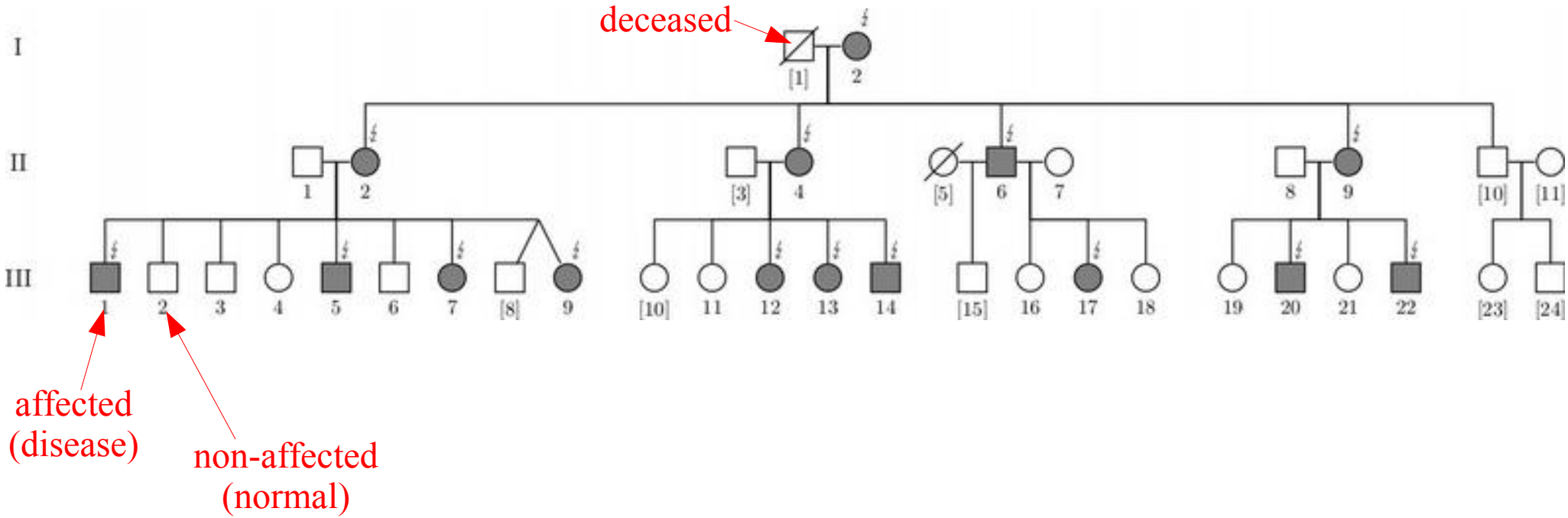

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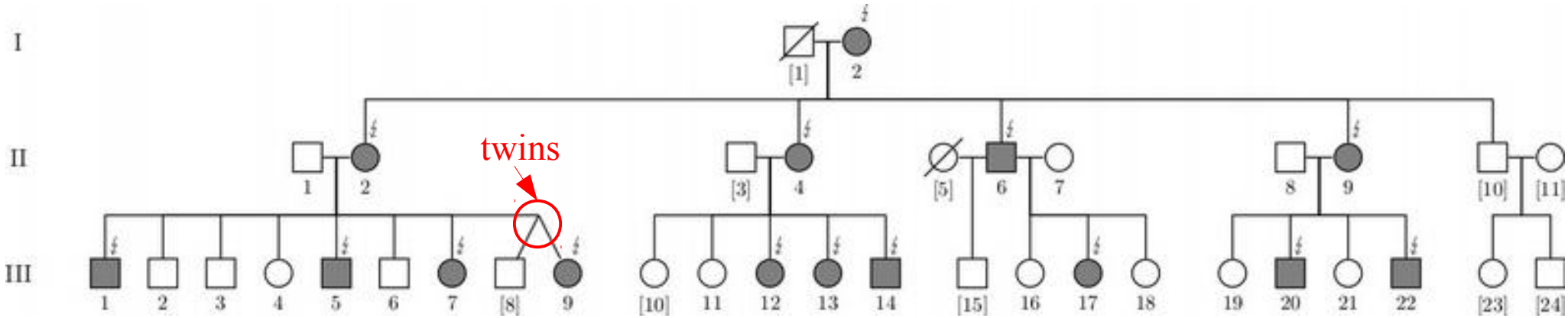

Linkage

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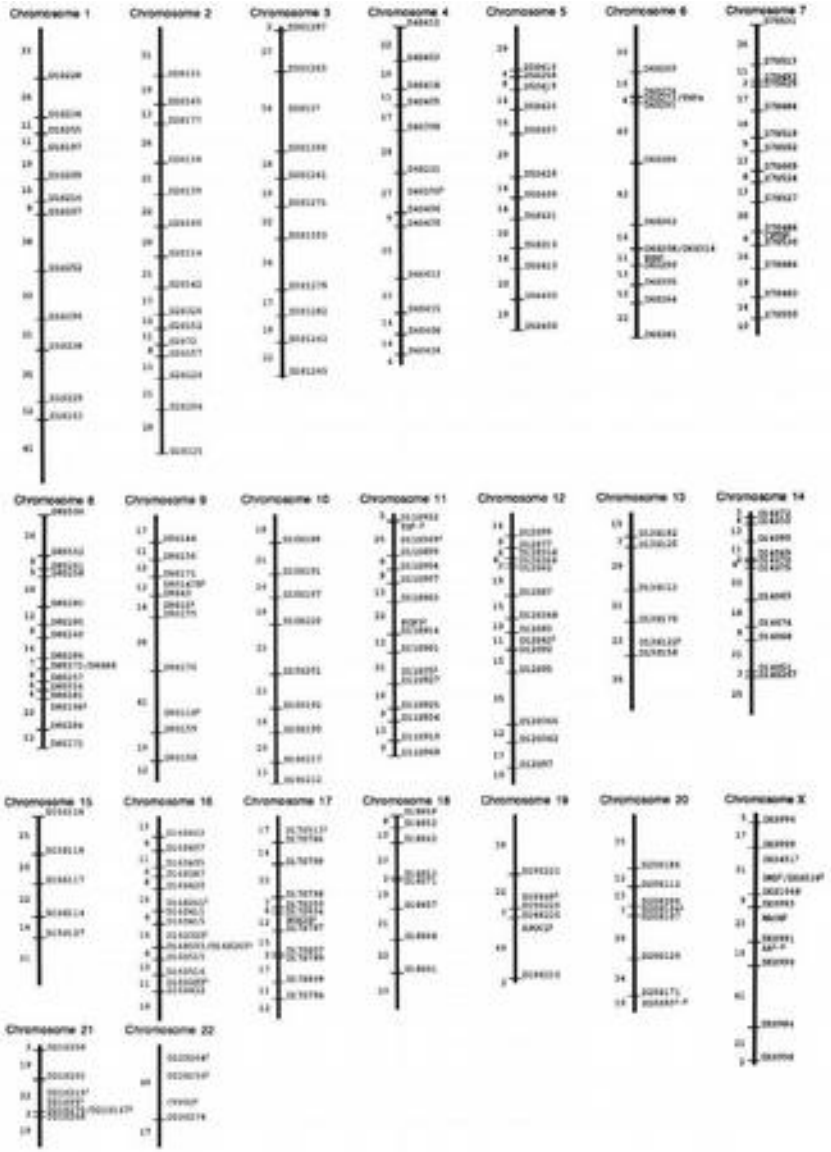

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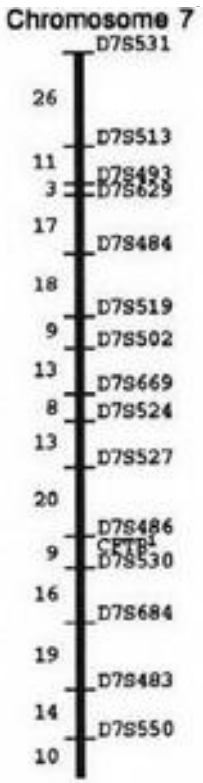

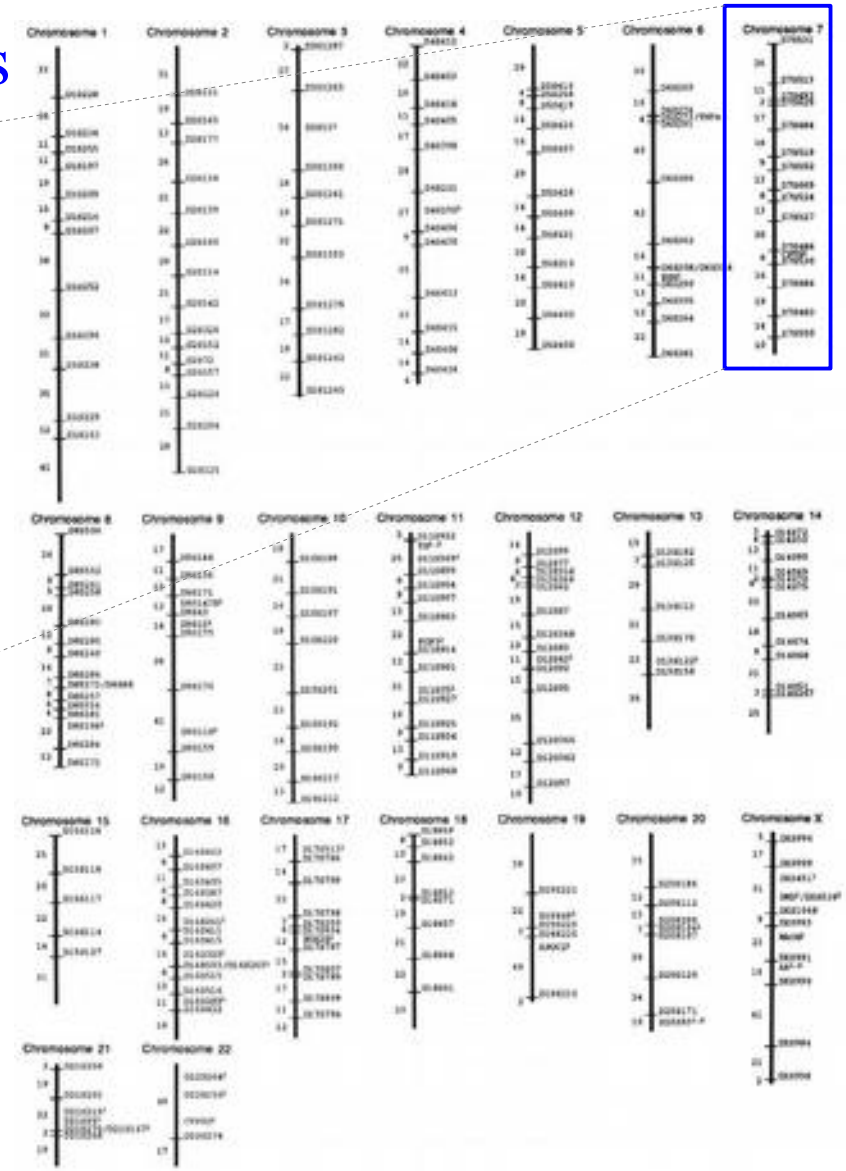

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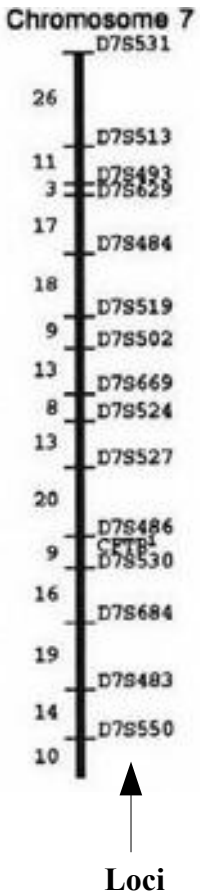

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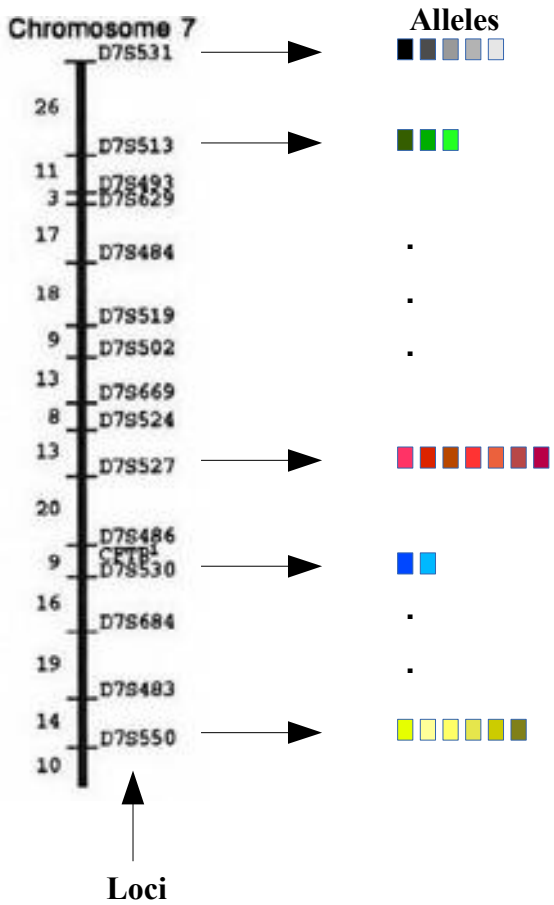

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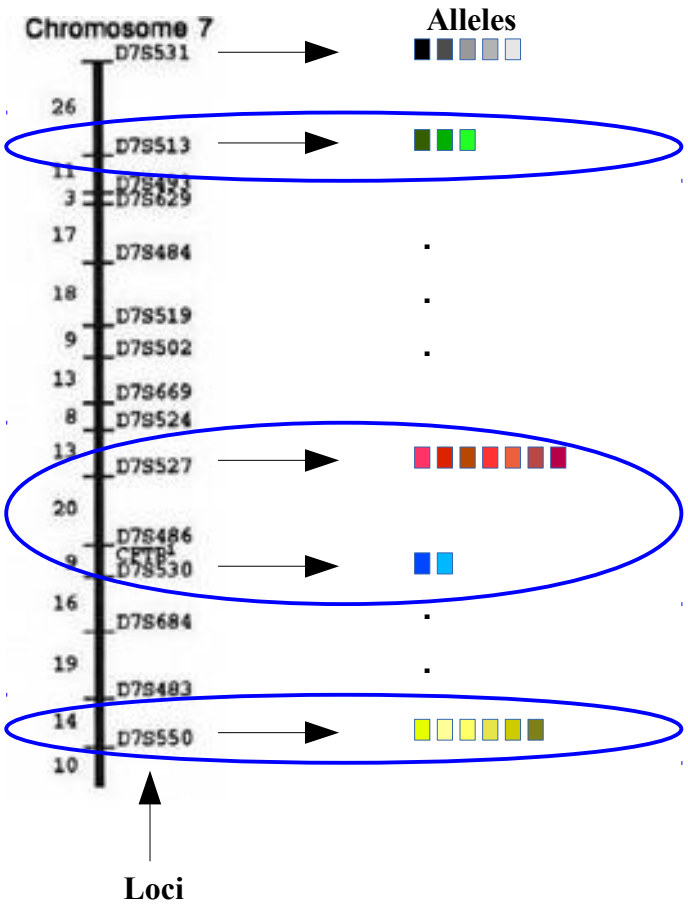

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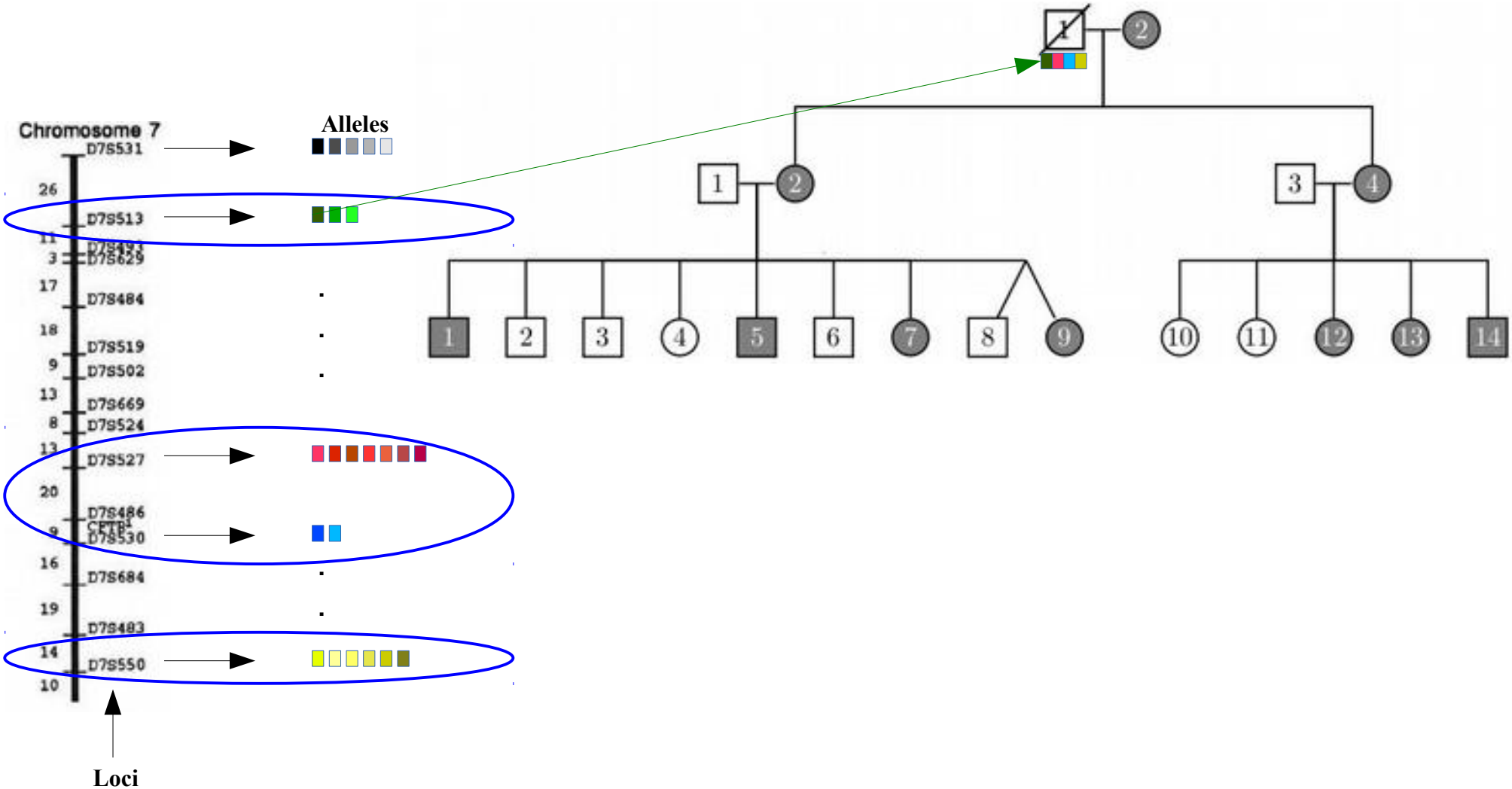

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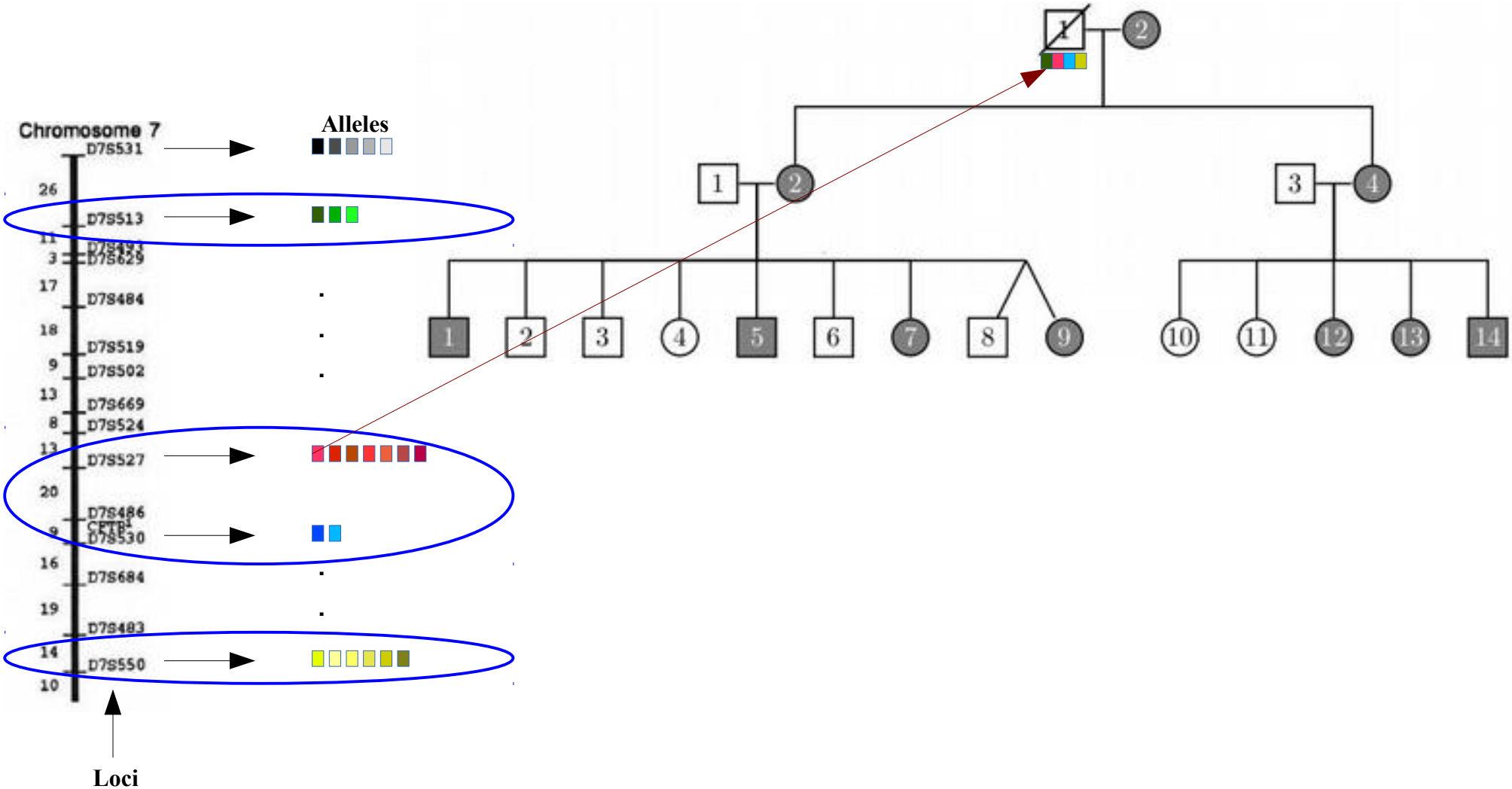

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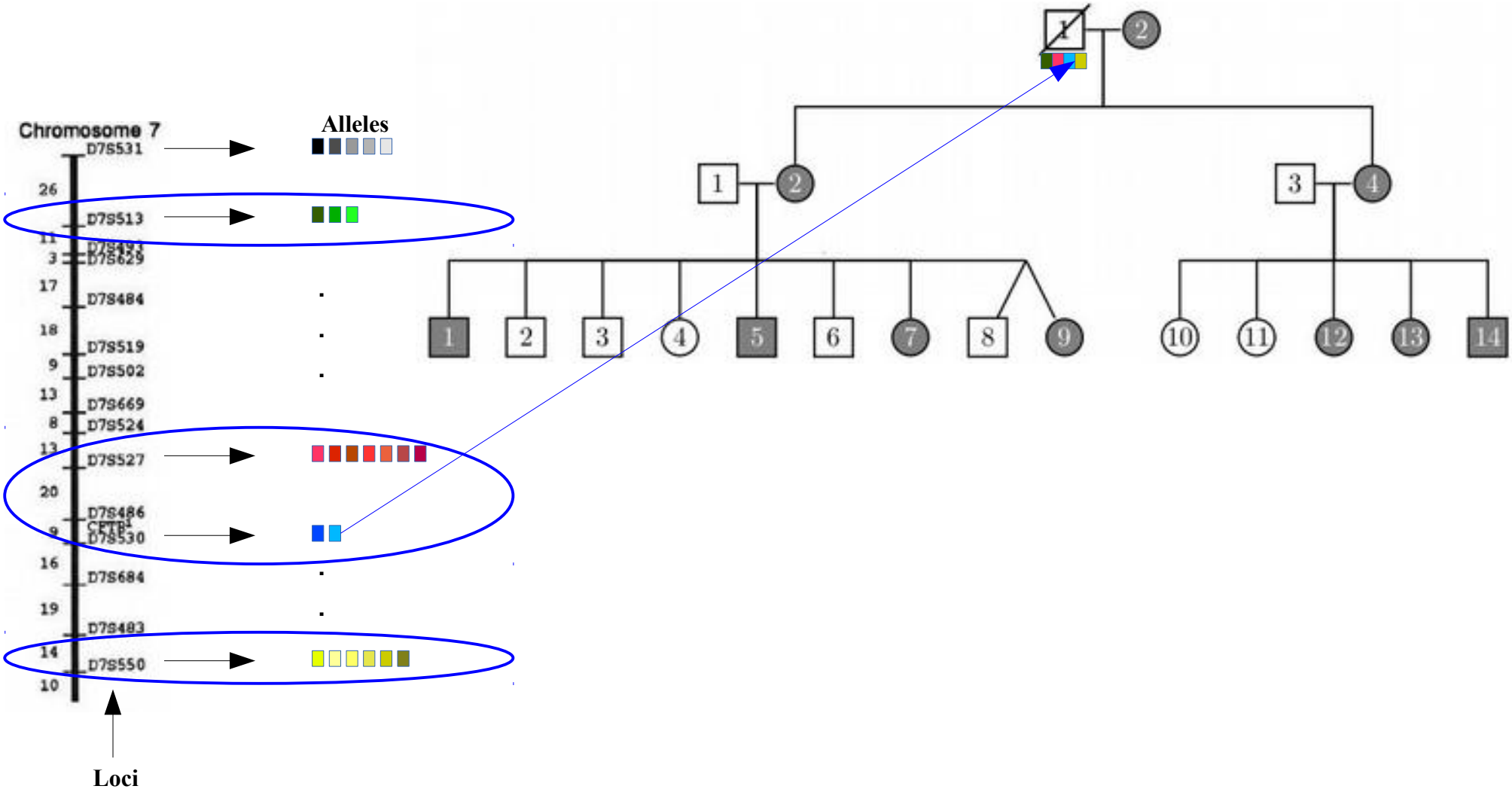

