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DNA Coding strand 5'->3'
DNA Template strand 3'->5'
mRNA strand 5'->3'
5'->3' direction of translation

G->S->M->telo->mei->tel1->tel2
2n 2n 2n 2n 2n n n
46 92 92 46 92 * 46 **23

*homolog pair separation
**sis chromatid separation

organism	Gene dosage
Fly 1X=♂	X expressn x2
marsupial	Dad X inactivated
Bird/reptiles ZW=♀ ZZ=♂	
man	Xist on hetrochrom X code RNA, coats the X, makes barr body (diff X inactivated each cell)

Lead to allele freq changes /H-W assumes none of
Natural selection
Migration
Mutation
Genetic Drift
non-random mating

Loss function	Gain function
*Dominant–ve	*Hyper-morphic
*Null/amorphic Leaky/	*Neo-morphic
*Hypomorphic [Most Recessive]	[Most Dominant]

Genetic Dissection
Investigate steps of a Biosynthetic pathway
growth medium A B C
1 (prototroph) + + + (ctrl)
2 - - +
3 3 2 1 - + +
Order is ->a->b->c

Genetic Heterogeneity
Mutations in diff genes have phenotype. Genetic Complementation-2 mutants have wild type offspring. Fail to complement= on same gene

Centromeric position and arm length

Dominant
Achondroplasia
Brachydactyly
C Night Blindness
Ehler-Danlos
Huntington's
Marfan
Neurofibromatosis
PTC Tasting
Widow's Peak
Wooly Hair
Hypertrichosis*

Recessive
Albinism
Alkaptonuria
Ataxia Telang...
Cystic Fibrosis
Galactosemia
Glycogen storage
Phenylketonuria
Sickle Cell
Tay-Sachs
Duchenne Muscle D

X-linked Rec.
Hemophilia
Red-Green C.B.

X-linked Dom.
Hypertrichosis*

Variable express
Waardberg

Maternal
LHON

Nondisjuction
Trisomy 13,18 21=DSCR 2x 2 many Jacob (47, XYY) Turner=SHOX

Sex Influenced
Pattern Baldness

Environmental
Sex Limited, Temp

Incomplete/Co dominant, Y Linked Epistasis, Delayed Age of Onset, pleiotrophy, Penetrance

Terminal deletion
Cri-du-chat

$$r = \frac{\text{number of recombinant gametes}}{\text{total number of meioses}}$$

Interference=1-C [c= obs. Int./Exp. Int.]
>0⇔less double crossovers than exp.
m.u. = ½r*100% P(recomb. Gamete)
m.u. = ½(1-r)*100% P(parental)
VP = VG + VE; VG = VA + VD + VI
VP = VE + ½VG (DZ twins)
H2 = VG /VP (broad sense)
h2 = VA /VP (narrow sense)
$R = S(h^2)$ [S= μ pop. - mating pop. μ]
$(p+q)(p+q) = p^2 + 2pq + q^2 = 1$
$p^2 + 2pq + q^2 + 2pr + r^2 + 2qr = 1$
# Phenotypes = 2*(# genes) + 1
Xlinked=♂-freq =p, ♀-freq= (pm+pf)/2
P = (2/3)pf+(1/3)pm; f(qn)=qi/(1+n*qi)
Stable equilibrium of p
pE = t/(s+t); qE = s/(s+t) s=1-w for p

Double Crossovers	
#stranded	#recomb. Prods.
2	None
3	2;(+2 parental)
4	All 4

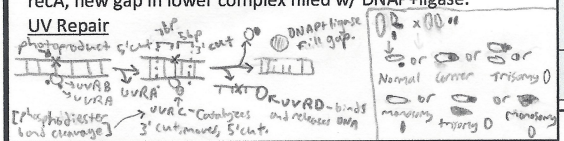
PEV=inversion moves genes to heterochromatin {HCT}. Mutations:
E(VAR)= ↑ variegation, ↑HCT
Su(VAR)=↓ HCT->Defective
HP1,HMT HP1-helps Methylate DNA.
HMT -Methylate DNA at certain Histones.
Su(VAR) genes=↑HCT

10nm- H1, H2A-H2B, H3-H4
H1=most variable.
146bp core DNA+50 linker DNA
30nm-10nm coils into solenoid structure. (6-8 nucleosomes per turn). Loops form rosettes, which condense into bundles.
300nm-variable (20-100kb) loops of 30nm fiber anchored to chromosome scaffold by nonhistone proteins at MARs sites (repetitive ATC sequences)
Chromatin Remodeling-displace nucleosomes-expose promoter-using epigenetic markers-takes place on N terminal end of histone proteins. Transcription ↓=Methylation; ↑=Acetylation

Coding Sequences
-Silent, -Missense, -Nonsense } base-pair substitn mutation. (transition or transversion P<Y)
-Frameshift
Nonsense creates: TAG,TAA or TGA,assume 5'->3' non template
Regulatory Mutation-amount of gene product changes
-promoter
-Splicing->AT...TG at sides Intron
Cryptic Splice Site new splice site

Forward mutation-wild->mutant
Reversions: True-restore wild type codon by mutation in same codon. Intragenic- mutation elsewhere on same gene. 2nd site-mutation in 2nd gene, both restore wild type.
Suppressor- mutation on 2nd site compensates for original.