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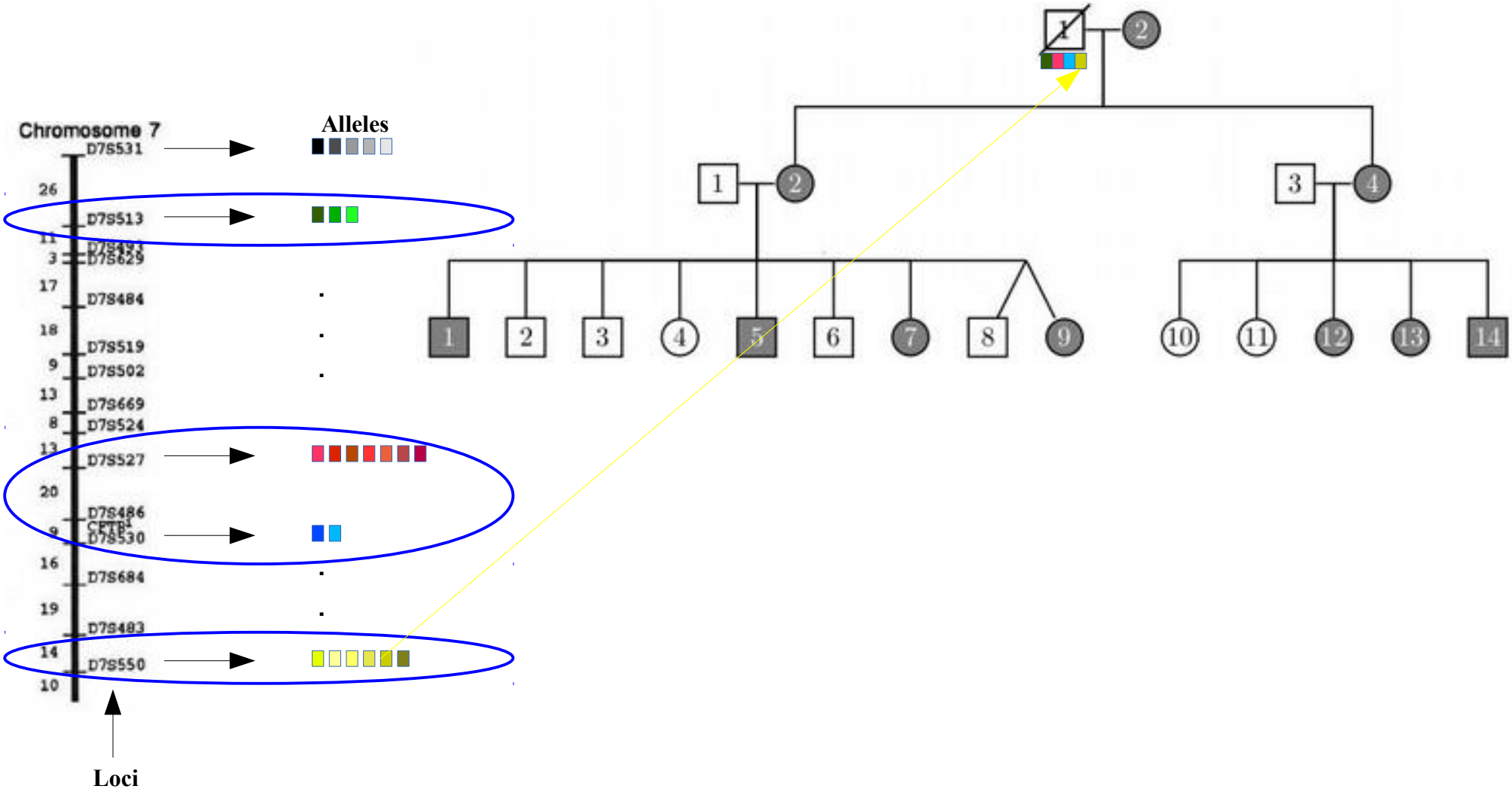

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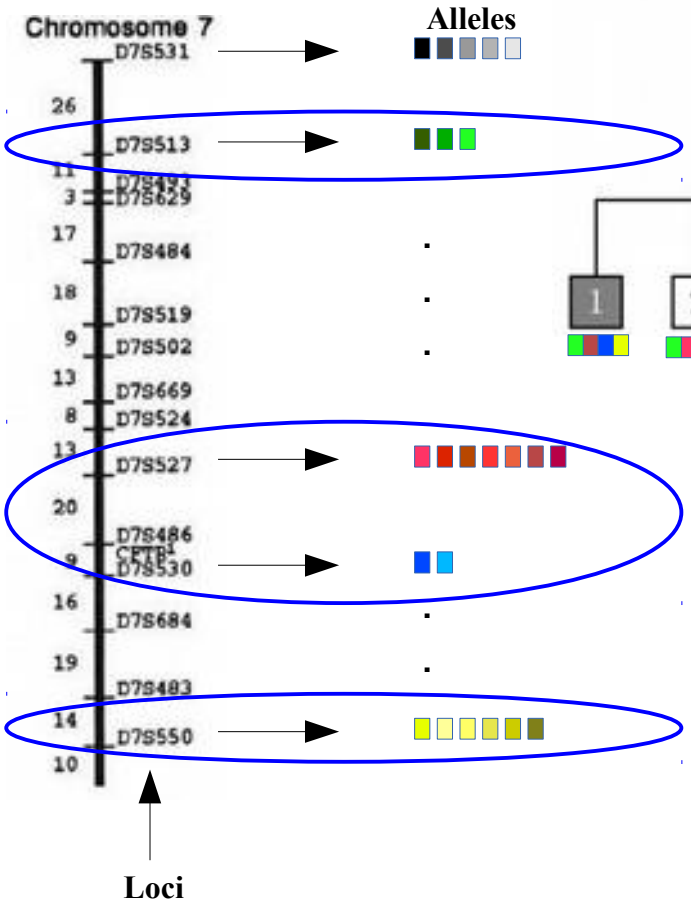

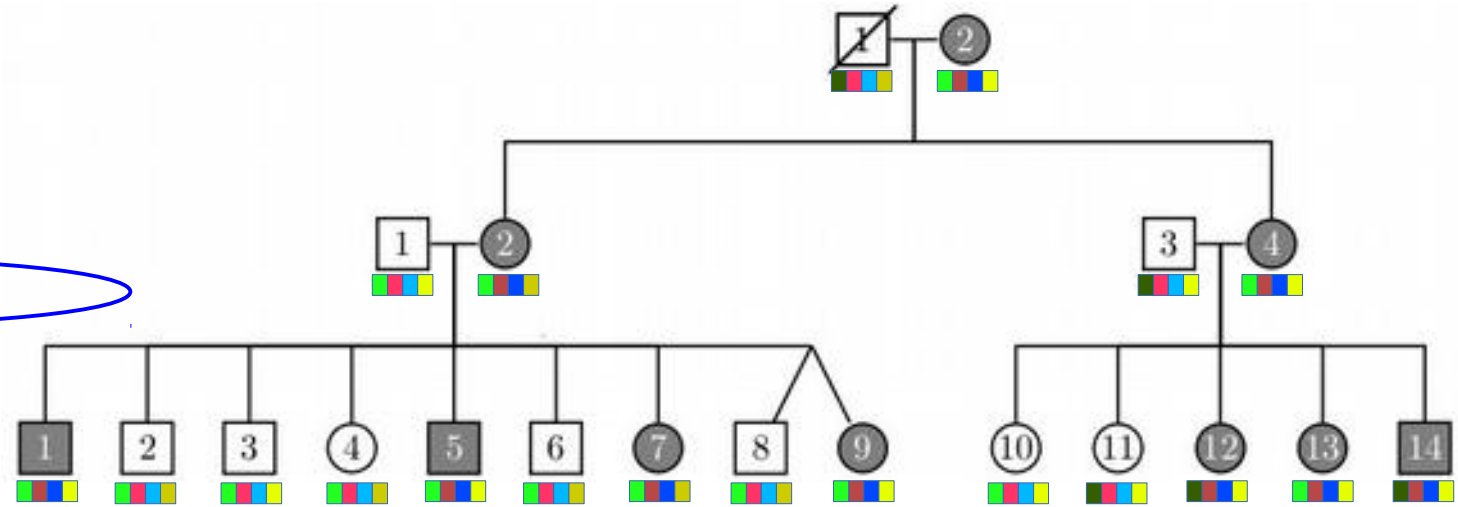

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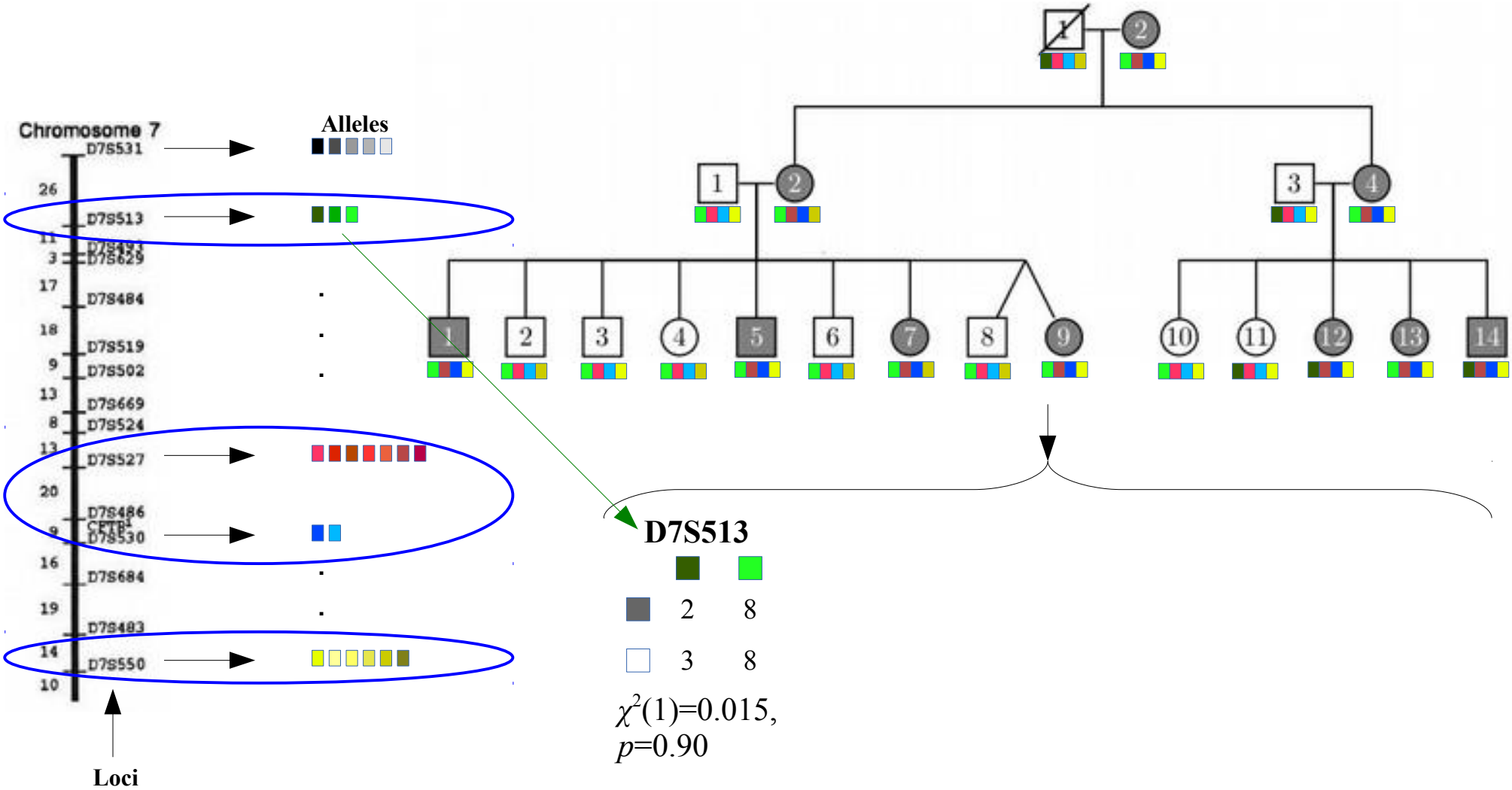

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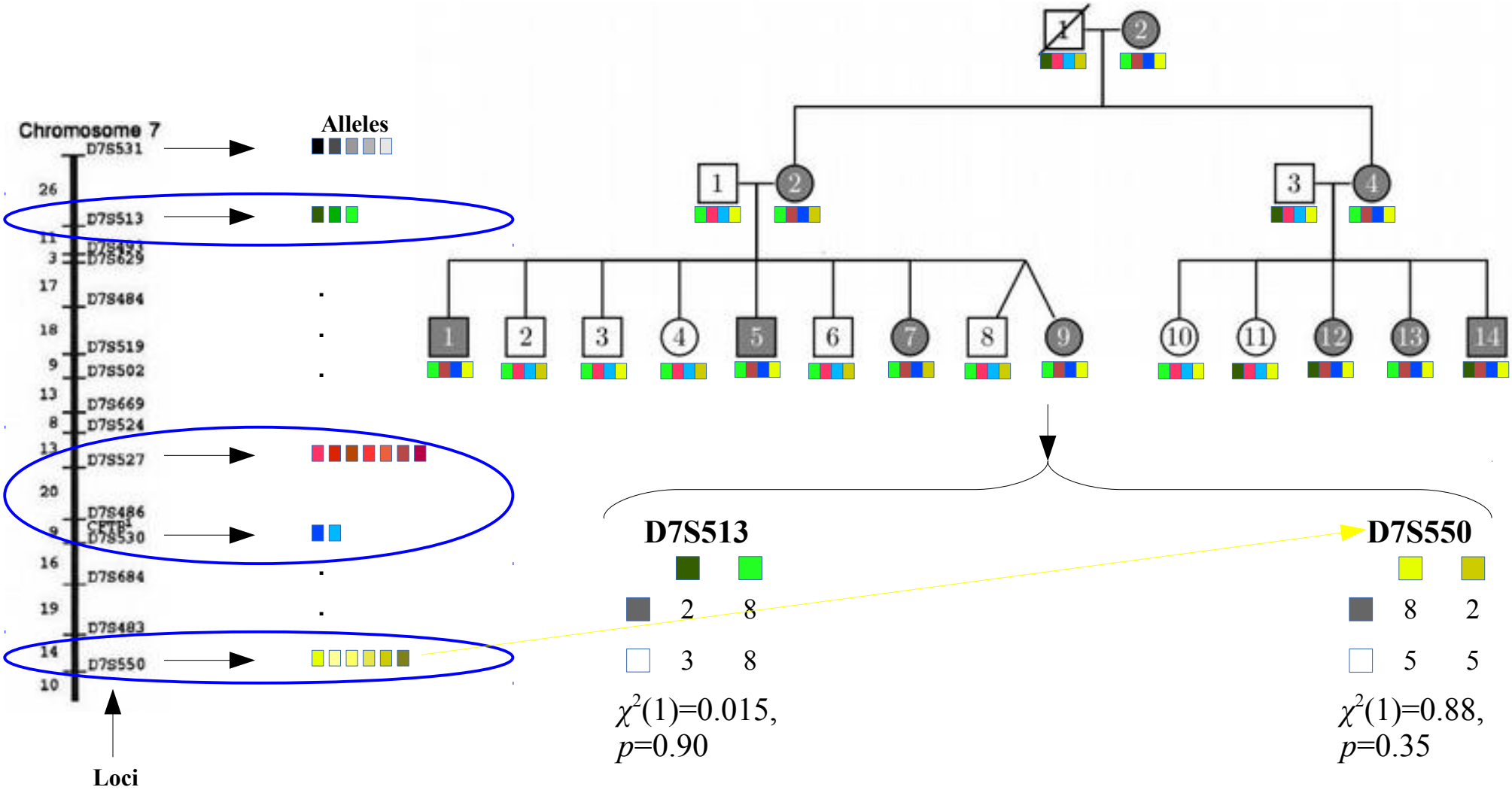

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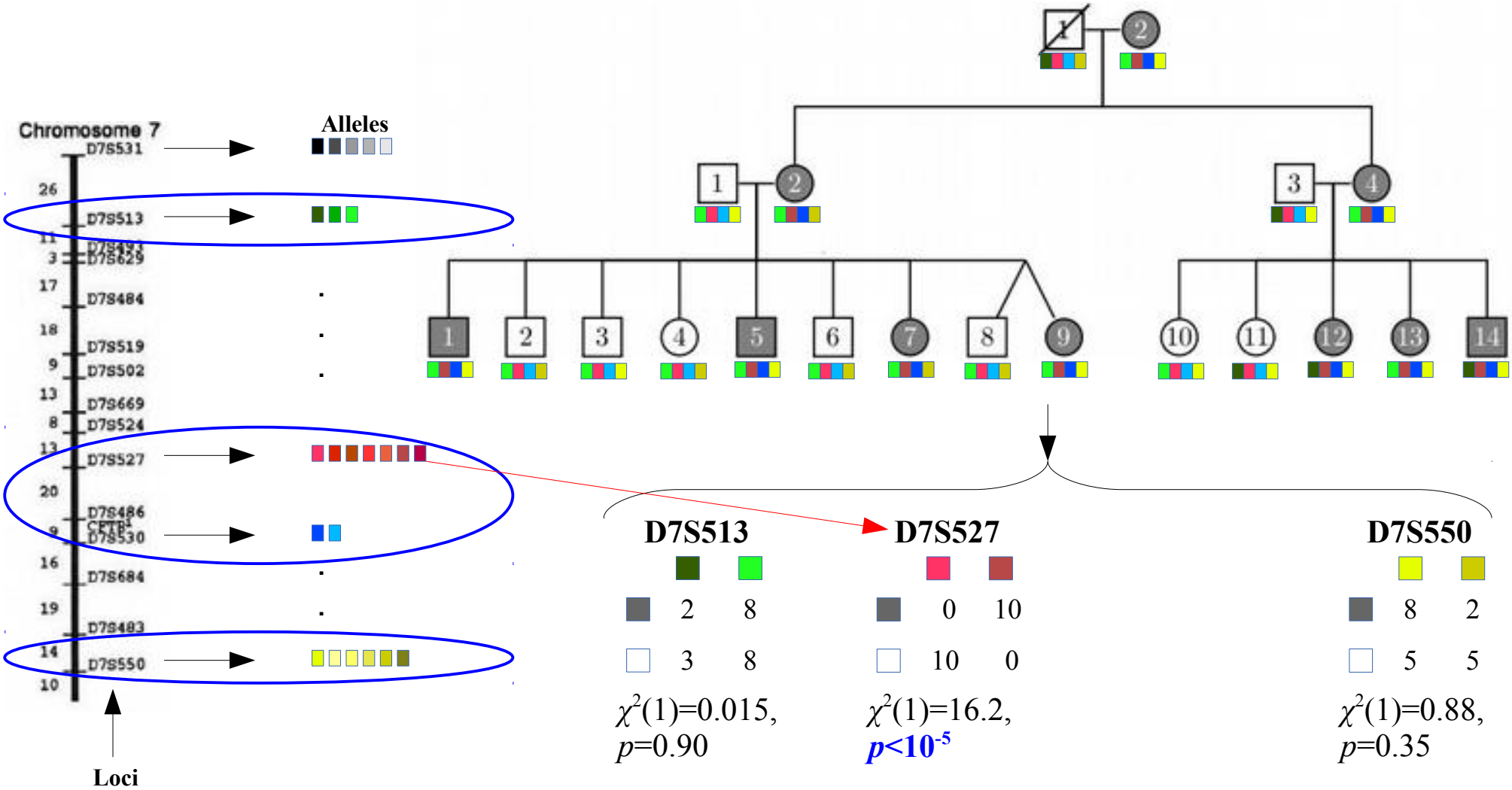

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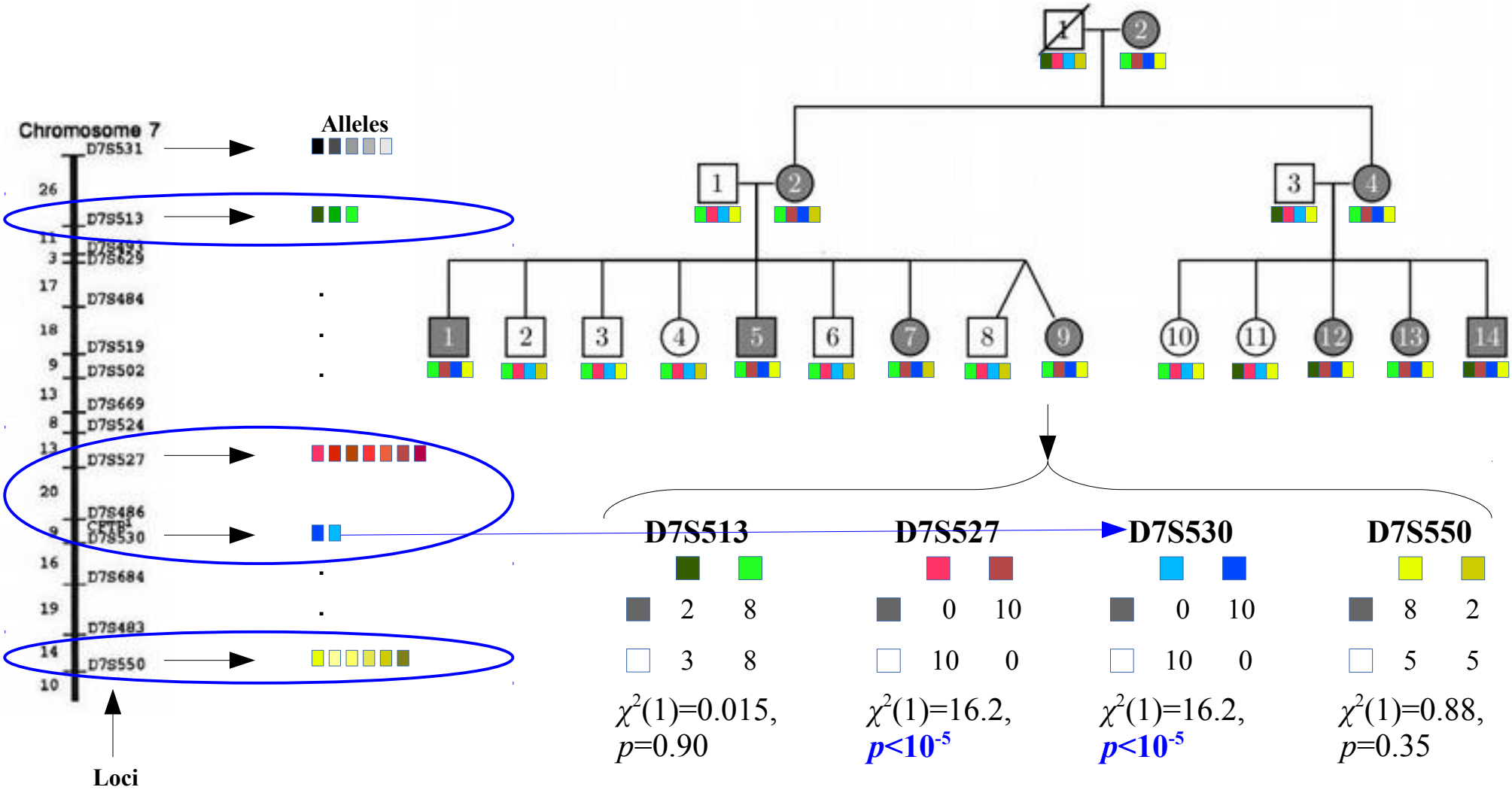

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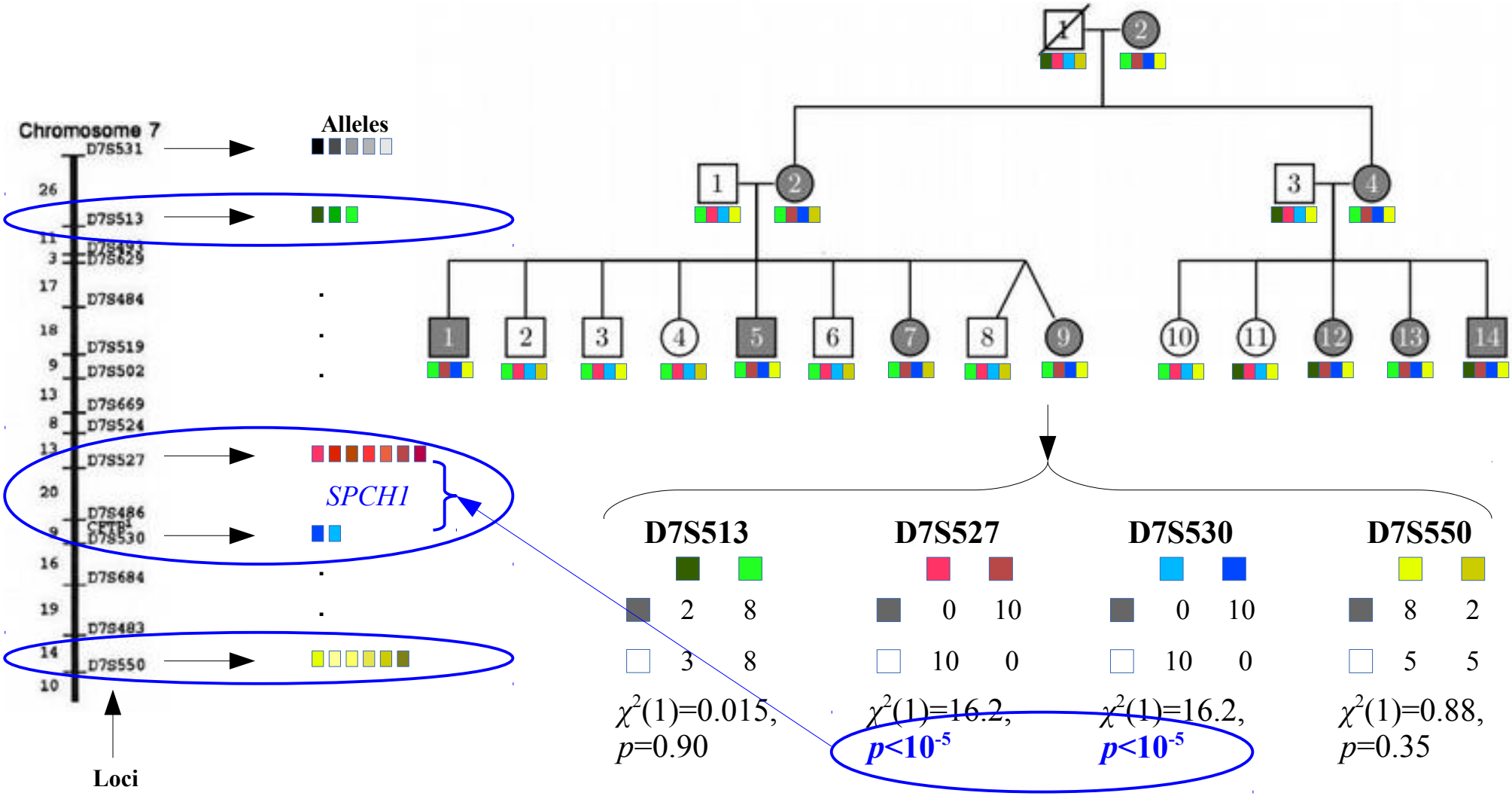

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    → complementary techniques

here, a case (CS) unrelated to KE

  - with same phenotype
  - chromosomal abnormality affecting the *SPCH1* interval on chromosome 7 → more precisely *FOXP2*

Association studies

- Large unrelated samples → variation in the phenotype of interest

Association studies

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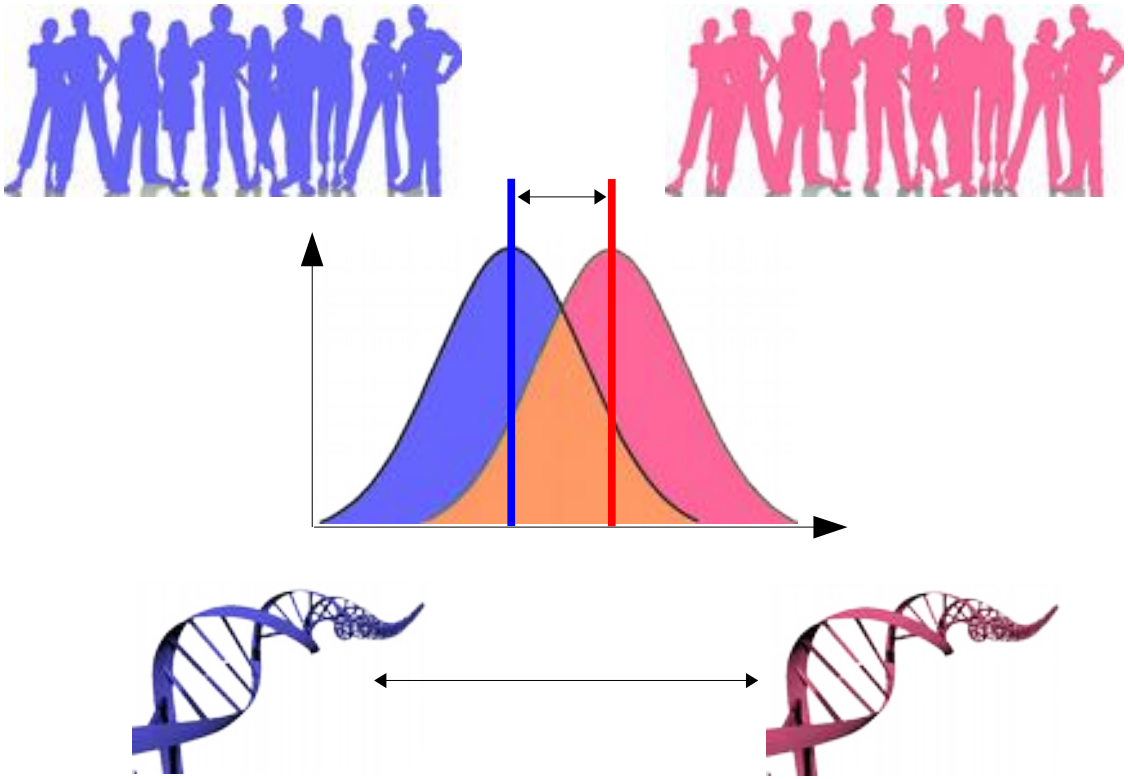
- Correlation between each marker and differences in phenotype



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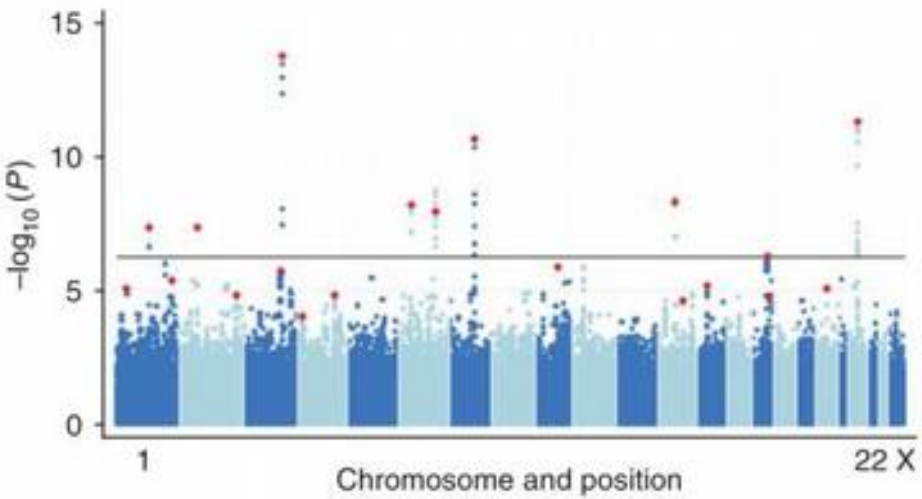
Association with height
in 13,665 individuals



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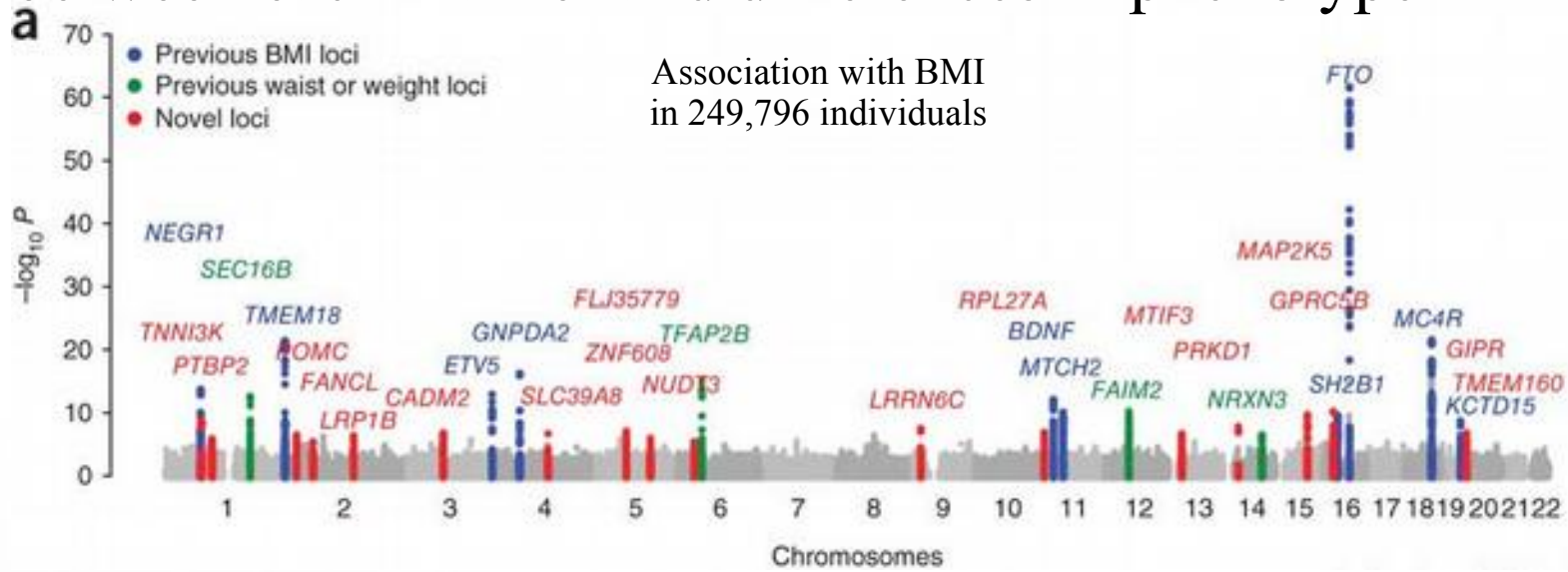
Association with BMI
in 249,796 individuals



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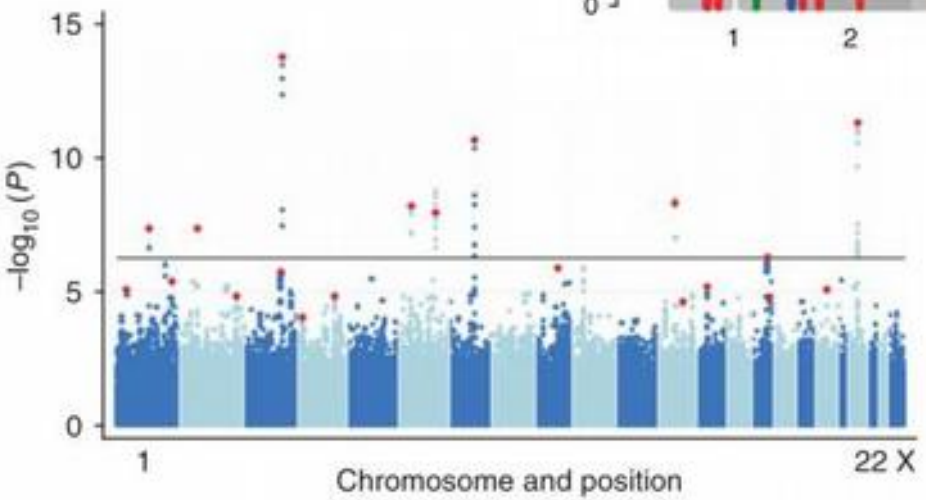

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  - huge sample sizes (1,000+ → 100,000+) → tiny effect sizes

Exome & genome sequencing

- Sequencing → full message instead of (dense) landmarks

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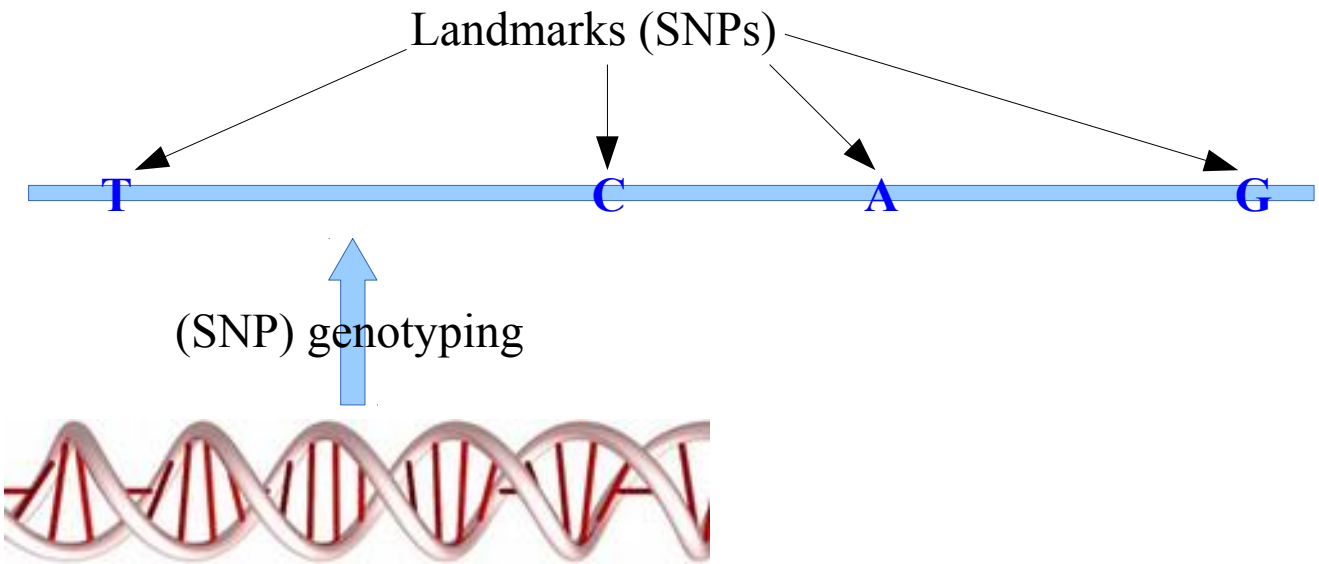

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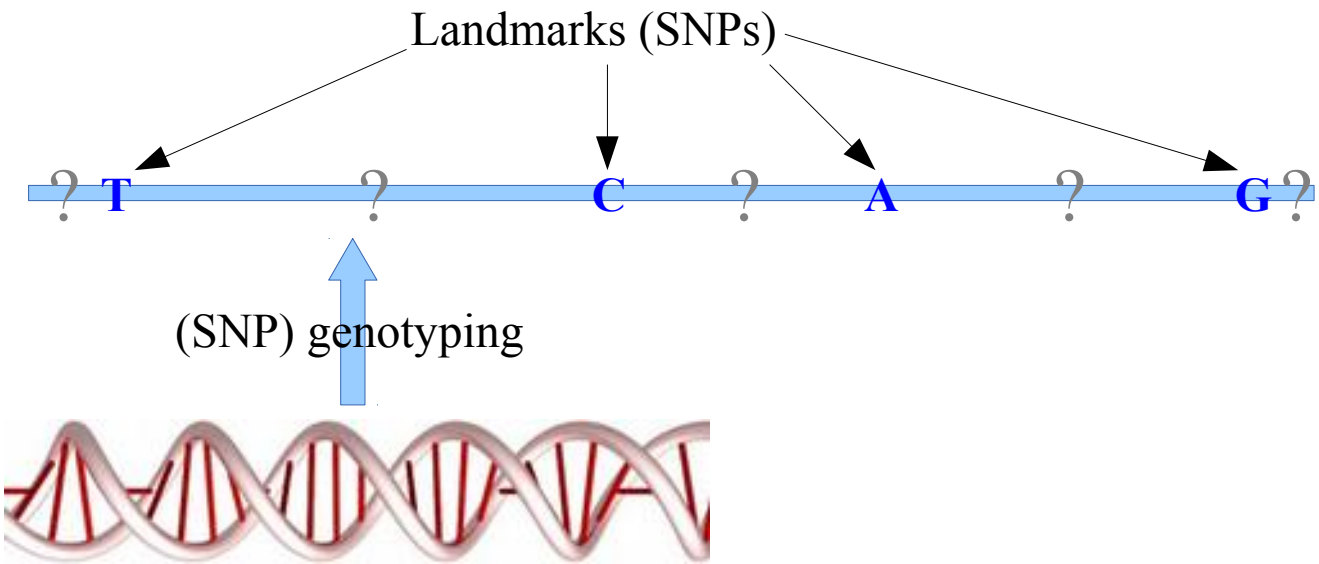

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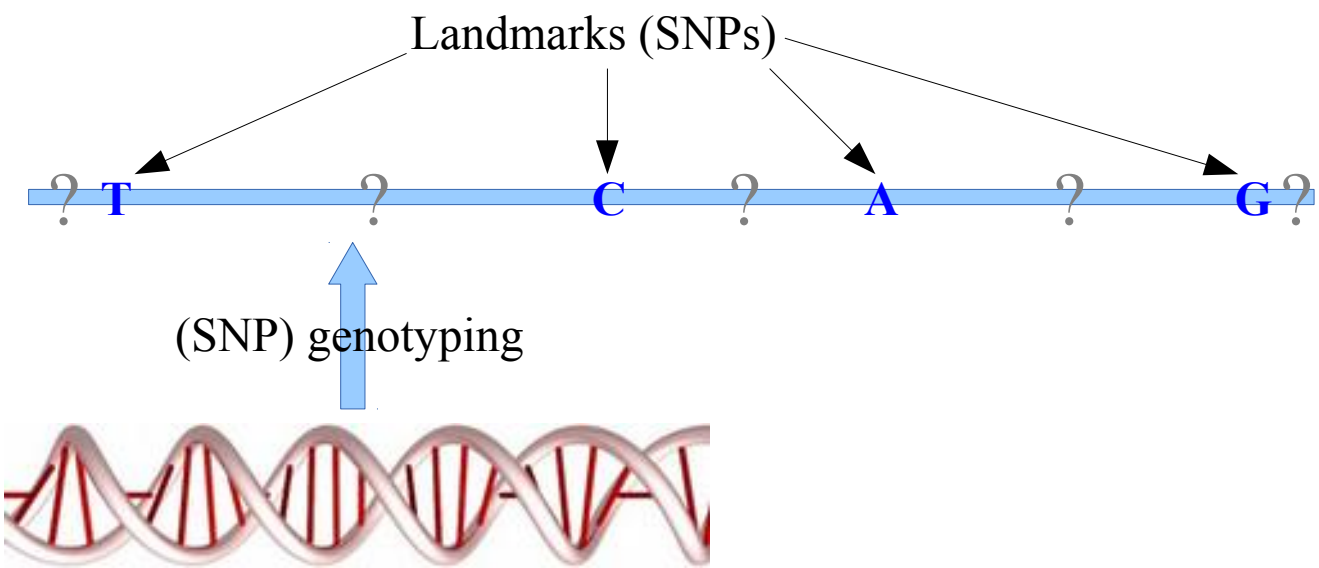

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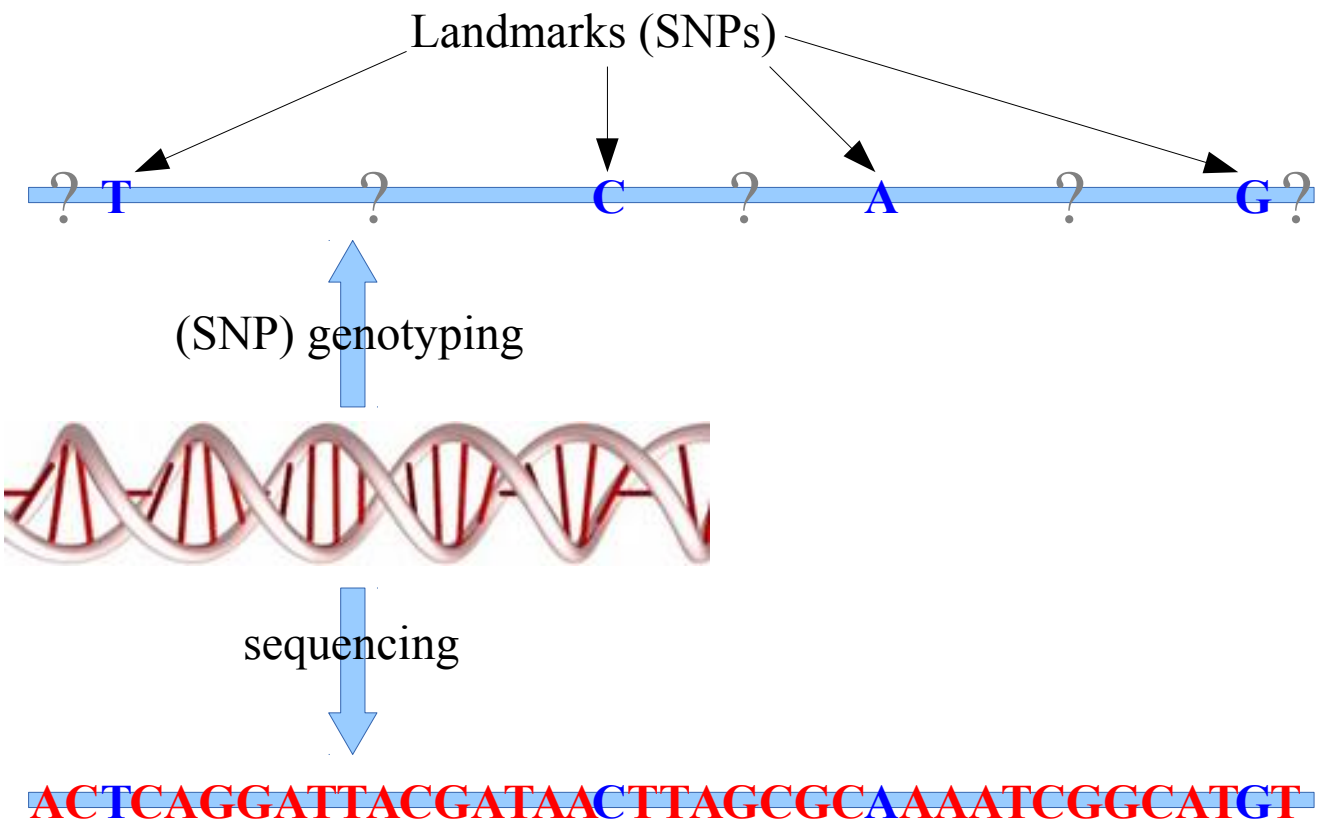

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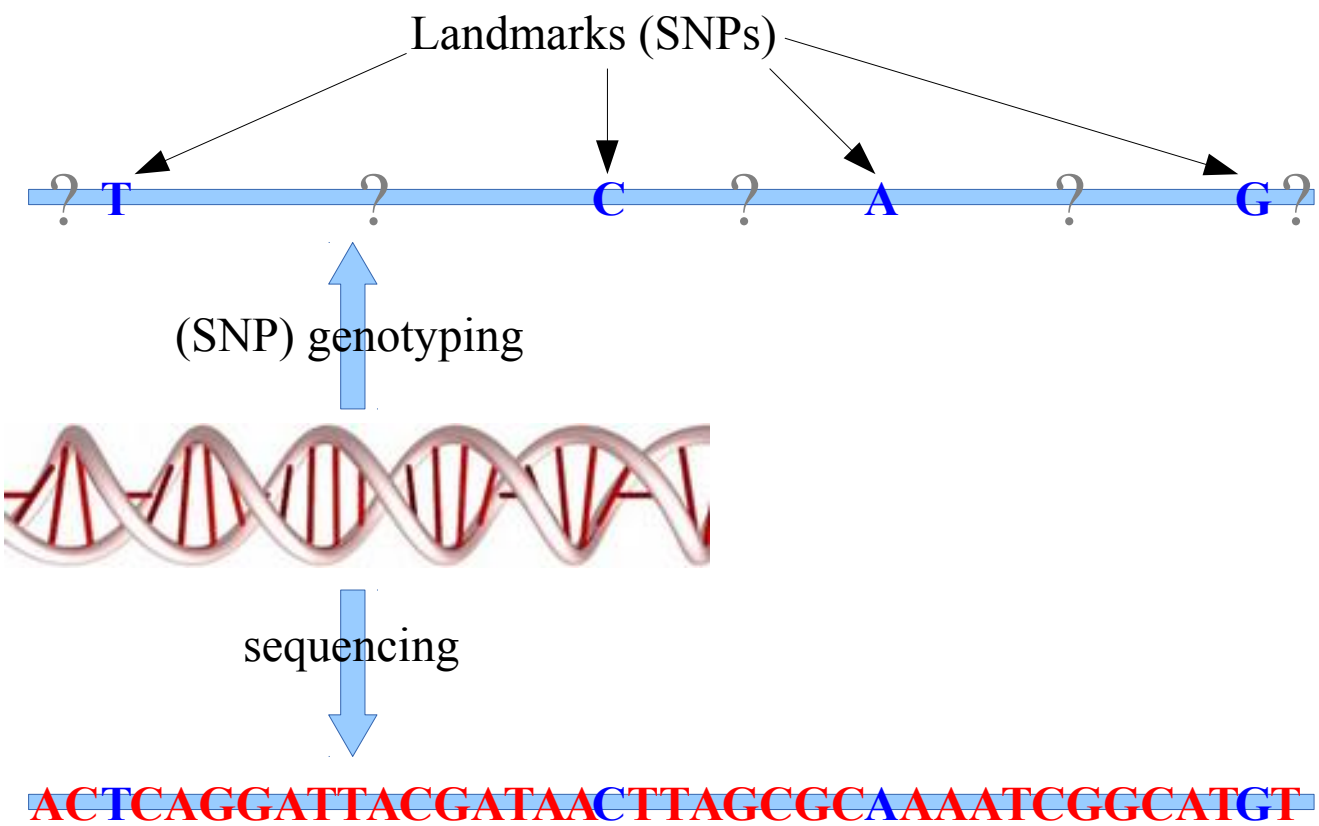