Direct Repair: DNA proofreading, Photoreactive repair-photolyze enzyme uses light to break pyrimidine dimers.
Indirect Repair: Nucleotide Excision Repair-DNA glycosylase removes pyrimidine, leaves apuranic site. AP nuclease removes sugar+P. DNAP+ligase fill gap. Recombination Repair-recomb of broken strand w/ complementary strand using recA, new gap in lower complex filled w/ DNAP+ligase.
UV Repair

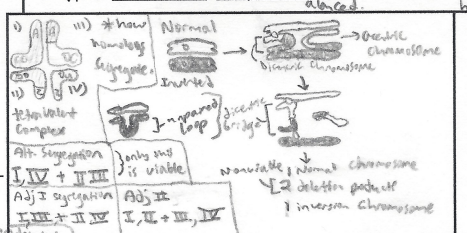


Mutations: **Spontaneous**-DNA replication->Strand Slippage= trinucleotide repeat disorders; changes to nucleotide structure->tautomeric shift-isomer w/ H in diff/spot, more bp mismatches; nucleotide lesions->deamination, depurination. **Induced**-mutagens-> chem. Agents: deaminating->substitution, nucleotide base analogs->transition, alkylating-> distorts DNA structure, Oxidizing->transversion, hydroxylating->transition, intercalating-> Frameshift.

Deletion mapping-pseudodominance of recessive allele if dominant is deleted

Inversion->pERIcentric=includes centromere;~=PARAcentric. Inversion loop needed in synapsis of invers. Hetero. Reattach to nonhomlg=translocation->semisterility if large=crossover suppression
3 types: unbalanced, reciprocal b. (parts of 2 nonhomologs switch place), Robertsonian (fusions)

Changing genomes=Chromosome aberrations, transposition
Euploid->whole # multiple of n (haploid #), ~->Anuploid
Polyploidy->n>3->Hybrid Vigor-allo/auto (from single species) multiple fertilizations or meiotic or mitotic nondisjunction.
Monosomic 2n-1; Trisomic->2n+1->trivalent or univalent and bivalent structure so semisterility. Nondisjunction->meiosis1=2tri,2mono->meiosis2=1mono,1tri, 2 normal.
Hypoploid->organism w/ chromosome segment underrepresented. Hyperploid->overrepresented. Uniparental disomy-both from single parent->trisomy rescue or 2 nondisj.
Unequal Crossover-repetitive regions of homologs misalign.



Homologous nucleotides-Orthologs=same anscestry; Paralog=duplication event
New genes form: **duplication**, " "by unequal crossover, Exon Shuffling, RT, from transposon, lateral transfer, Gene Fission, De Novo derivation (introns->exons); become: Pseudogenes, Subfunctional, Neofunctional
Synteny-conserved gene order CNV-

genotype	None	Complementary GeneInteract	Duplicate GeneAction	Dominant GeneInteract	Recessive Epistasis	Dominant Epistasis	Dominant Suppressive
1/16AABB	A-B- 9/16	A-B- 9/16 Need A and B	A-B-,A-bb, aaB- 15/16 A and B do same thing	A-B- 9/16 Need both for full phenotype	A-B- 9/16 aa negates B effects	A-B- A-bb 12/16 A- negates bb effects	A-B-, 13/16 B- suppresses A- or aa
2/16AaBB							
2/16AABb							
4/16AaBb							
1/16AAbb	A-bb 3/16	A-bb, aaB-, aabb 7/16		A-bb aaB- 6/16	A-bb 3/16		A-bb 3/16
2/16Aabb							
2/16aaBb	aaB- 3/16				aaB- aabb 4/16	aaB- 3/16	aaB-, aabb 13/16
1/16aaBB							
1/16aabb	1/16		1/16	1/16		1/16	

Transposable Gene Element-> transposition within genome. Cause mutation= insertional inactivation.
Autonomous=carries transposase gene, can do transposition (Ac); ~=non-autonomous (Ds)
Intraspecific comparison-SNPs within same species