Exome & genome sequencing

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Whole genome

sequencing

ACTCAGGATTACGATAACTTAGCGCAAAATCGGCATGT

Exome & genome sequencing

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Whole genome

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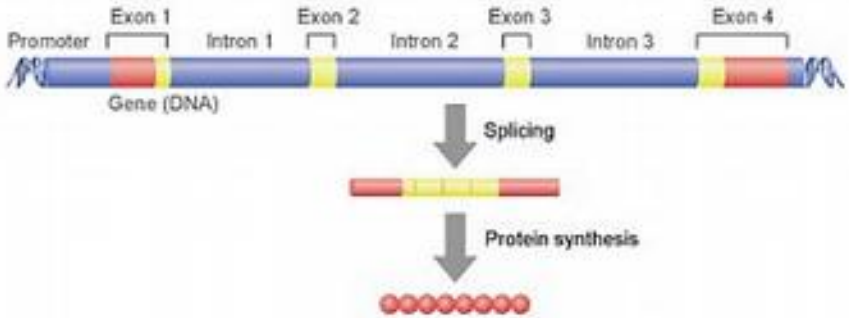

Exome & genome sequencing

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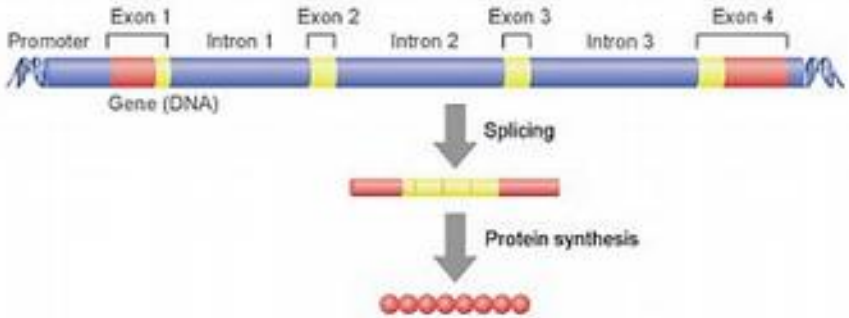
lots of data ←

Whole genome

Exome



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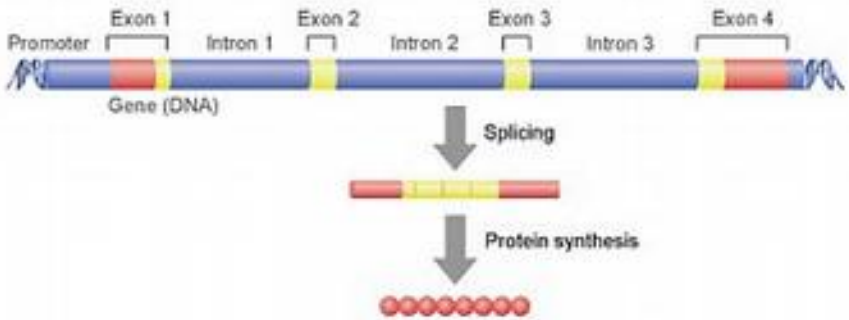


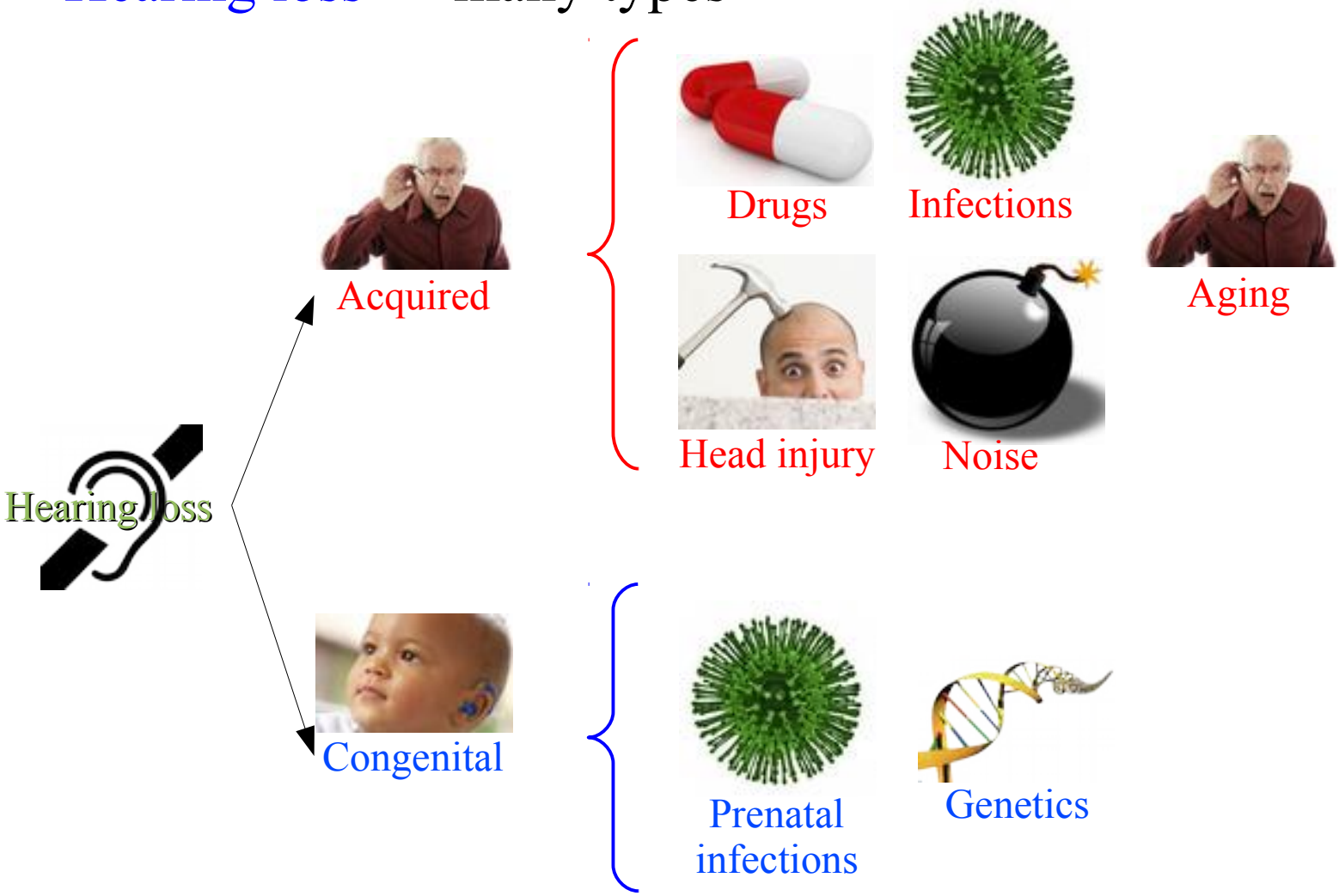
Difficult to analyze:
- heaps of genetic variation → what is relevant?

Examples of genes

- Hearing loss

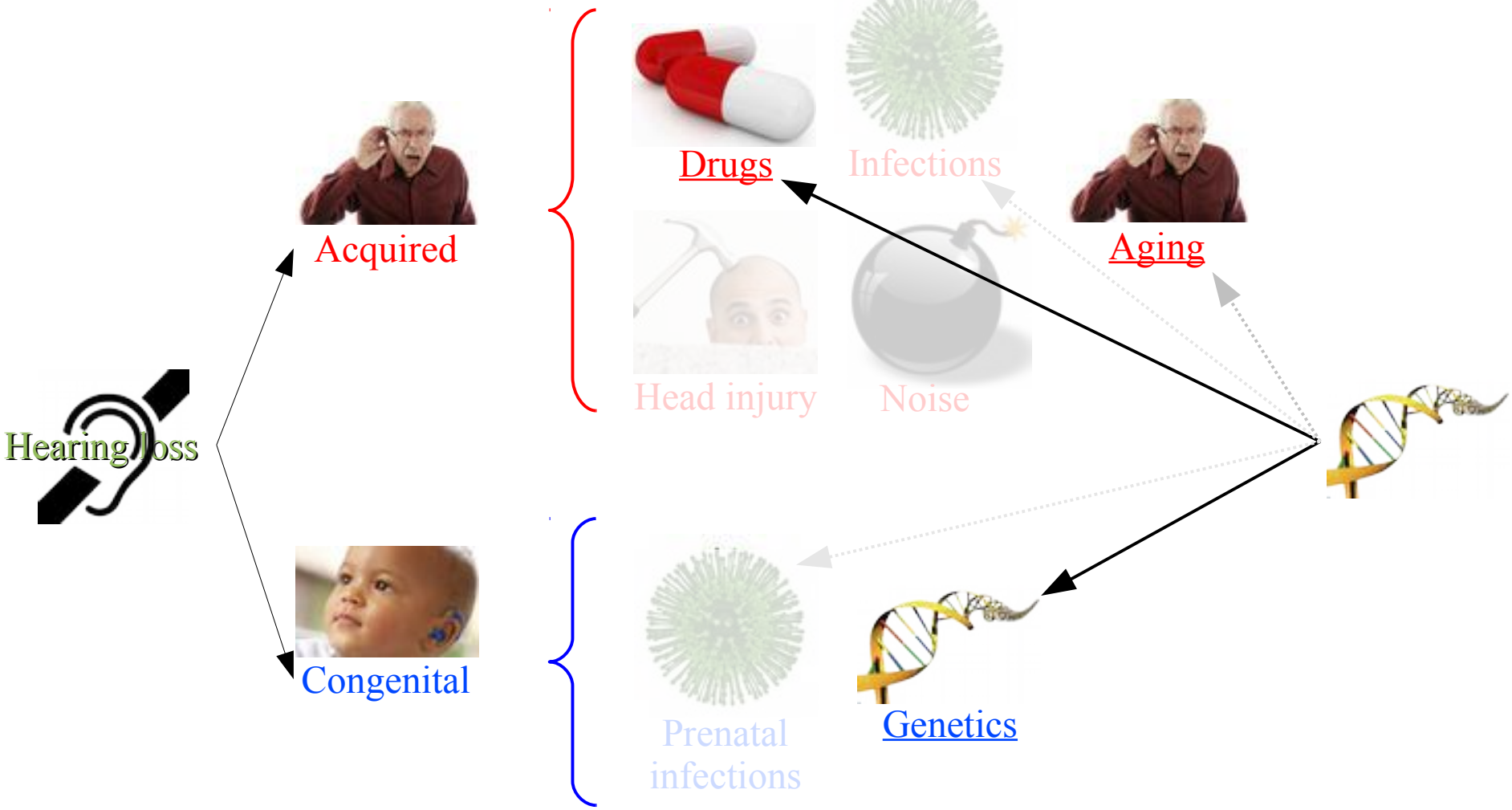
Examples of genes

- Hearing loss → many types

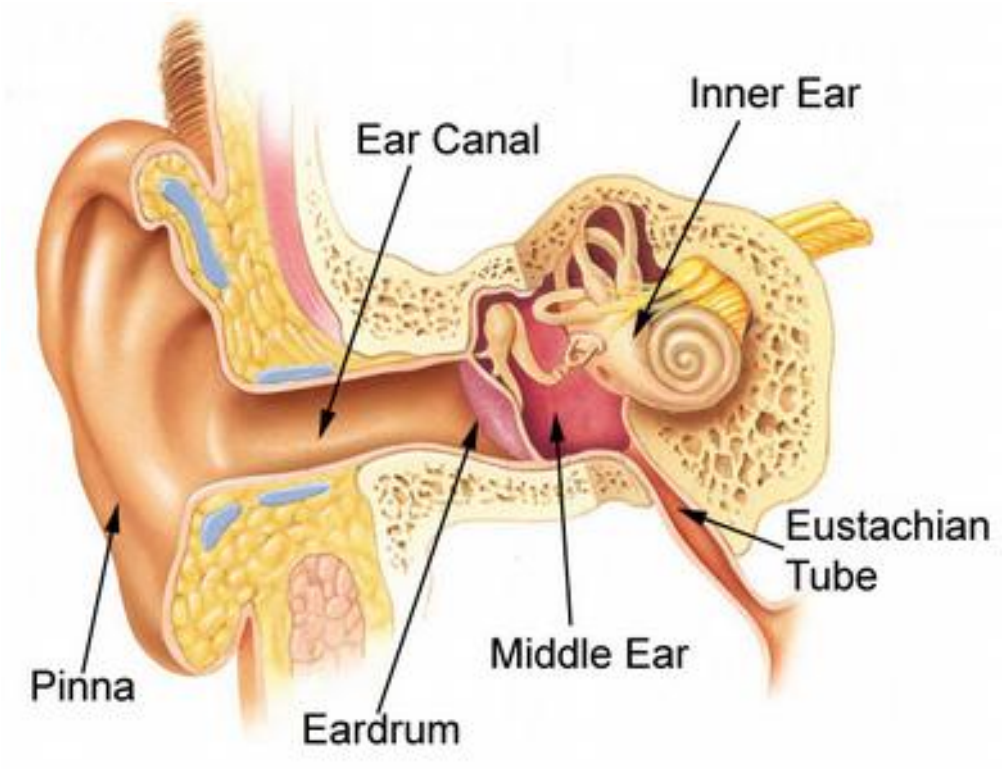


Examples of genes

- Hearing loss → many types → genetic component



Some examples: *TECTA*



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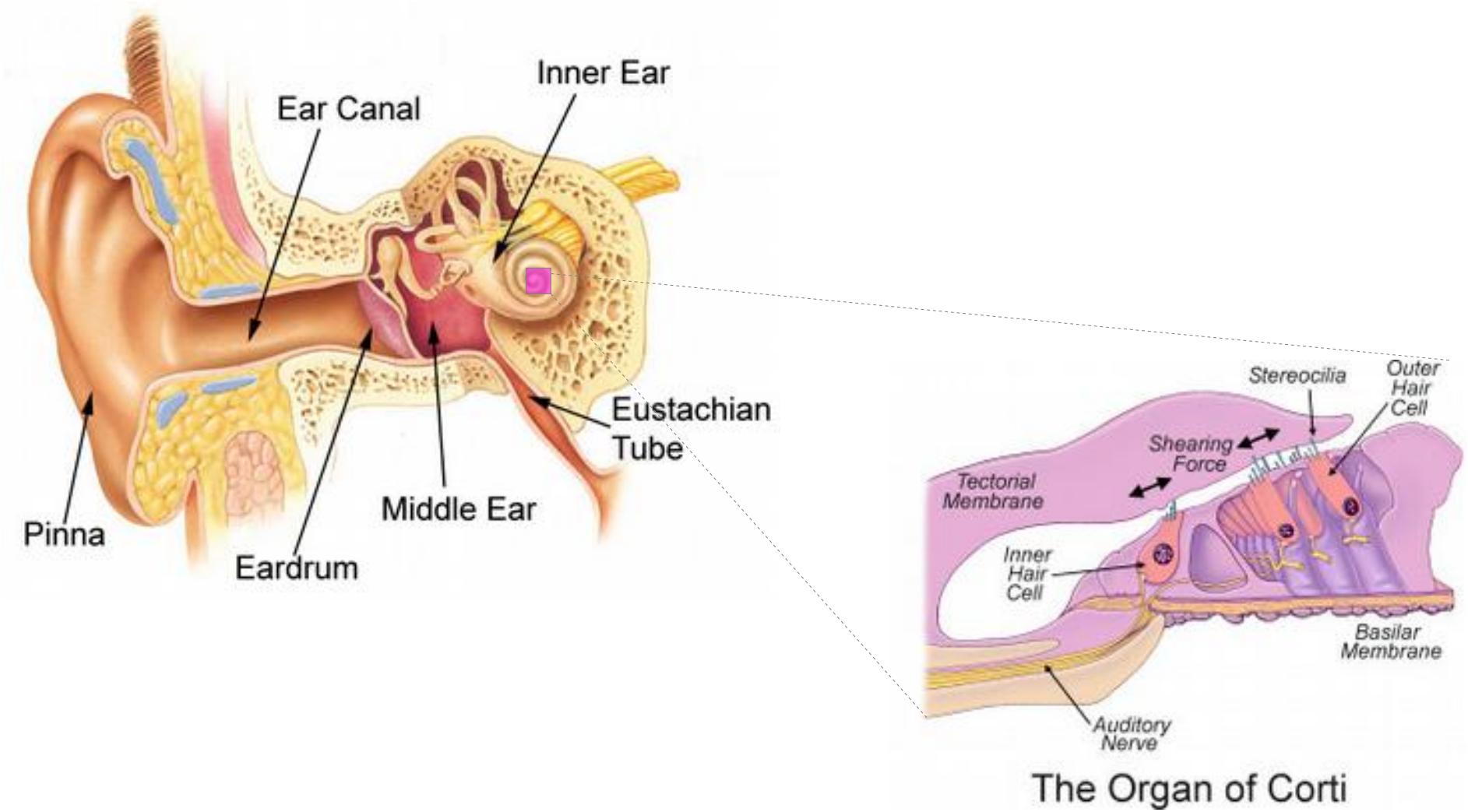
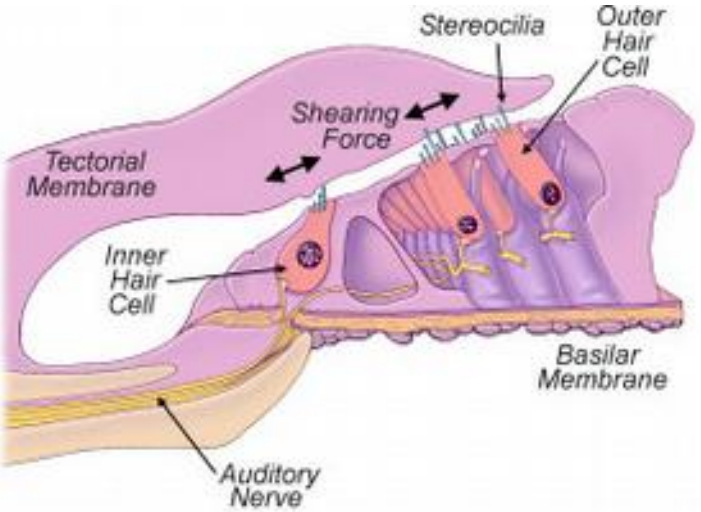


Some examples: *TECTA*

- Tectorial membrane:

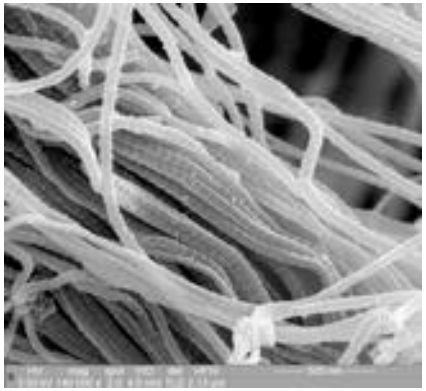


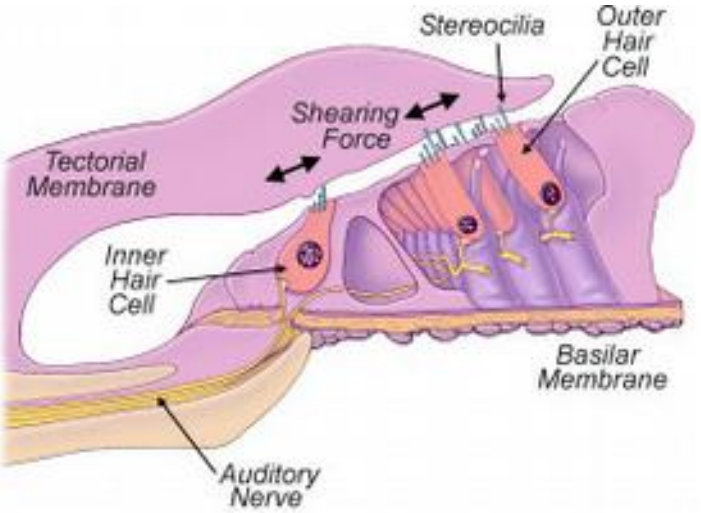
The Organ of Corti

Some examples: *TECTA*

- Tectorial membrane:

  → collagen





The Organ of Corti

Some examples: *TECTA*

- Tectorial membrane:

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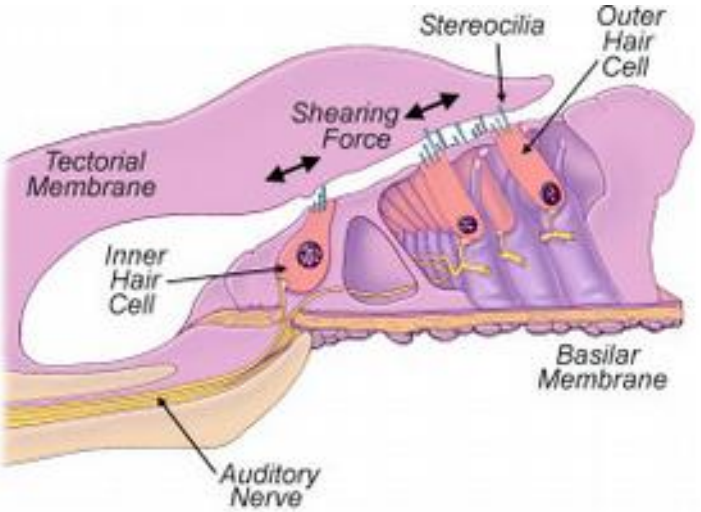
  → non-collagenous proteins



The Organ of Corti

Some examples: *TECTA*

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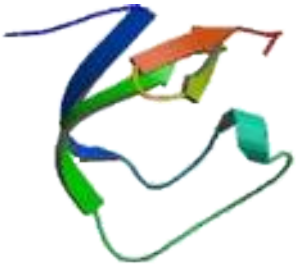

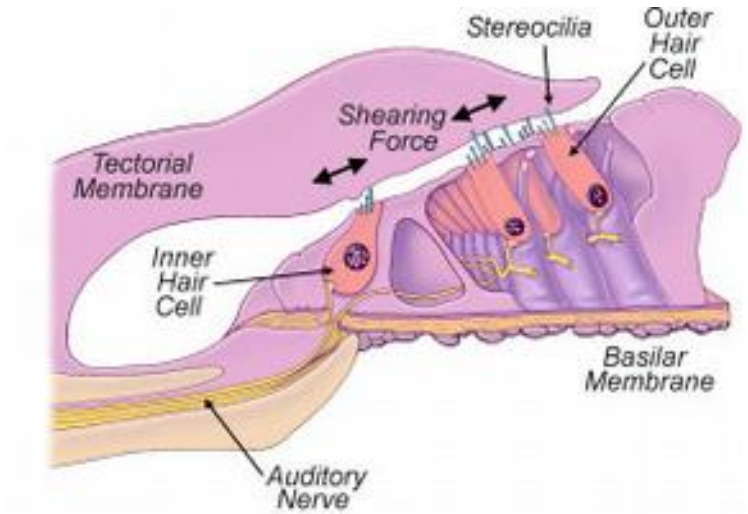

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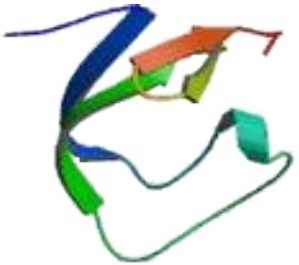
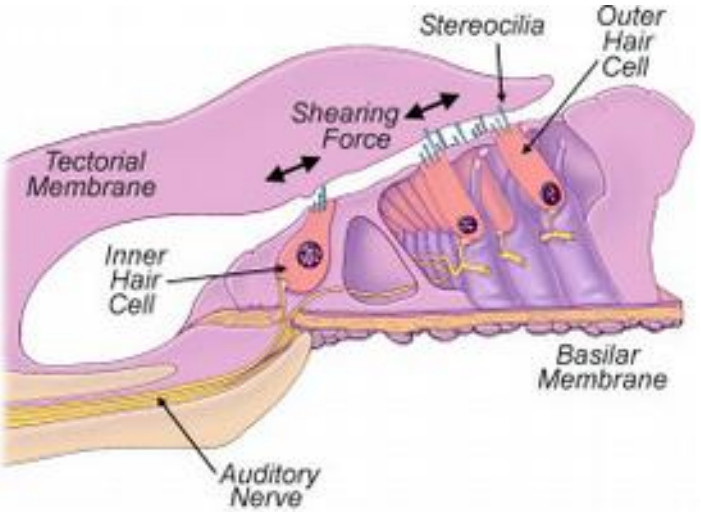


TECTA gene



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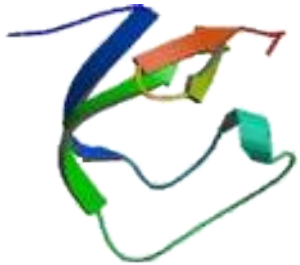
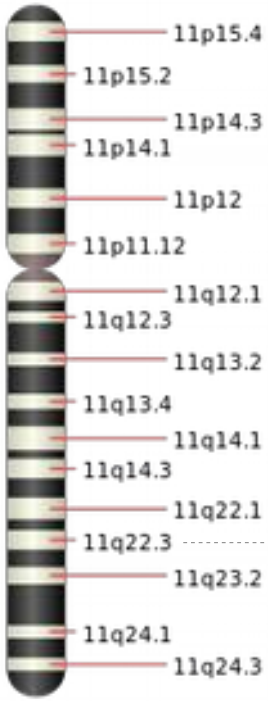
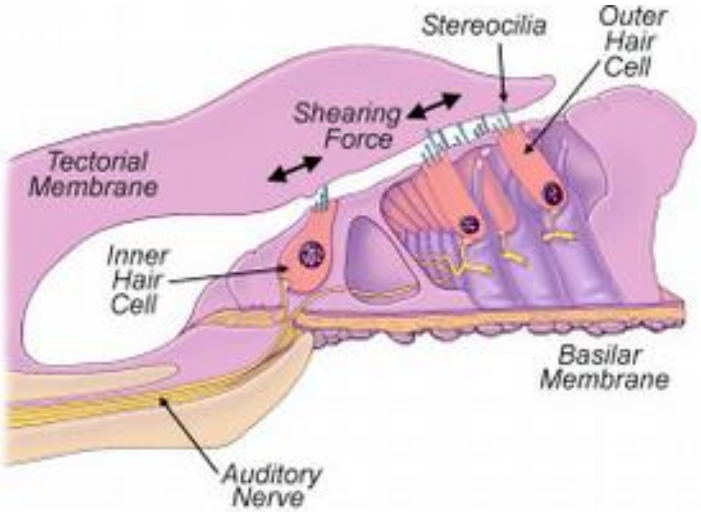




TECTA gene (11q23.3)



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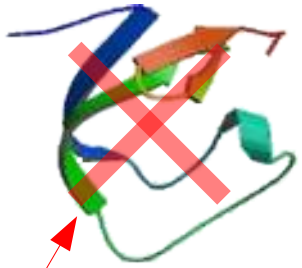

mutations

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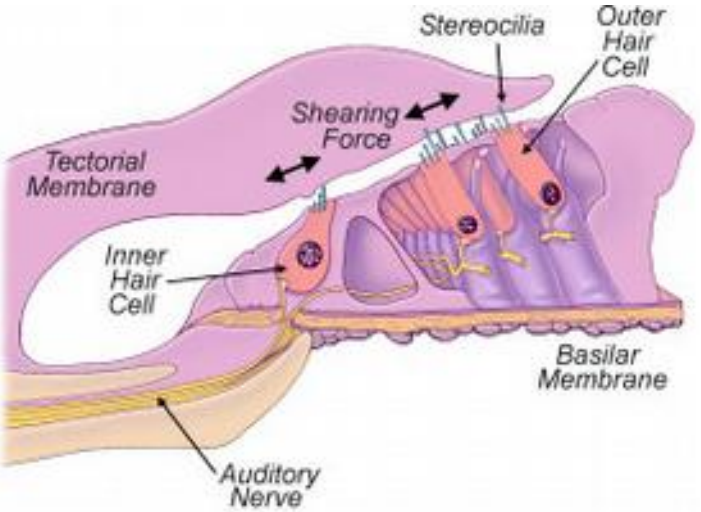

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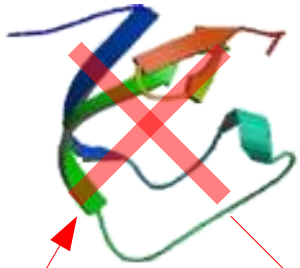

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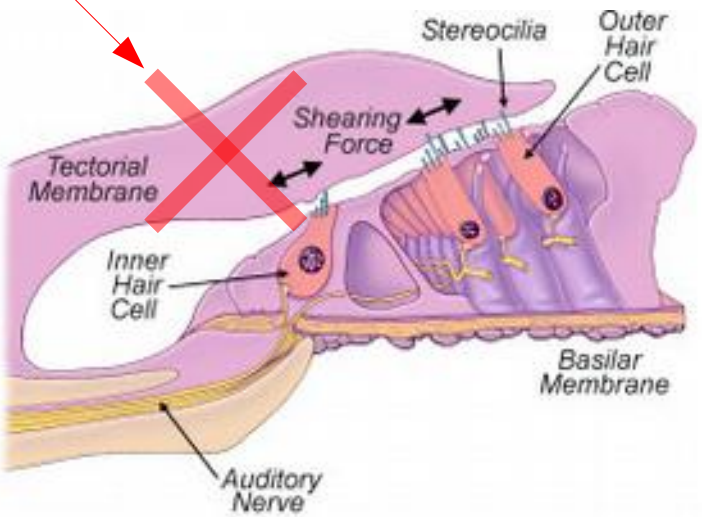

The Organ of Corti

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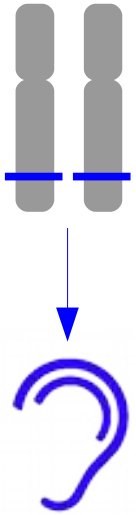

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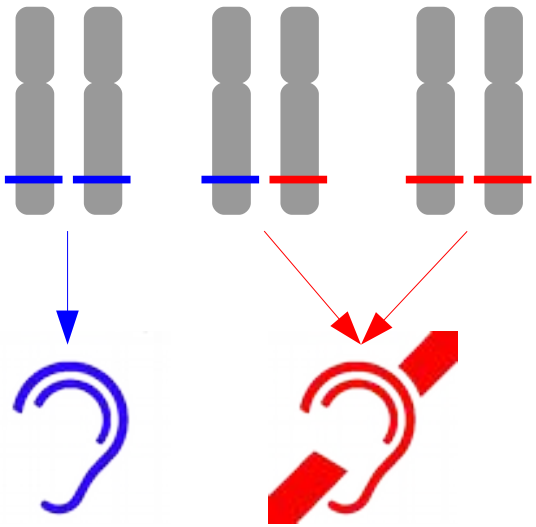

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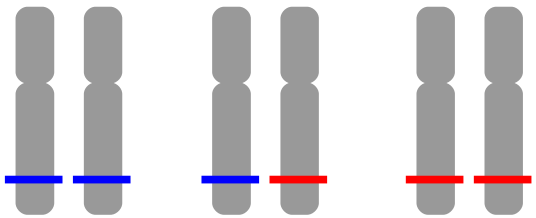

DFNA12 - dominant

DFNB21 - recessive

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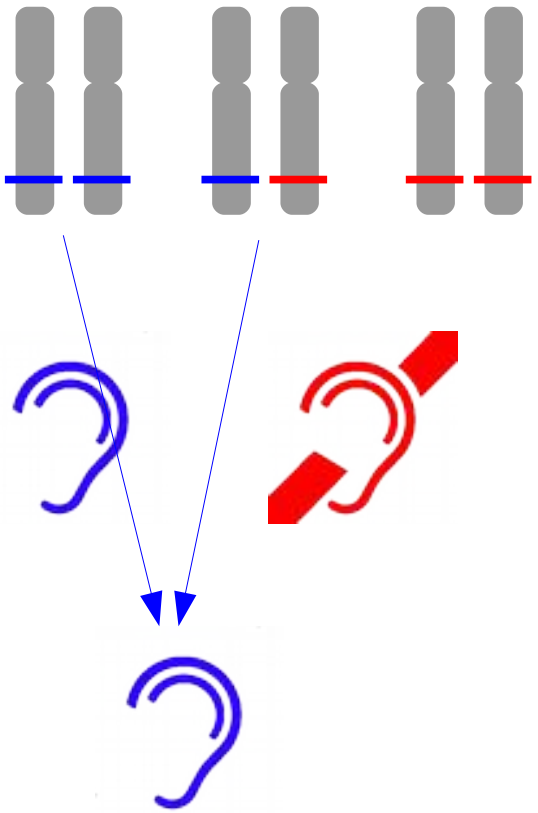

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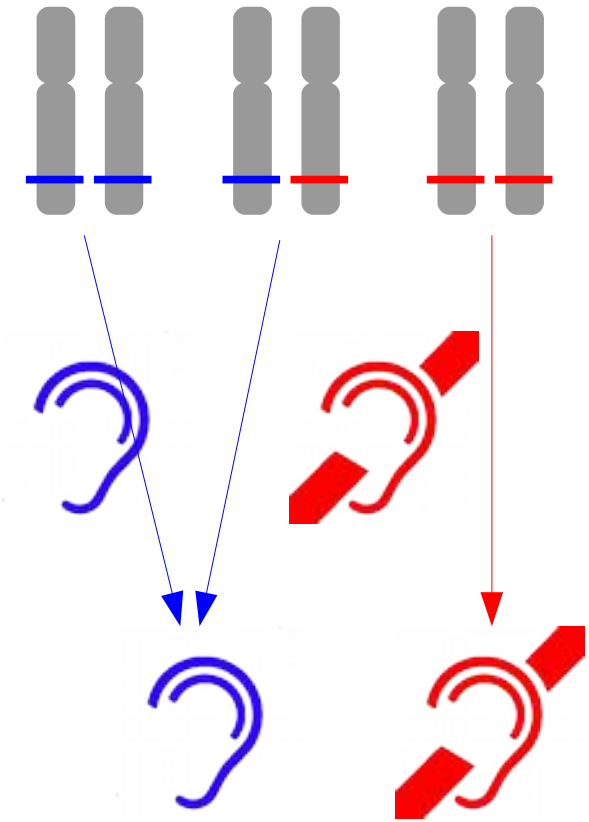

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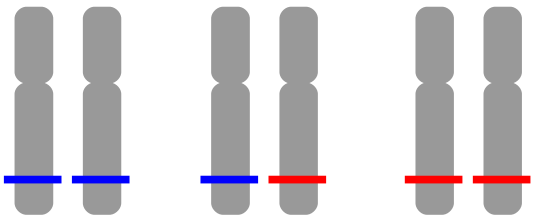

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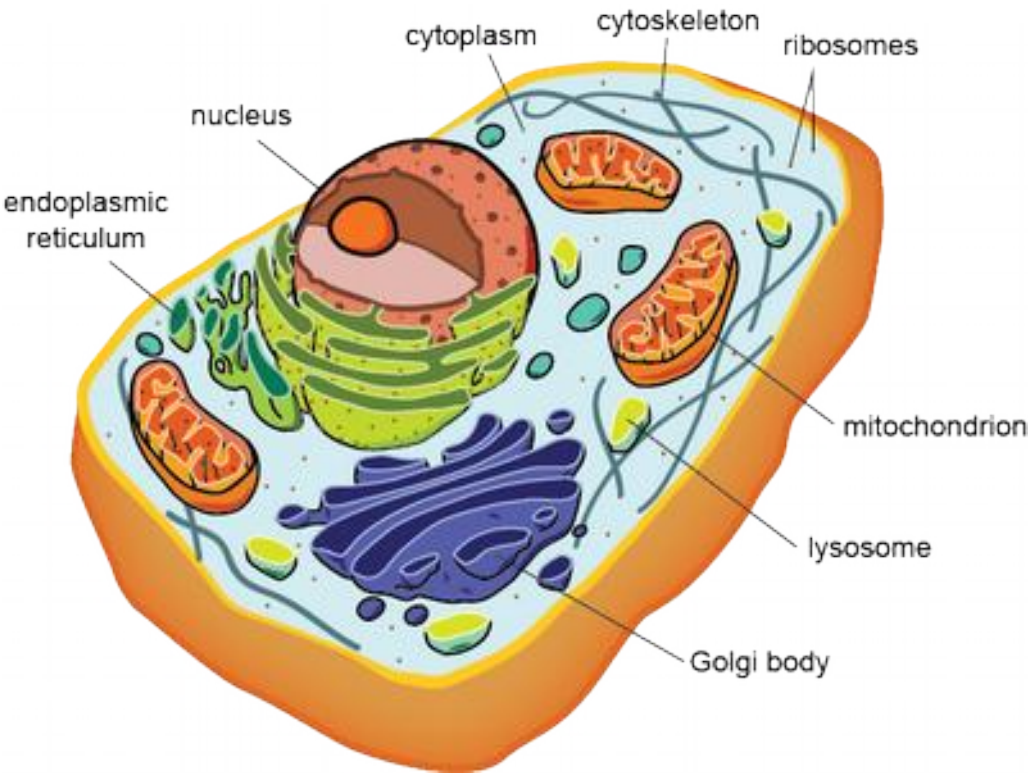
Some examples: mitochondrial *12S rRNA*



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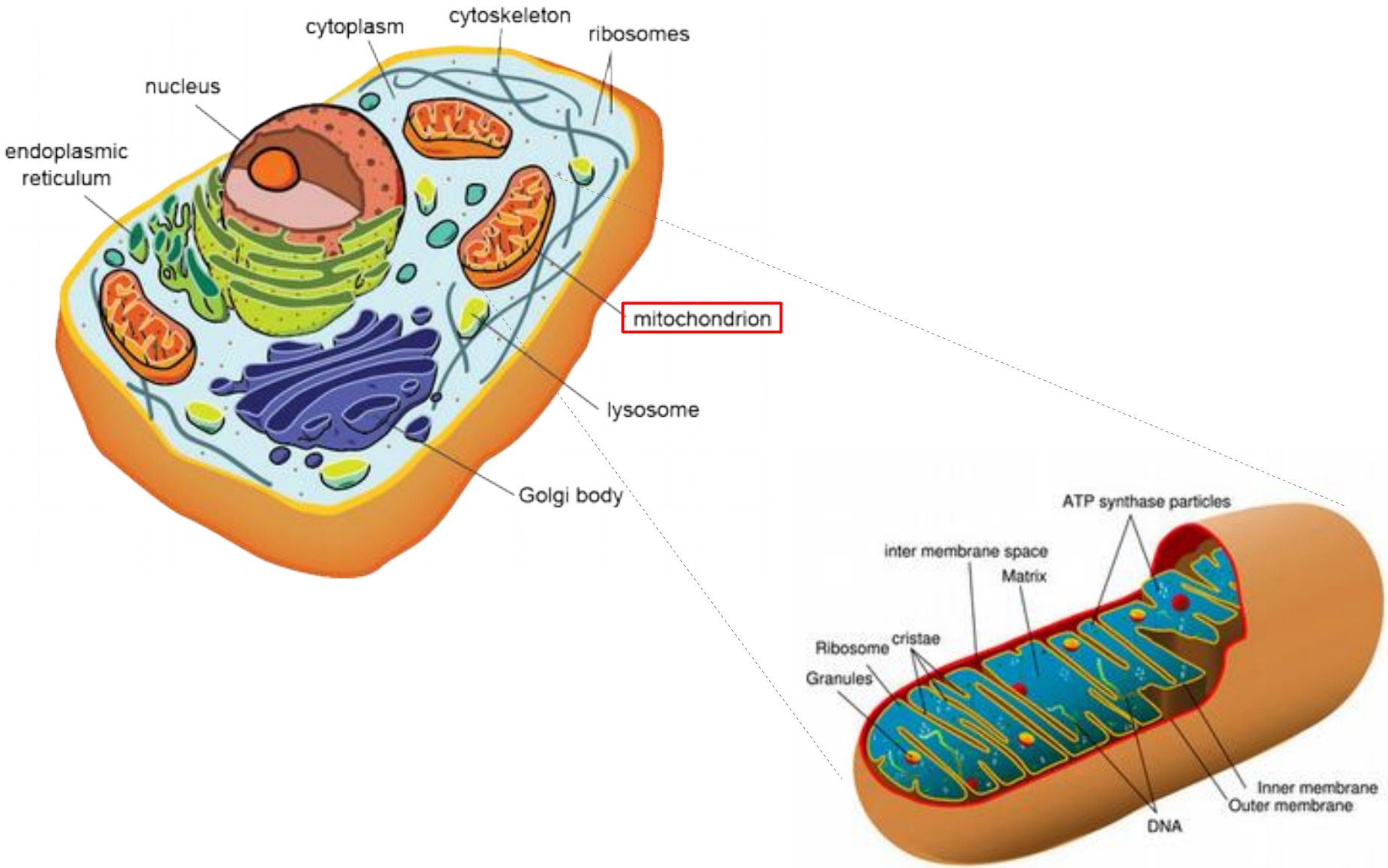

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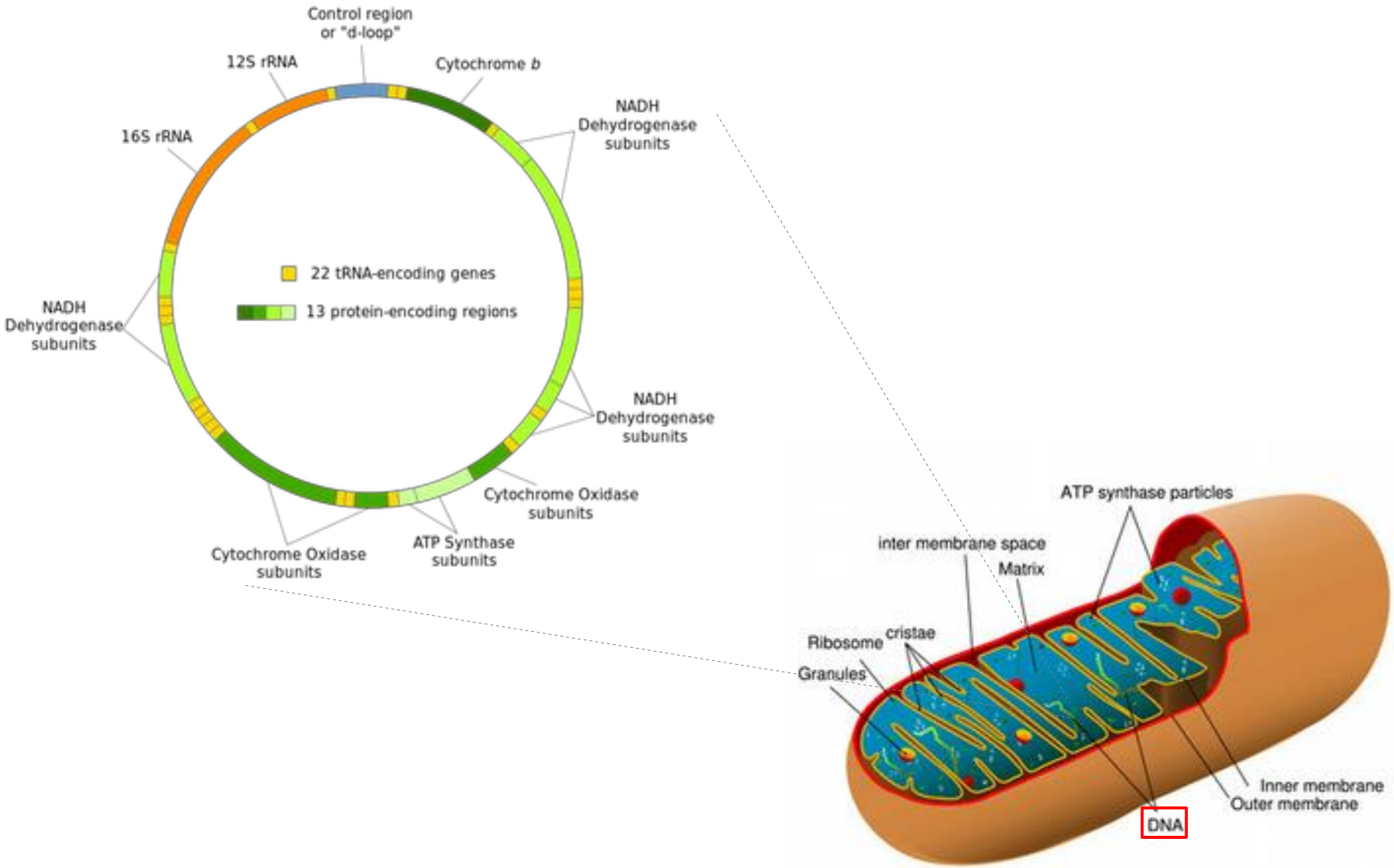

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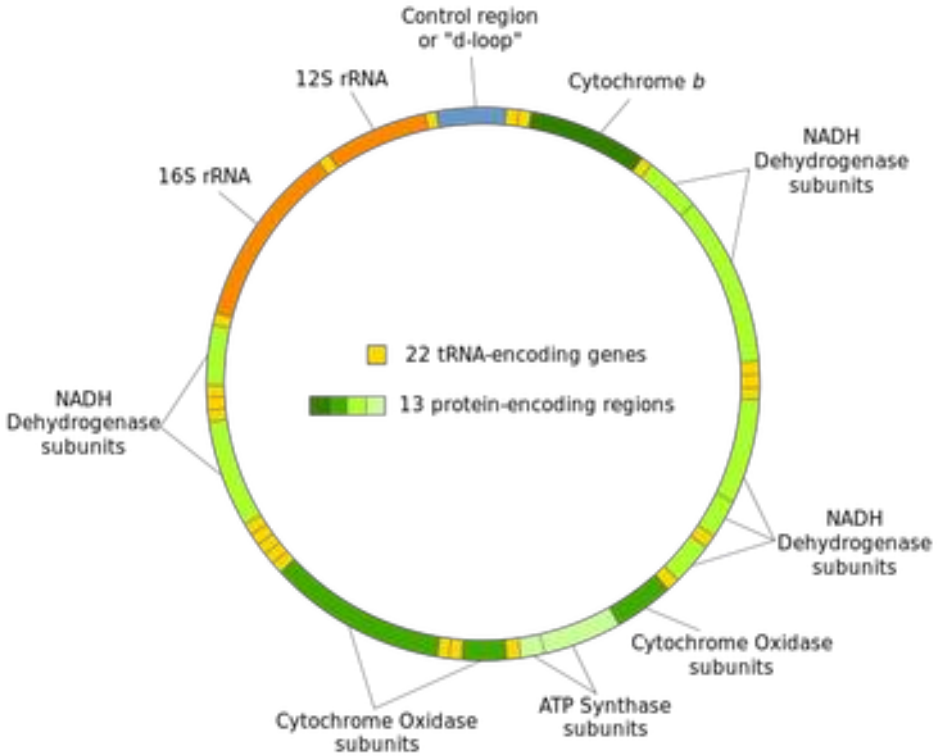
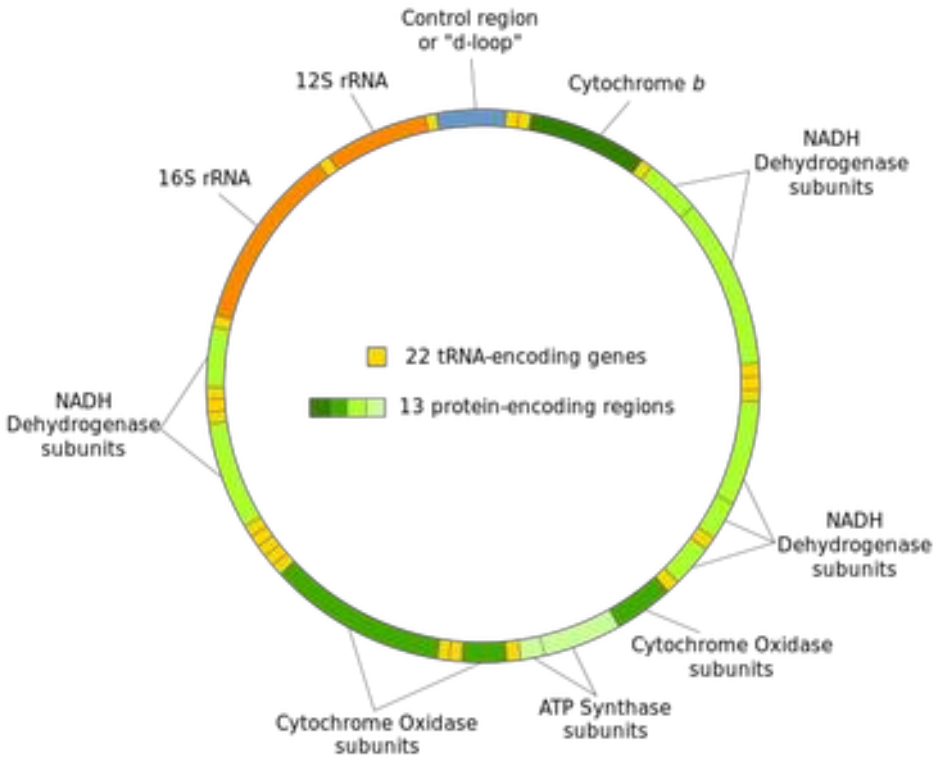


Own genetic code

Some examples: mitochondrial *12S rRNA*



Own genetic code

→ own translation machinery

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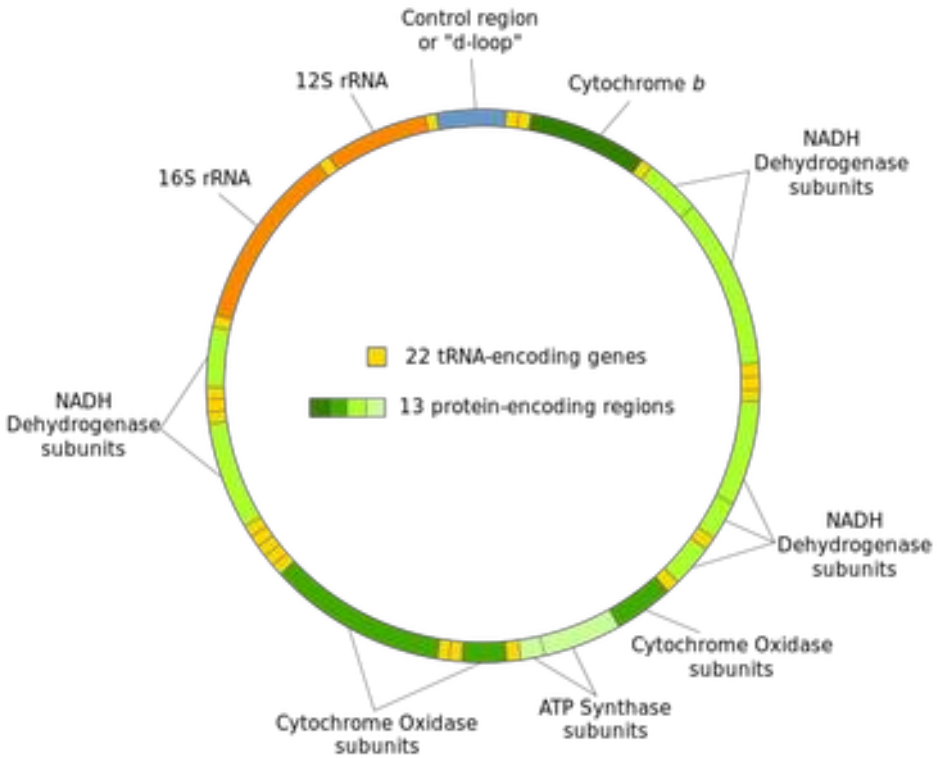

Own genetic code

→ own translation machinery

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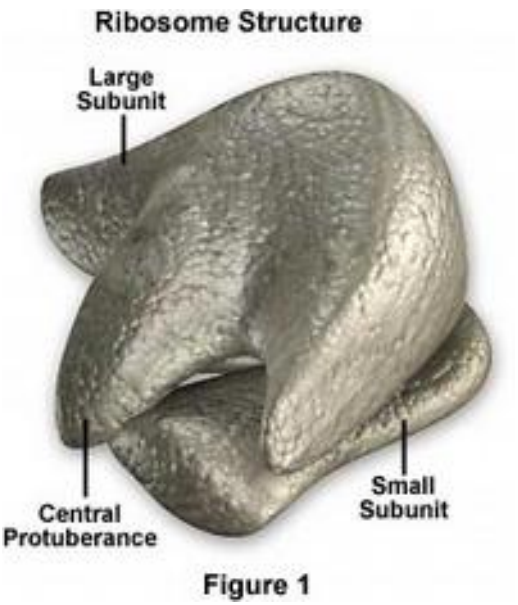
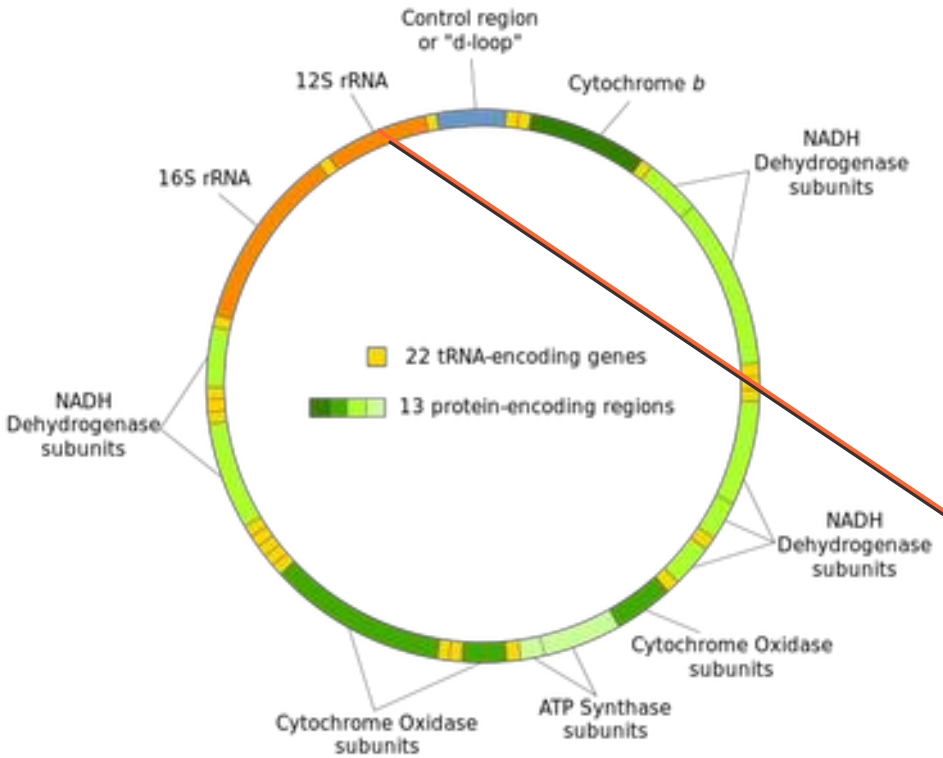


Some examples: mitochondrial *12S rRNA*



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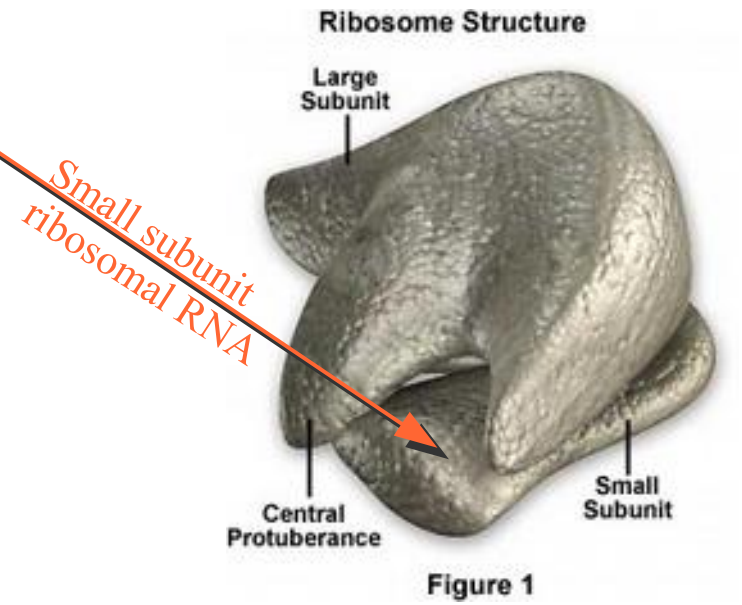


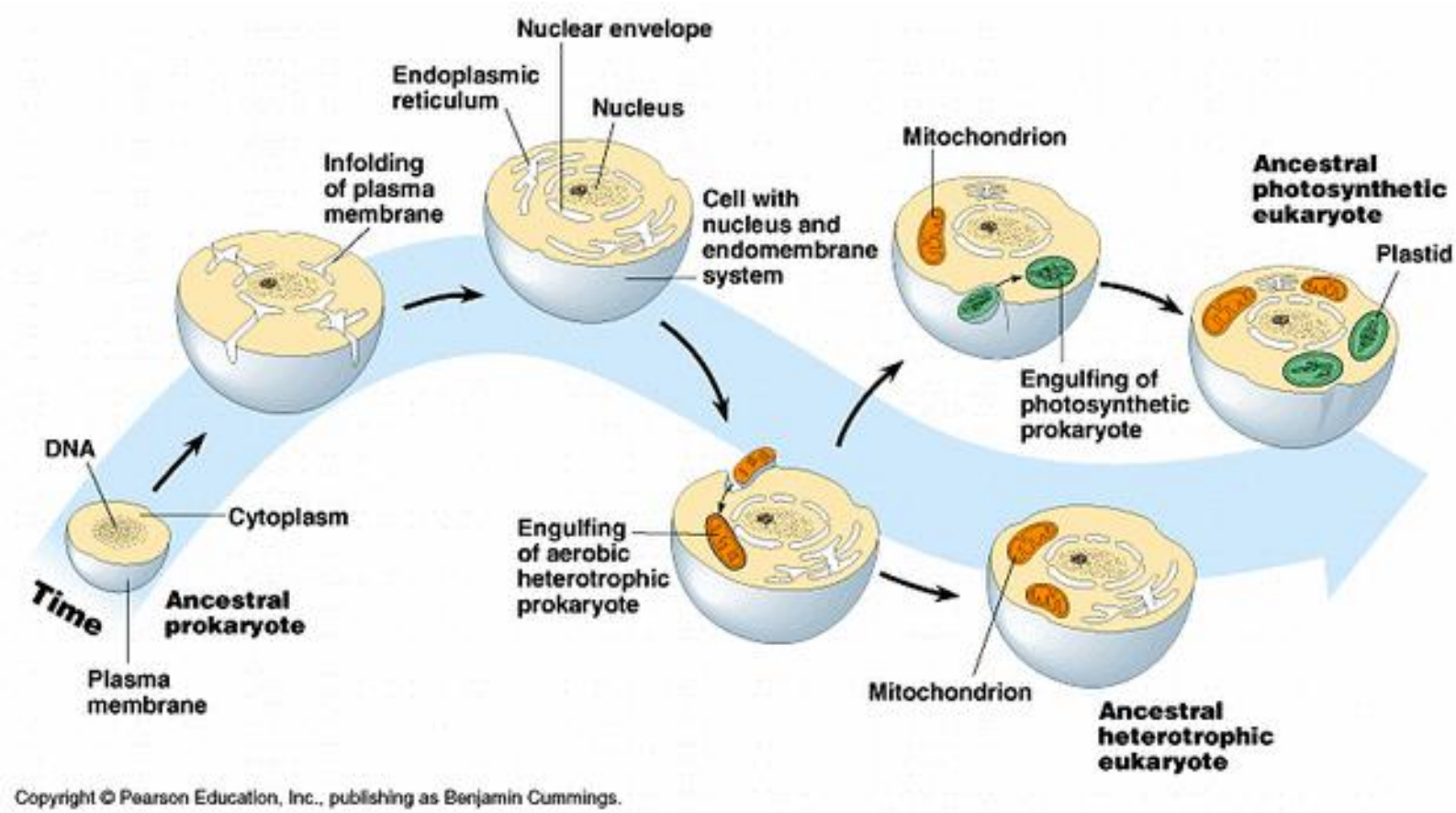
Small subunit
ribosomal RNA

Some examples: mitochondrial *12S rRNA*

Mitochondria → ancient bacteria

Some examples: mitochondrial *12S rRNA*

Mitochondria → ancient bacteria (endosymbiotic theory)



Some examples: mitochondrial *12S rRNA*

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→ mitochondrial ribosomes are very similar to bacterial ribosomes

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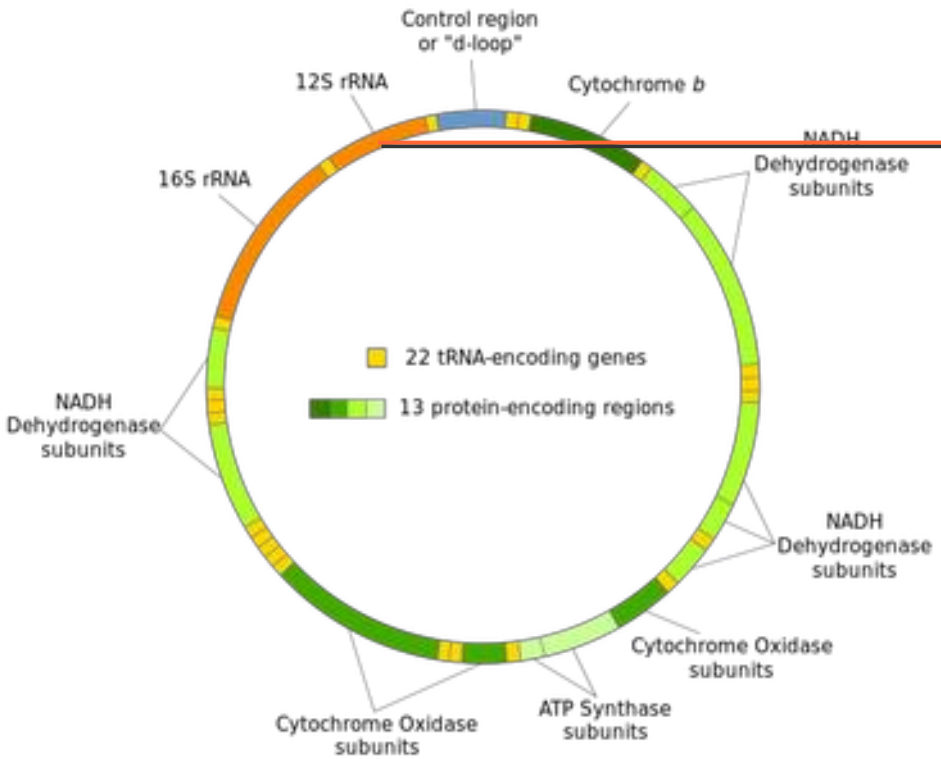

Mutations
(e.g. A1555G)

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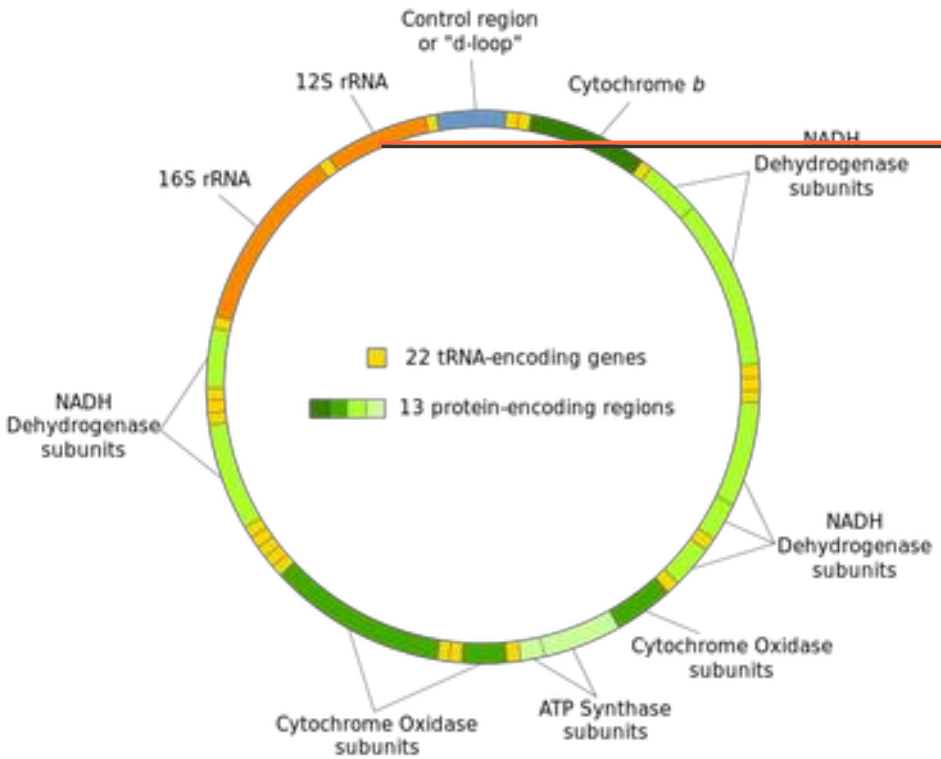

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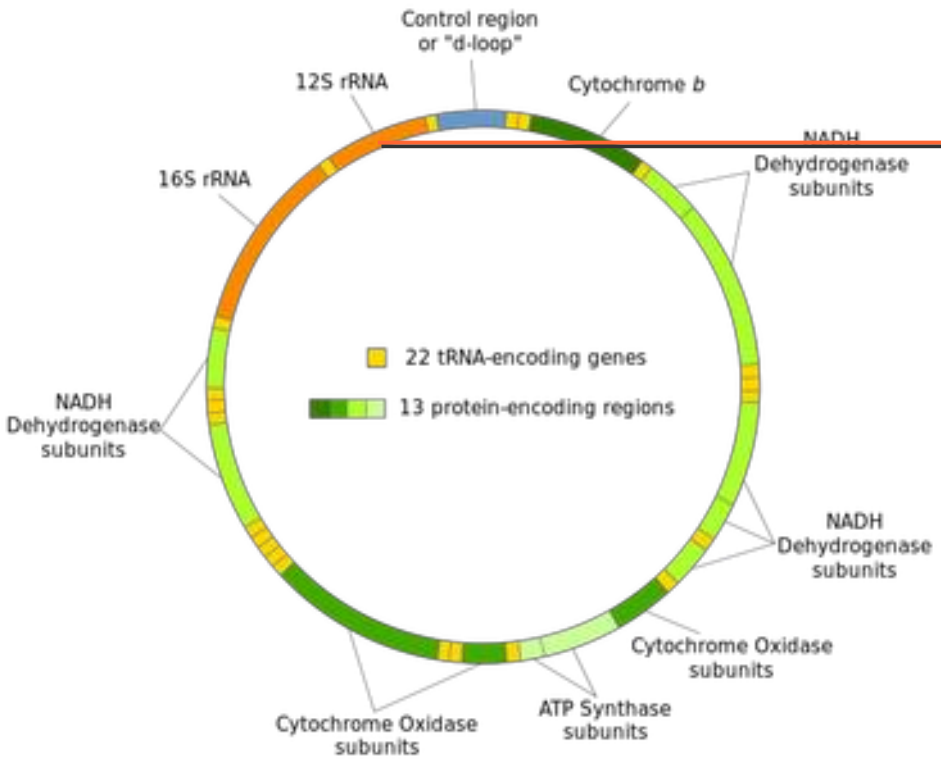

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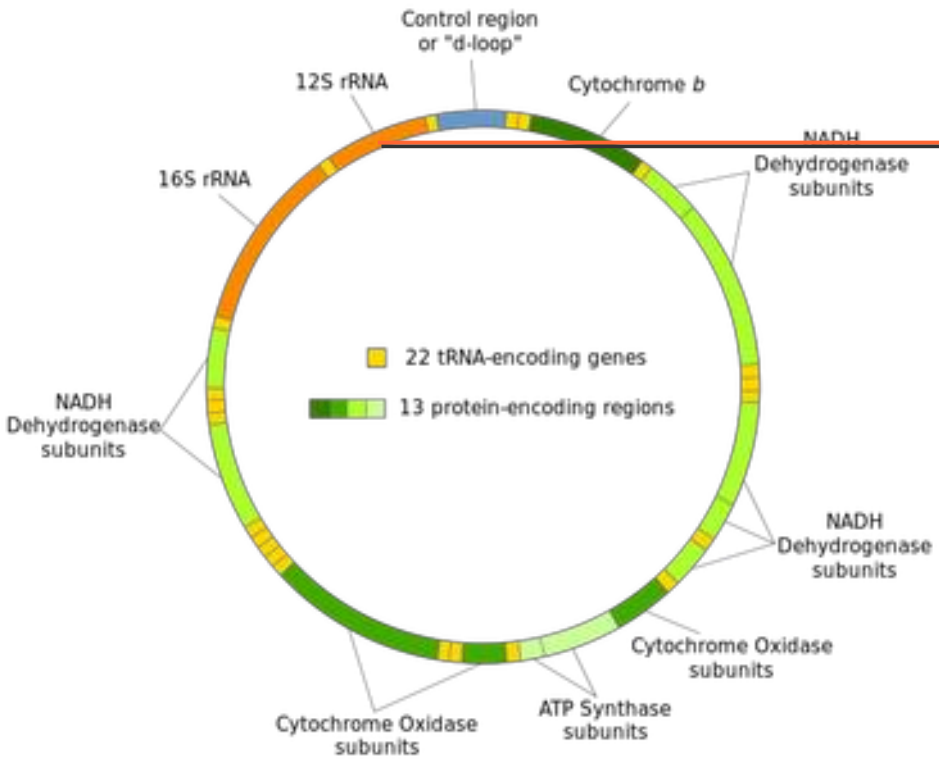
Some examples: mitochondrial *12S rRNA*

Hair cells are more affected by mitochondrial ribosomal impaired function more than other cells?



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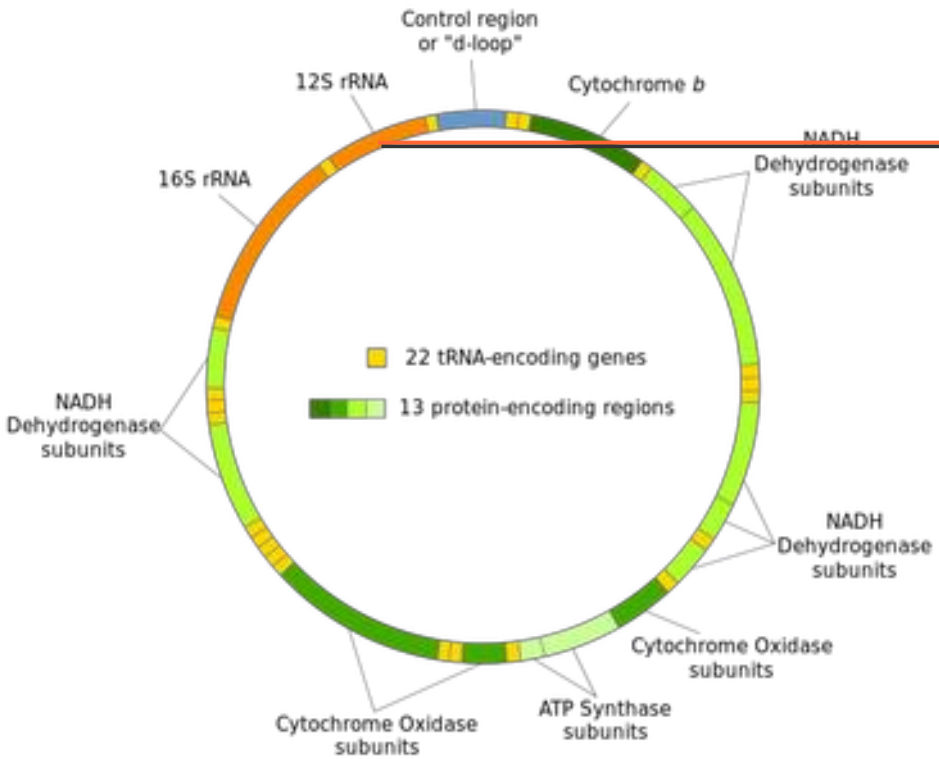
Some examples: mitochondrial *12S rRNA*

Hair cells are more affected by mitochondrial ribosomal impaired function more than other cells? → specific phenotype



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Congenital non-syndromic deafness

- Many loci (e.g., http://hereditaryhearingloss.org/main.aspx?c=.HHH&n=86163)

Congenital non-syndromic deafness

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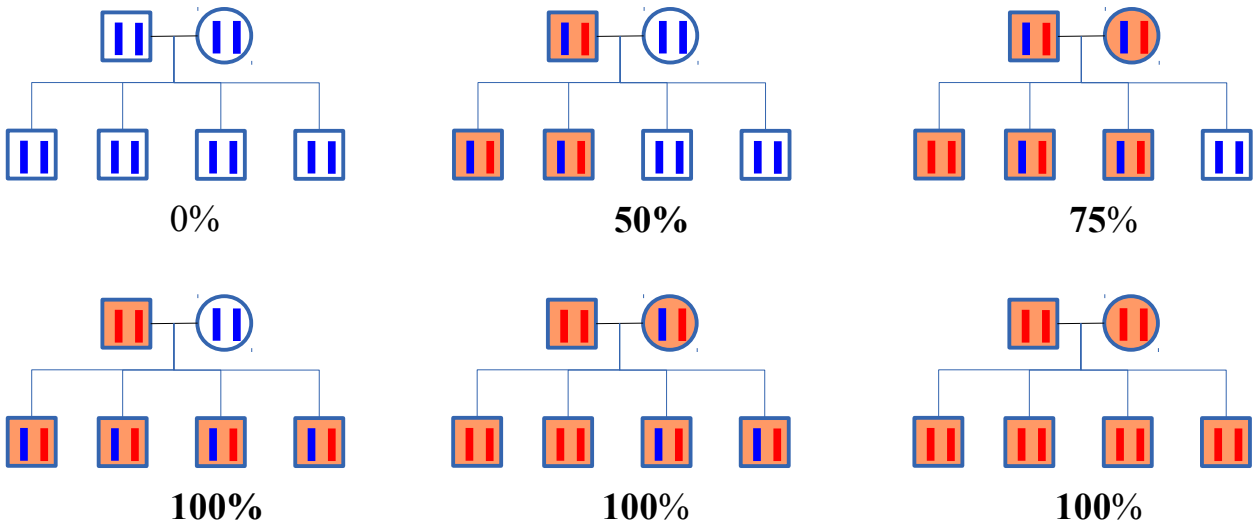
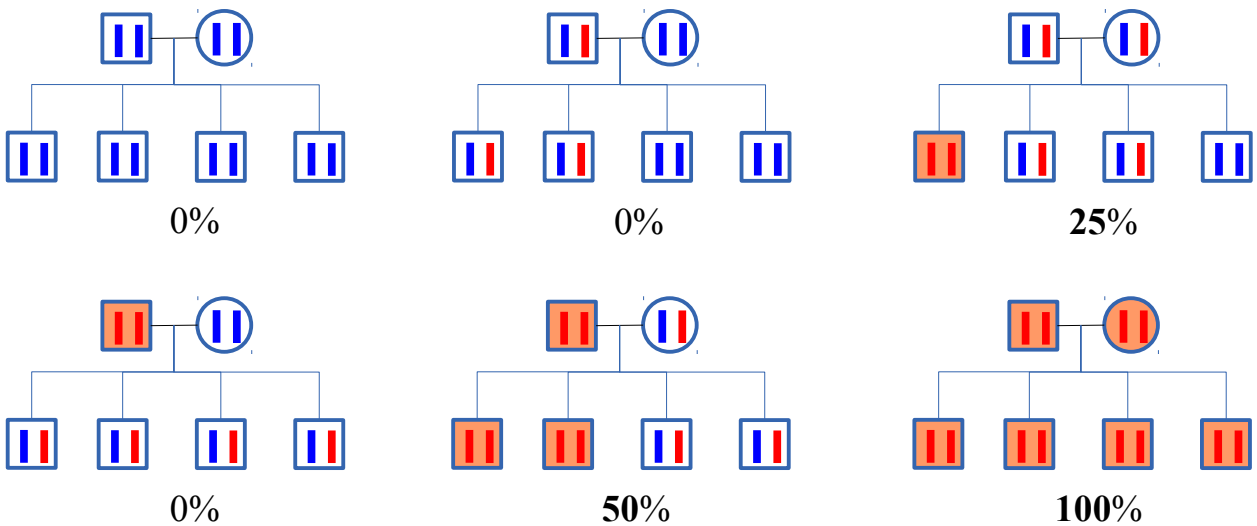


Congenital non-syndromic deafness

- Many loci (e.g., http://hereditaryhearingloss.org/main.aspx?c=.HHH&n=86163)
- Autosomal dominant: *DFN**A**nn*, recessive: *DFN**B**nn* (~40)



Congenital non-syndromic deafness

- Many loci (e.g., http://hereditaryhearingloss.org/main.aspx?c=.HHH&n=86163)
- Autosomal recessive: *DFNB1* and *DFNB3*

DFNB1A/B (*GJB2* and *GJB6*)

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- 13q12.11

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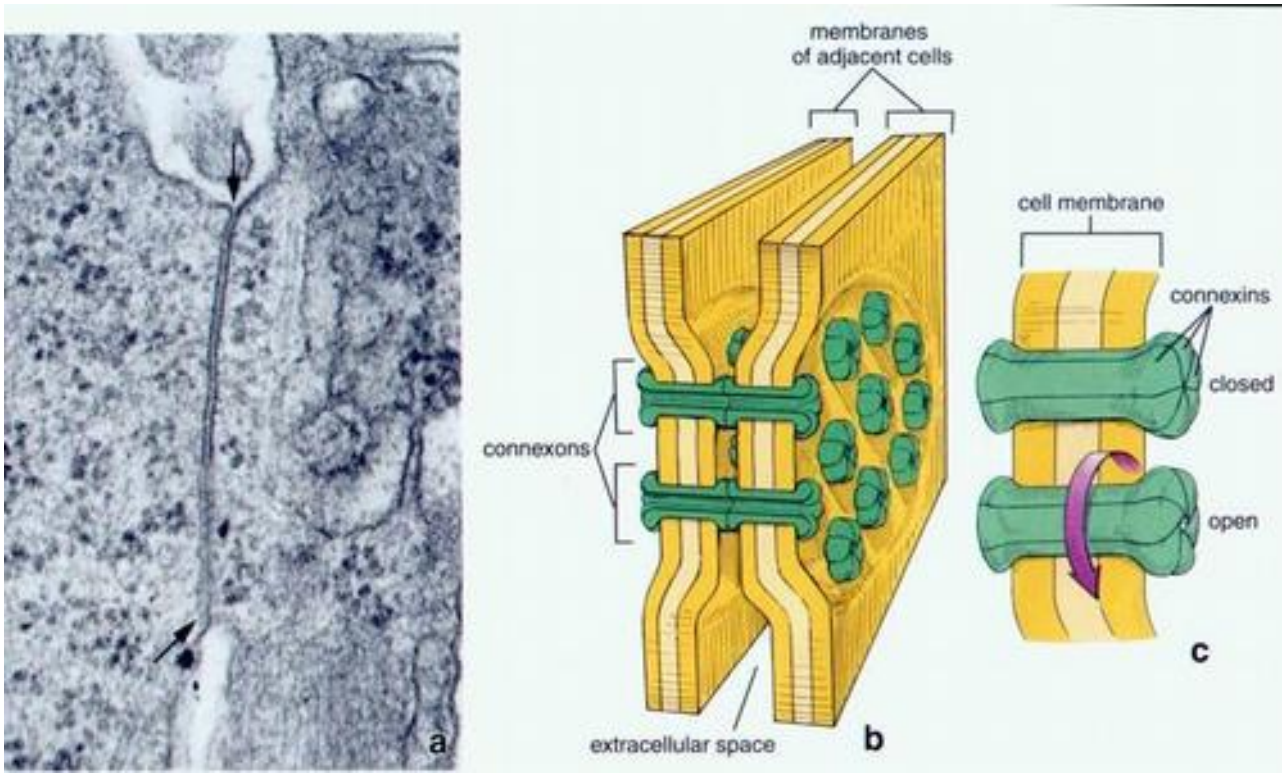

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  - other mutations: syndromes (skin + deafness)

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  - other mutations: skin disorders

→ potassium levels in the inner ear?

DFNB3 (MYO15A)

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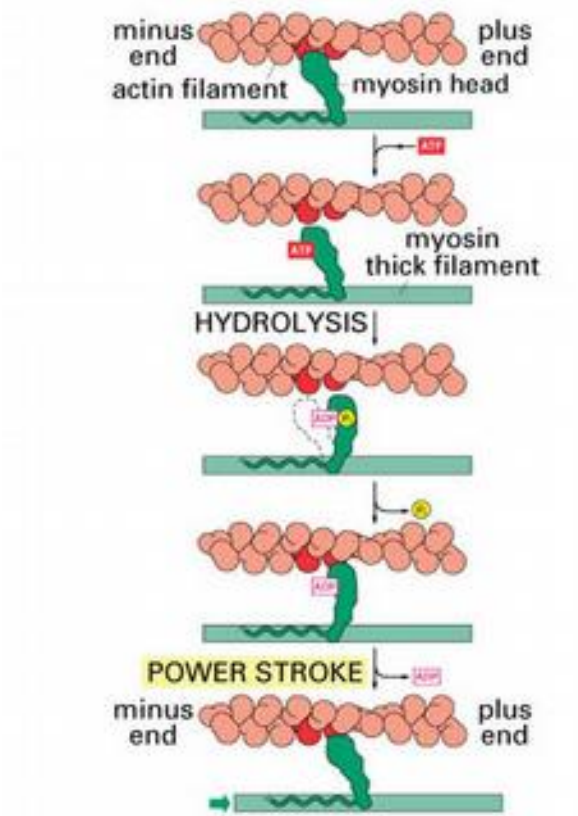

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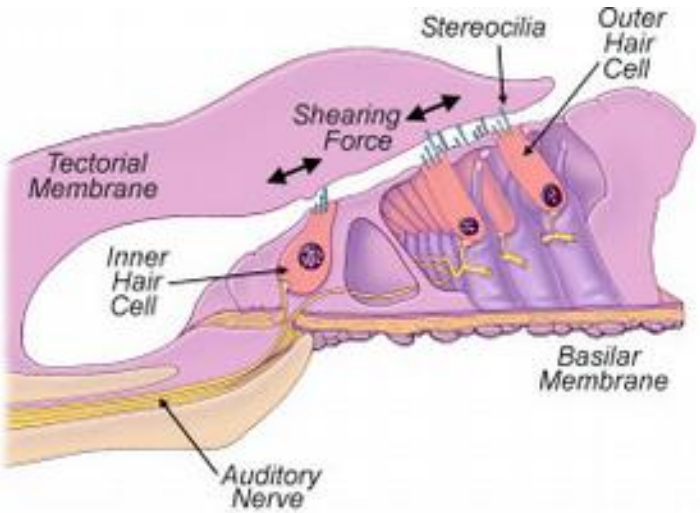
DFNB3 (MYO15A)

- Autosomal recessive
- 17p11.2
- *MYO15A* (unconventional myosin-15; myosin XVa)

  → sterocilia



The Organ of Corti

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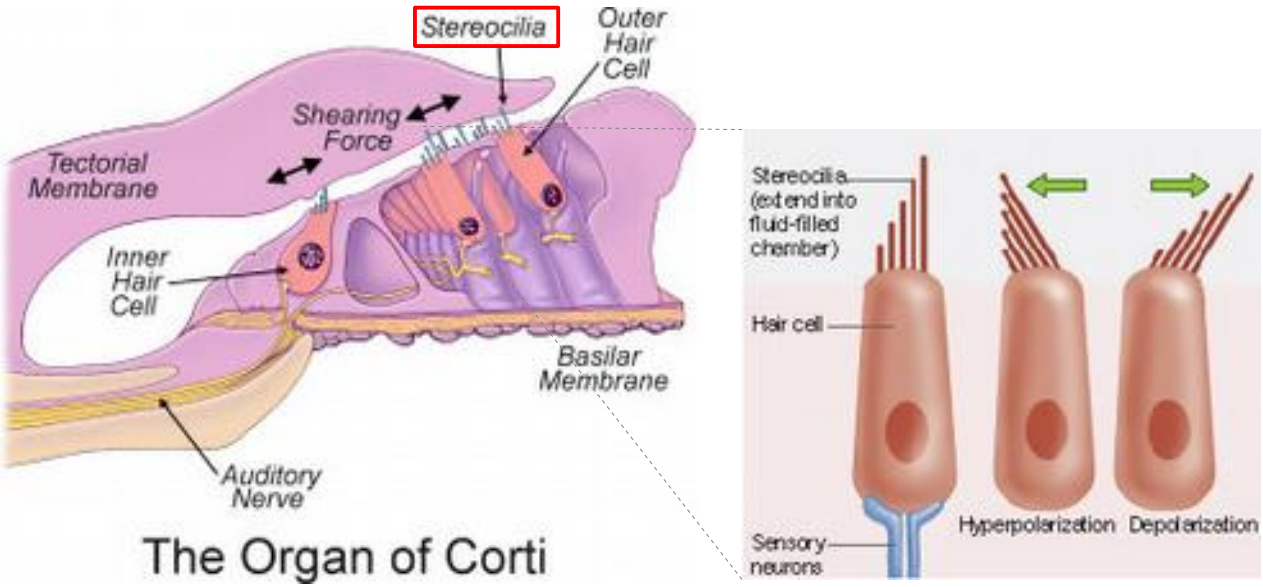

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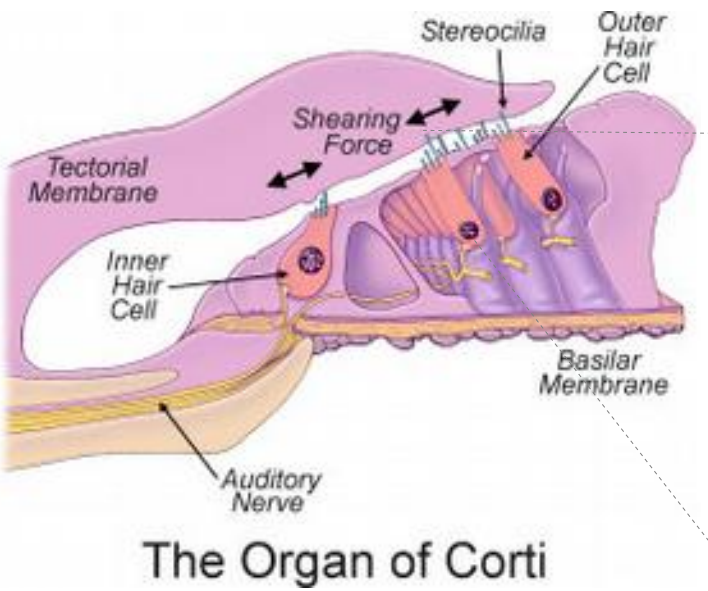

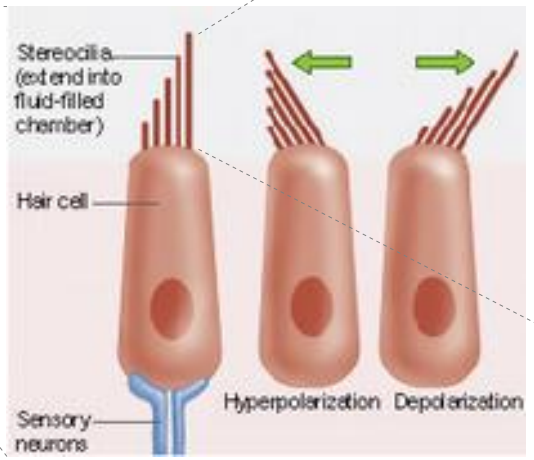

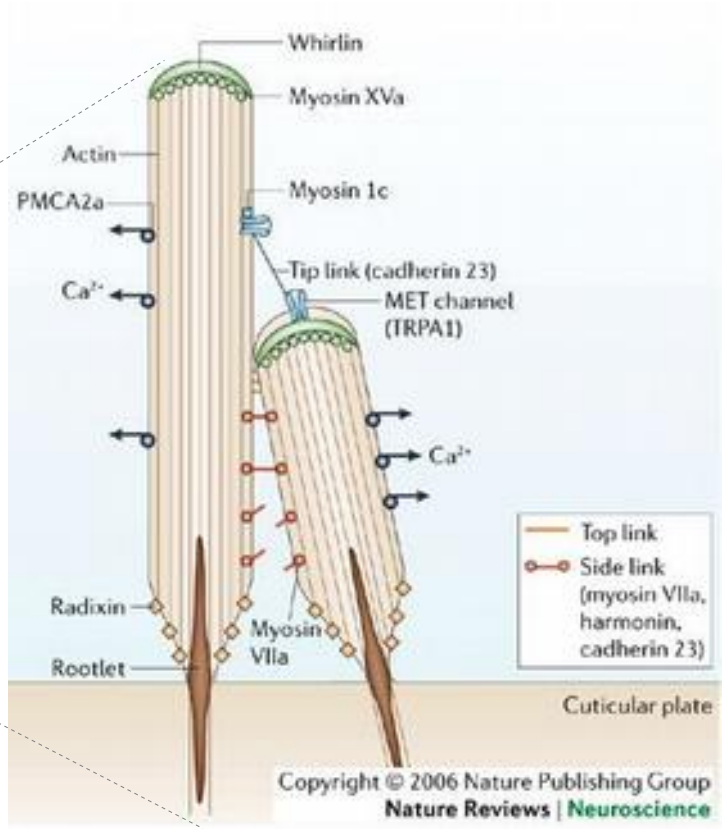

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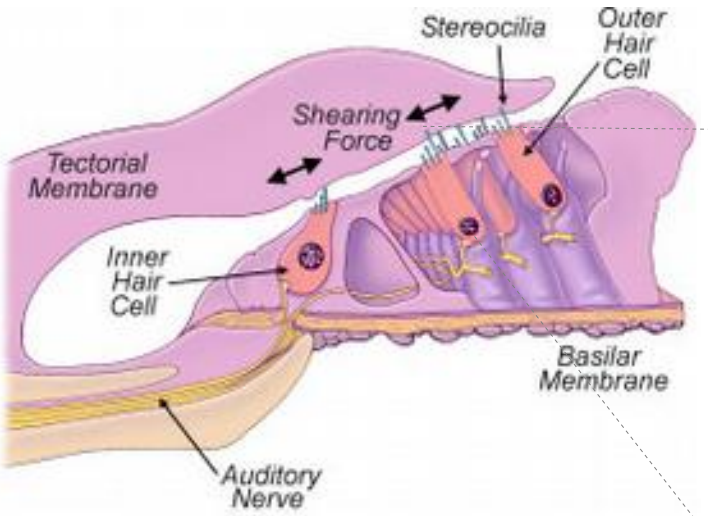
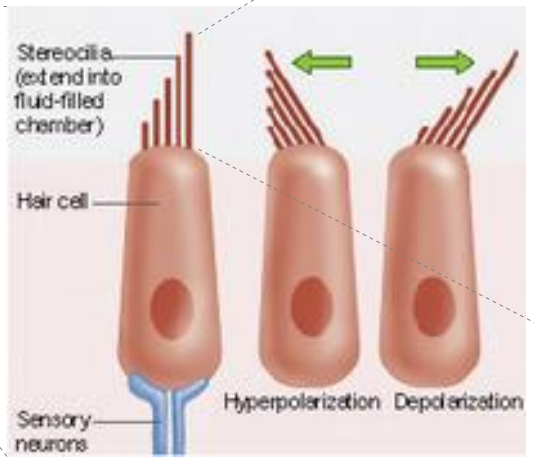
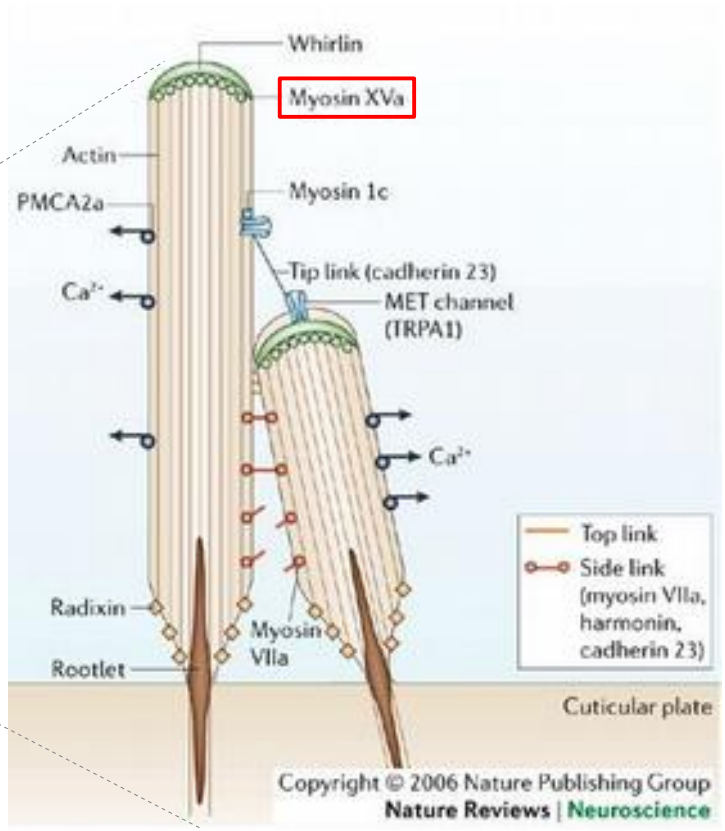


The Organ of Corti





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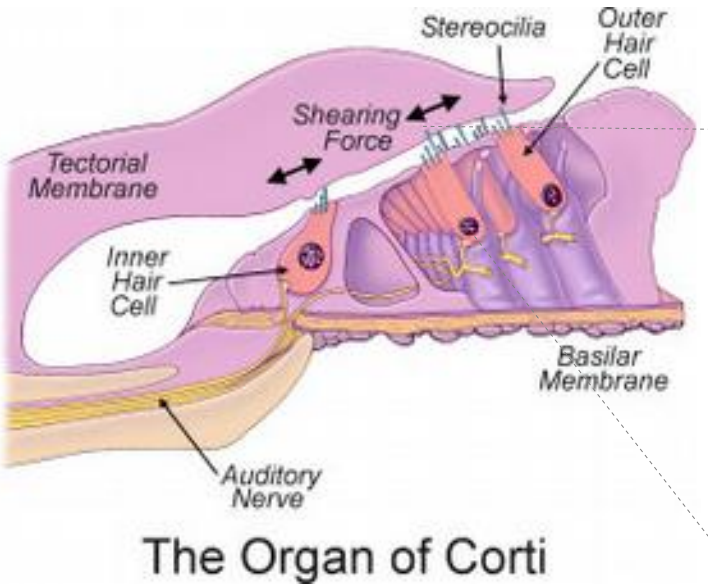

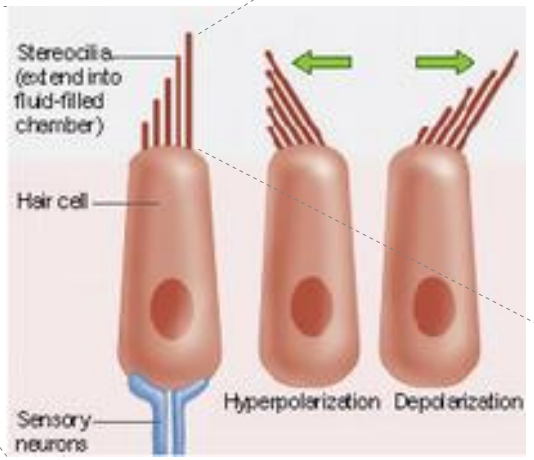

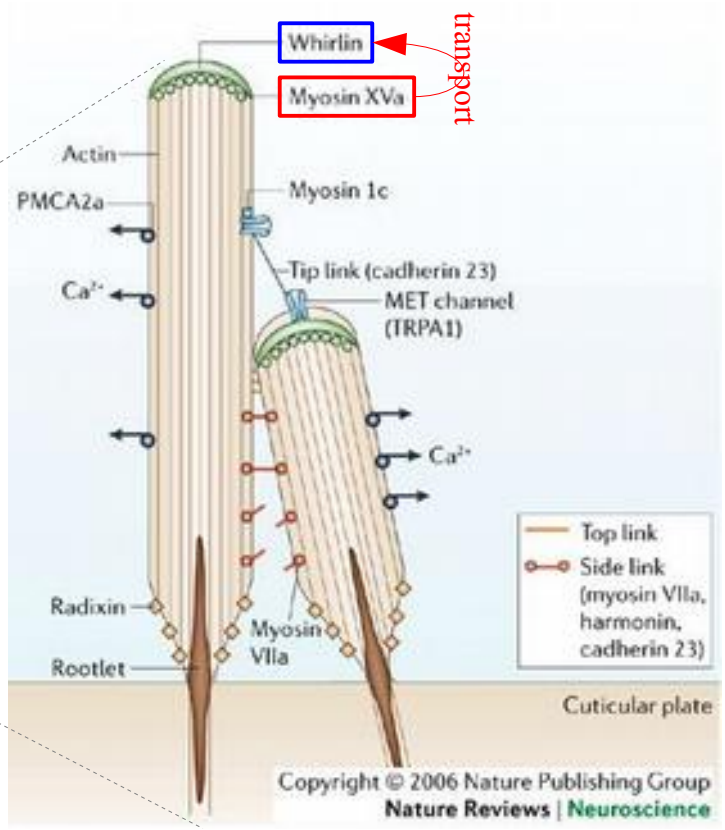

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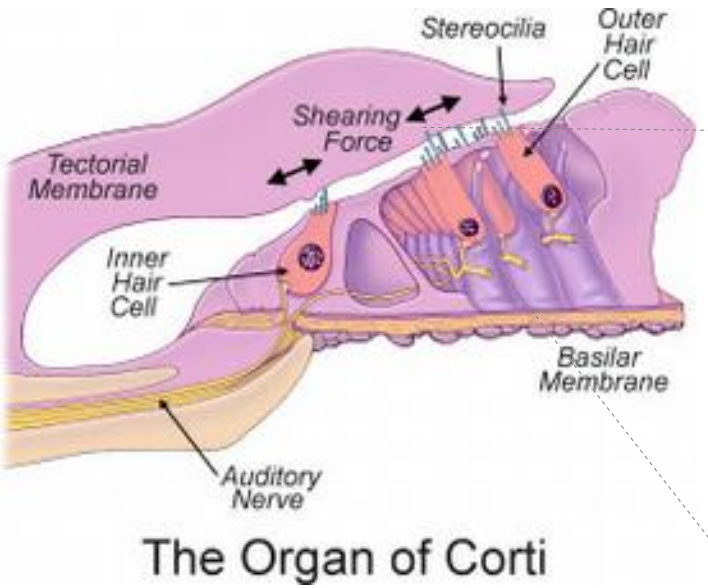

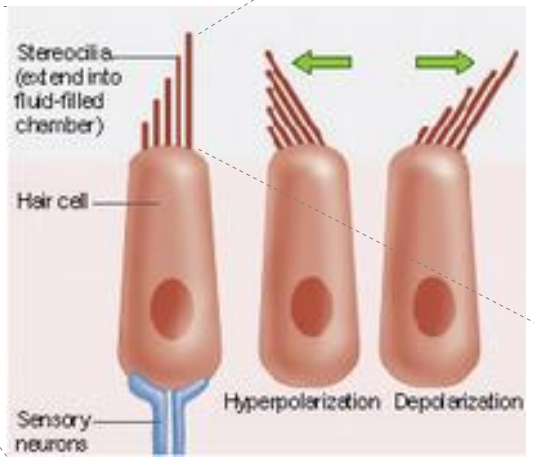

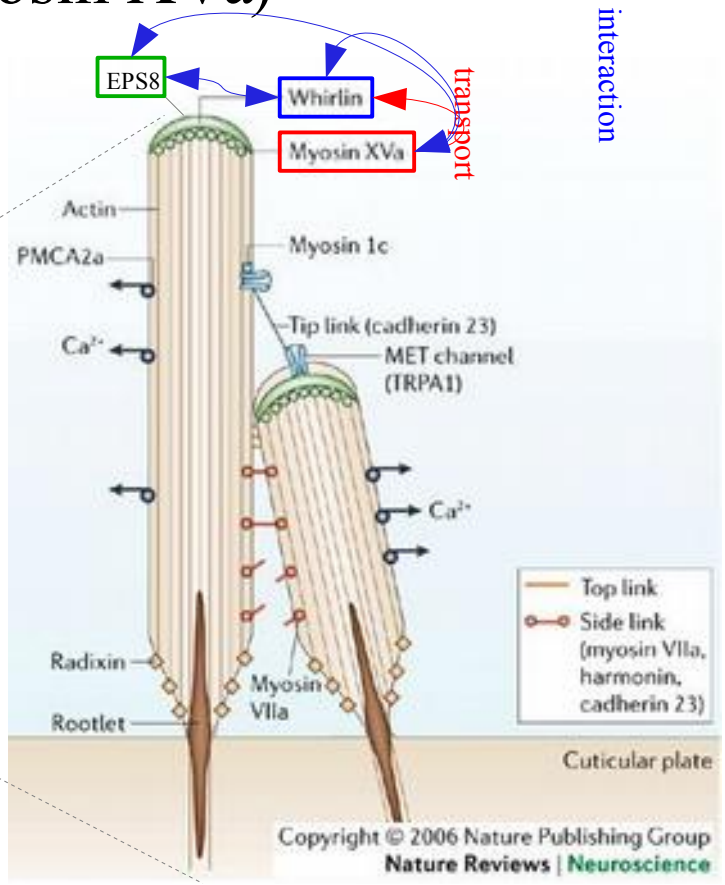

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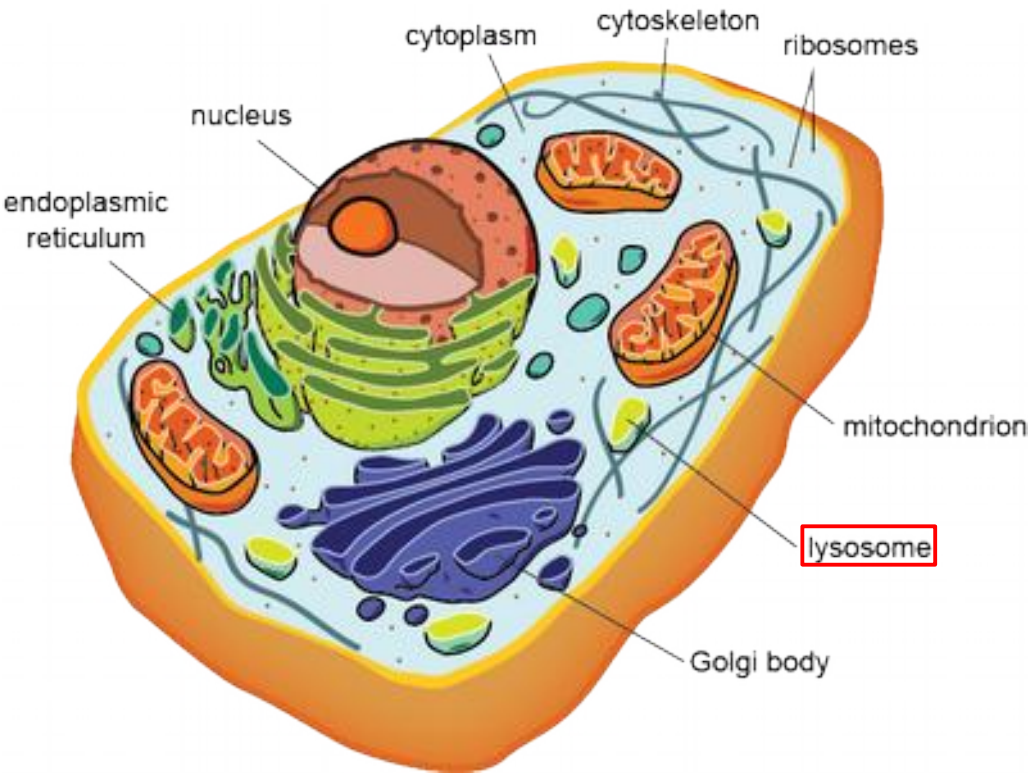

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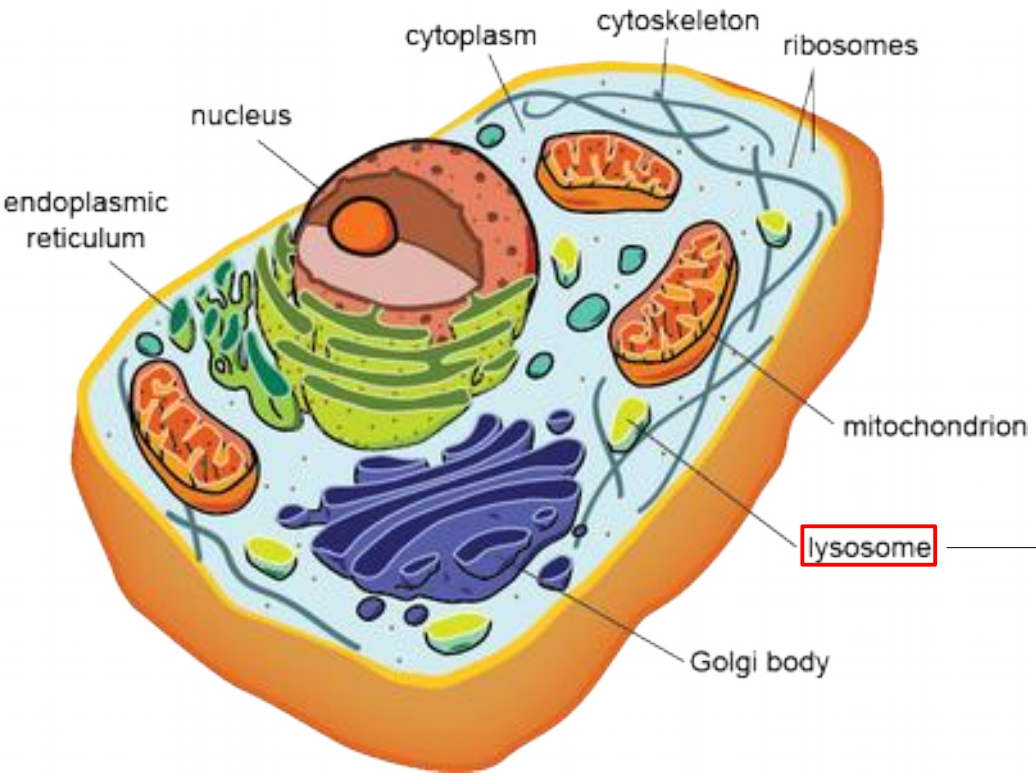

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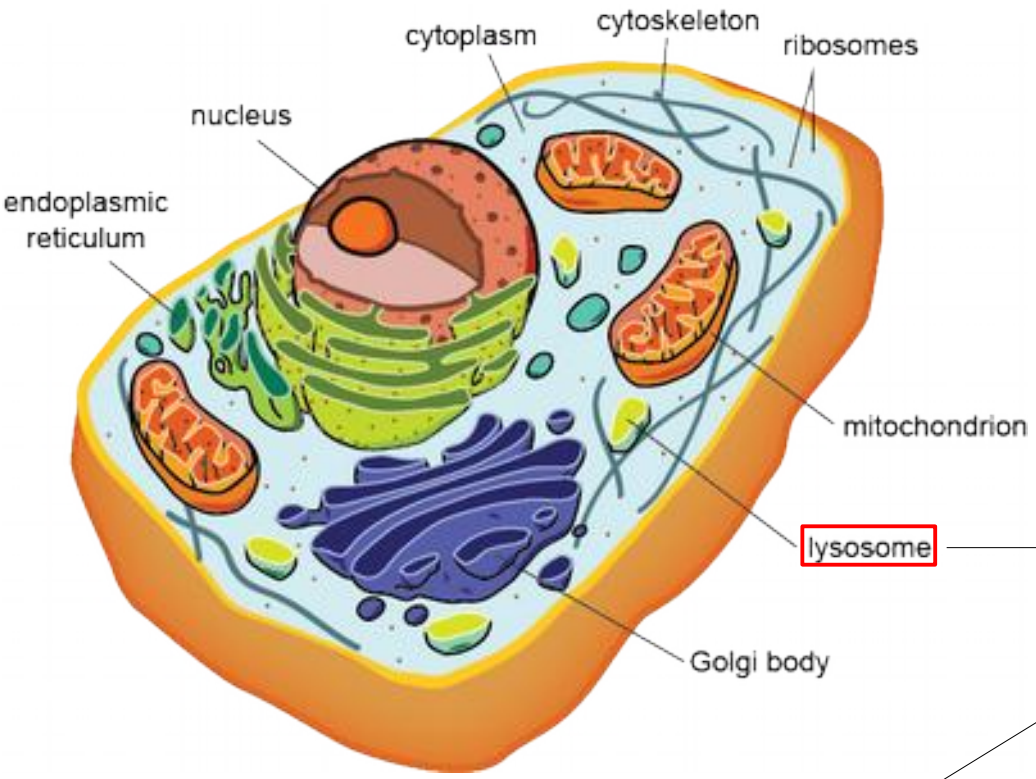

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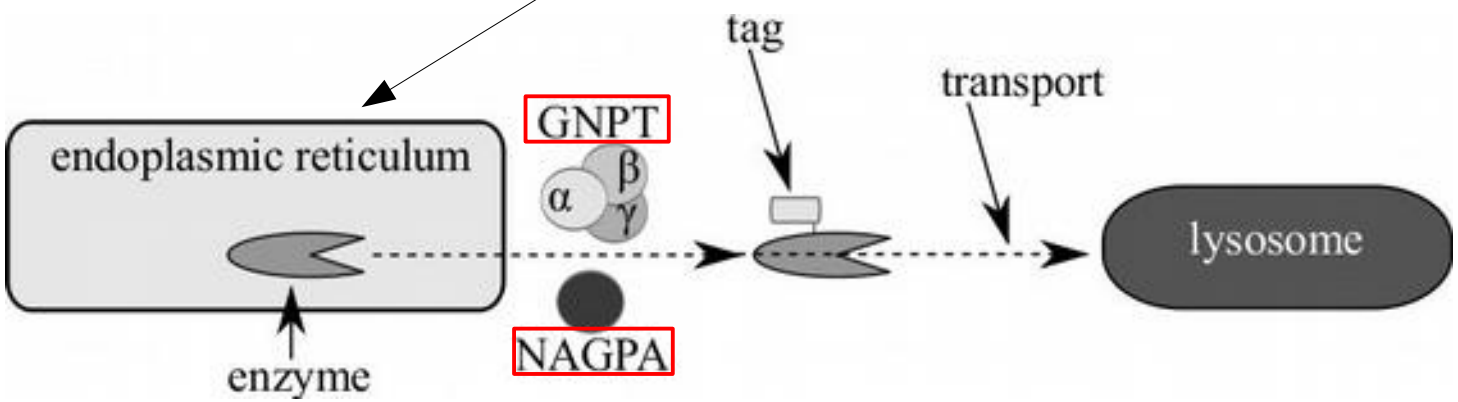

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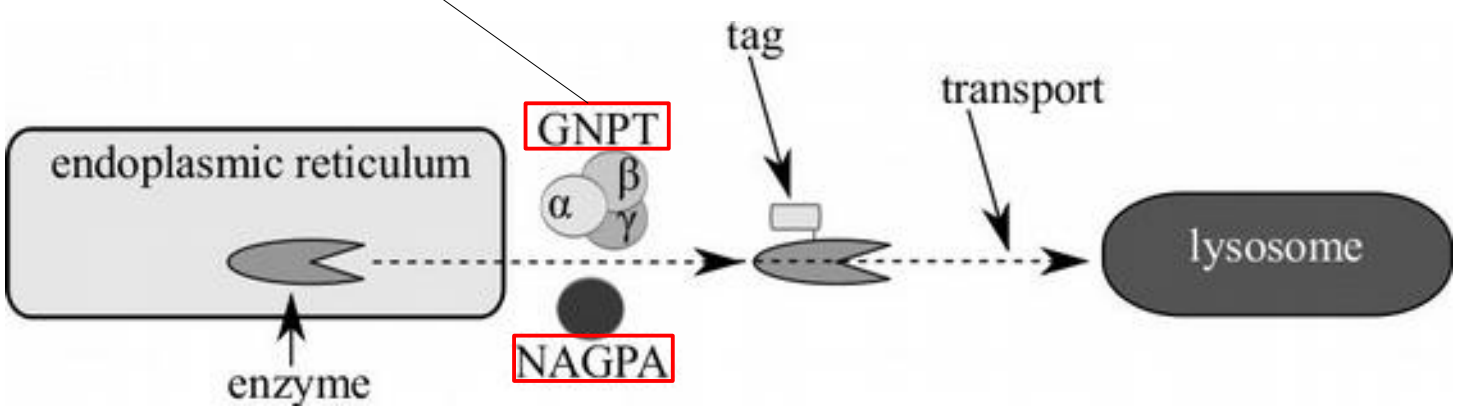
GNPT → 3 subunits (α, β, and γ)



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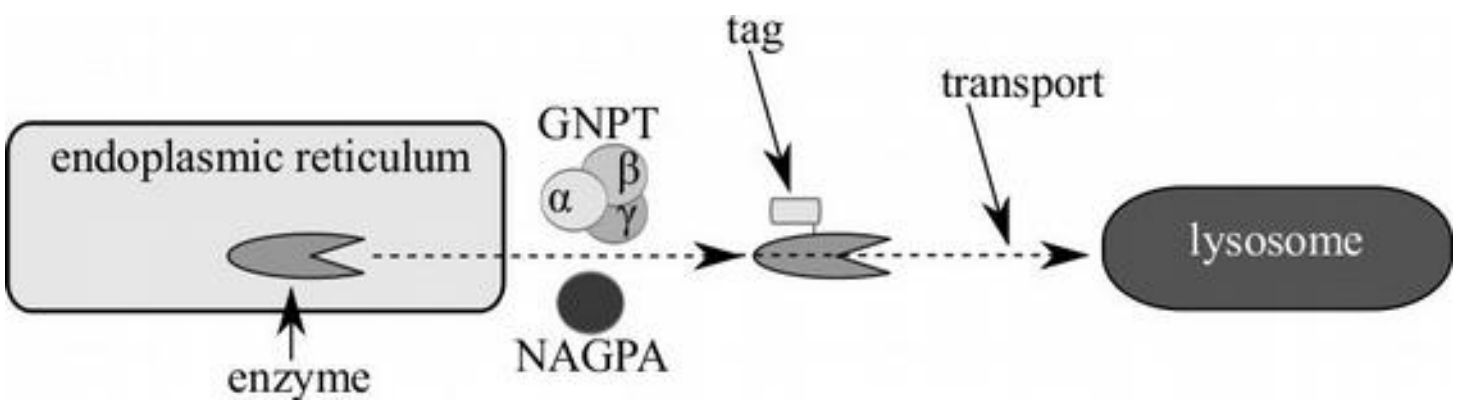

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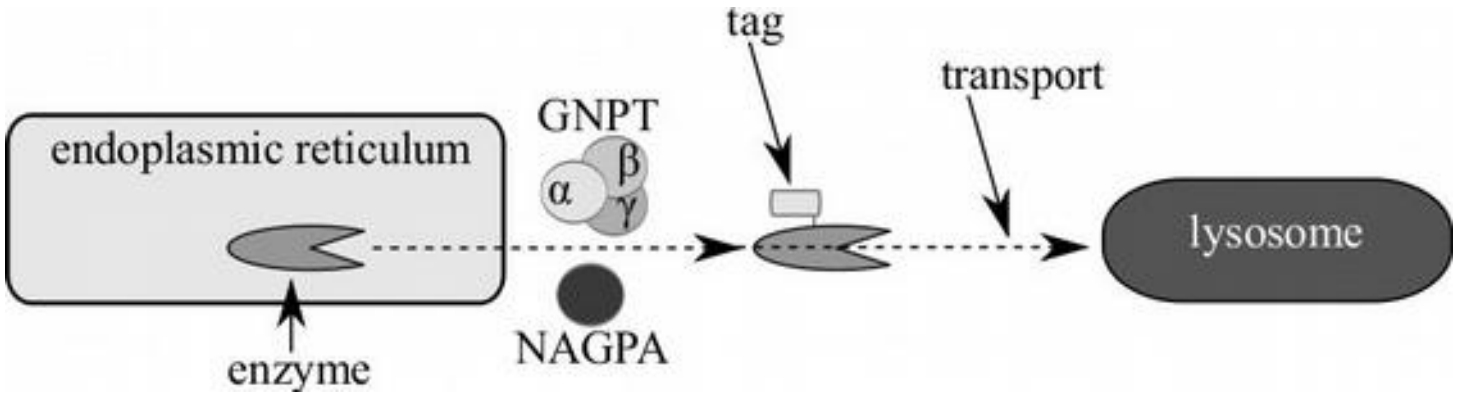

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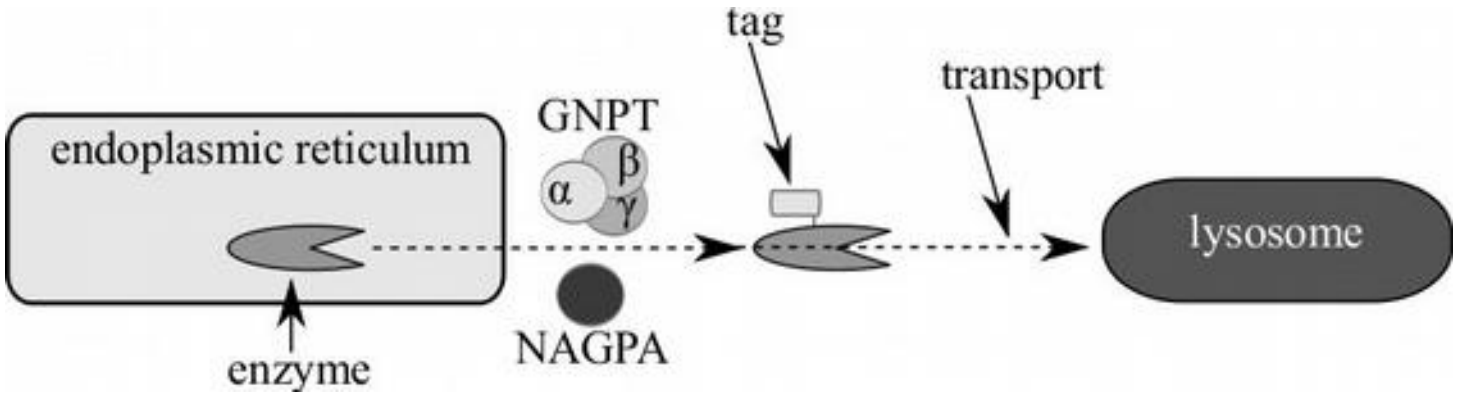

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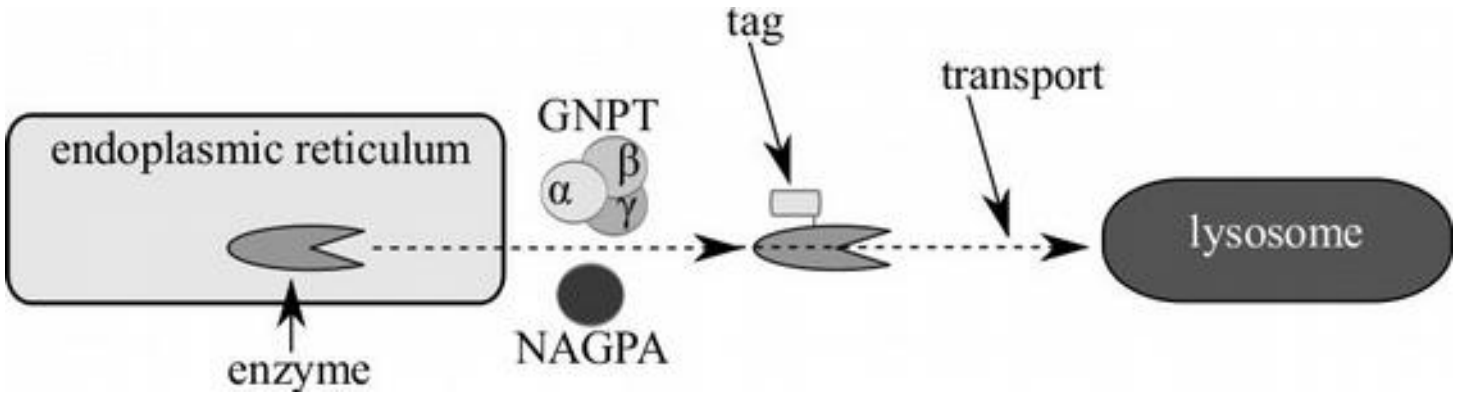

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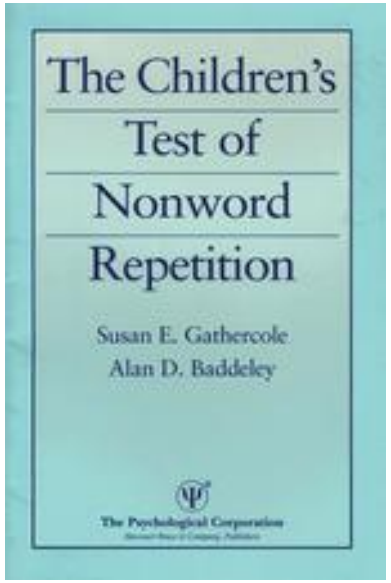

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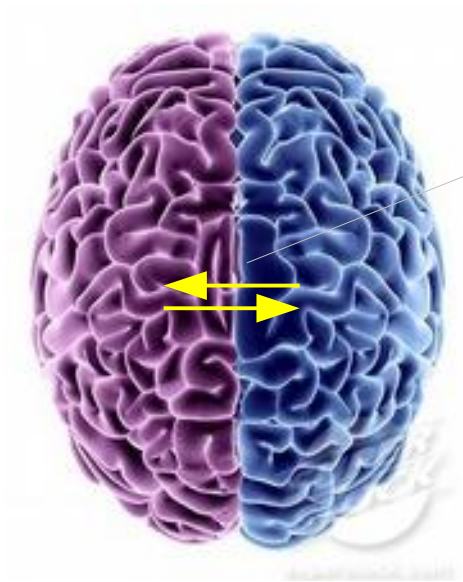

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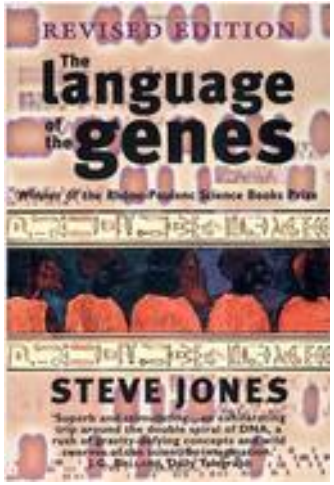
Thanks to: Alejandrina Cristia, Sarah Graham, Steve Levinson

Funding: Netherlands Organisation for Scientific Research (NWO) Vidi grant 276-70-022

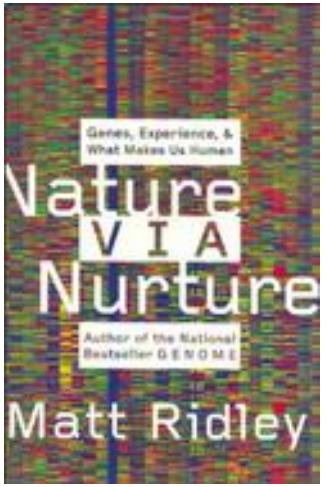
Suggested reading

- General books:

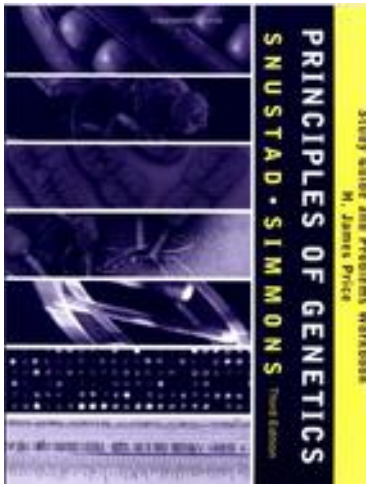


Jones, Steve (2000). *The language of the genes*. London: Flamingo.

Ridley, M. (2004). *Nature via nurture: genes, experience and what makes us human*. London: Harper Perennial.

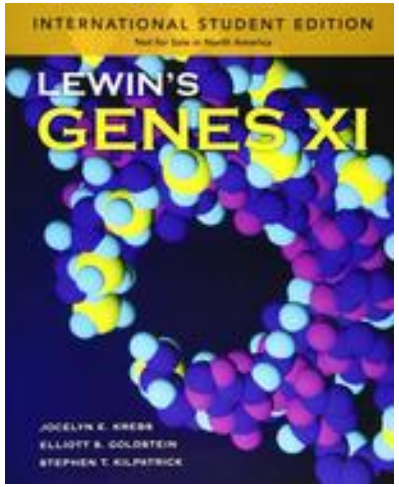


- Introductions to genetics:



Snustad, D. P., & Simmons, M. J. (2010). *Principles of genetics*. John Wiley & Sons, Inc.

Krebs, J. E., Kilpatrick, S. T., & Goldstein, E. S. (2013). *Lewin's Genes XI*. Jones and Bartlett Publishers, Inc.



Suggested reading

- Heritability:

Visscher, P. M., Hill, W. G., & Wray, N. R. (2008). Heritability in the genomics era–concepts and misconceptions. *Nat Rev Genet* **9**:255–266. doi:10.1038/nrg2322

Charney, E. (2012). Behavior genetics and postgenomics. *Behavioral and Brain Sciences* **35**:331–358. doi:10.1017/S0140525X11002226

Stromswold, K. (2001). The Heritability of Language: A Review and Metaanalysis of Twin, Adoption, and Linkage Studies. *Language* **77**:647–723.

- Linkage:

Dawn Teare, M., & Barrett, J. H. (2005). Genetic linkage studies. *The Lancet* **366**:1036–1044. doi:10.1016/S0140-6736(05)67382-5

- Association:

Hirschhorn, J. N., & Daly, M. J. (2005). Genome-wide association studies for common diseases and complex traits. *Nature Reviews Genetics* **6**:95–108. doi:10.1038/nrg1521

Balding, D. J. (2006). A tutorial on statistical methods for population association studies. *Nature Reviews Genetics* **7**:781–791. doi:10.1038/nrg1916

Suggested reading

- Sequencing:

Deriziotis, P., & Fisher, S. E. (2013). Neurogenomics of speech and language disorders: the road ahead. *Genome biology* **14**:204. doi:10.1186/gb-2013-14-4-204

O'Roak, B. J., Deriziotis, P., Lee, C., Vives, L., Schwartz, J. J., Girirajan, S., … Eichler, E. E. (2011). Exome sequencing in sporadic autism spectrum disorders identifies severe de novo mutations. *Nature genetics* **43**:585–589. doi:10.1038/ng.835

- Genetics of language:

Graham, S. A., & Fisher, S. E. (2013). Decoding the genetics of speech and language. *Current Opinion in Neurobiology* **23**:43-51. doi:10.1016/j.conb.2012.11.006

Kang, C., & Drayna, D. (2011). Genetics of speech and language disorders. *Ann rev genomics hum genet* **12**:145–164. doi:10.1146/annurev-genom-090810-183119

Smith, S. D., Grigorenko, E., Willcutt, E., Pennington, B. F., Olson, R. K., & DeFries, J. C. (2010). Etiologies and molecular mechanisms of communication disorders. *Journal of developmental and behavioral pediatrics* **31**, 555–563. doi:10.1097/DBP.0b013e3181ee3d9e

Bishop, D. V. M. (2009). Genes, cognition, and communication: insights from neurodevelopmental disorders. *Ann N Y Acad Sci* **1156**:1–18. doi:10.1111/j.1749-6632.2009.04419.x