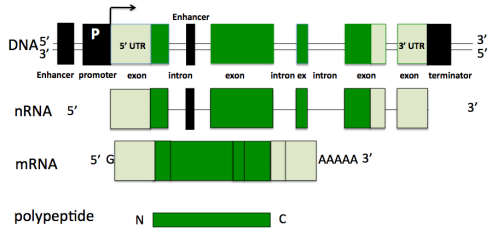
Diagnostics for pedigrees (how to solve any pedigree):

1. Information in the question: Does the question say the condition is “rare”? --if so that means we can assume people marrying in are unaffected unless there is evidence to the contrary. If it does not say this then some people marrying in might be carriers.
2. Attempt to determine dominance vs. recessiveness first Are there any unaffected parents that give birth to an affected child? If so then the condition MUST be recessive. For dominant conditions it tends to be observed in every generation. If you see two affected parents have any unaffected child then it MUST be dominant (but you often won’t see this in real pedigrees)
3. Is the condition more commonly observed in males? This could indicate X-linked recessive. We try to consider what condition requires the fewest number of affected individuals to explain it.
4. If affected males have all their daughters affected and none of their sons it strongly suggests X-linked dominance.



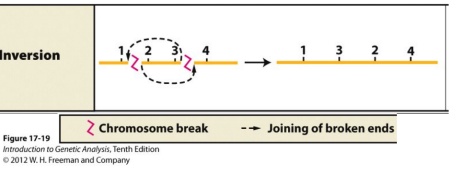


Figure 17-19
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Inversion (a chunk of the chromosome containing the gene (2) has flipped inside the chromosome)

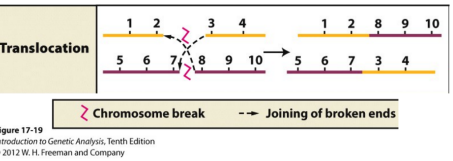

Figure 17-19
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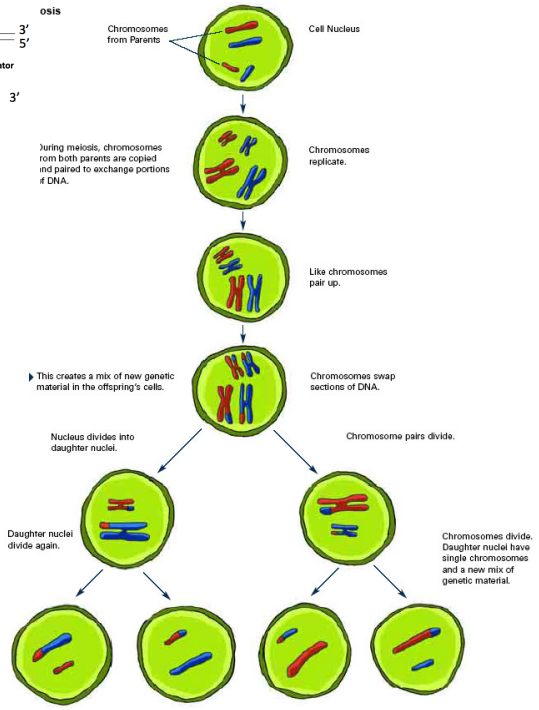
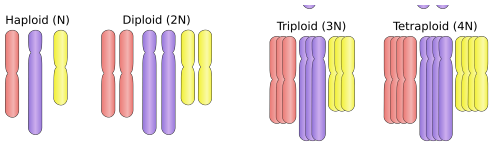
Translocation (a chunk of the chromosome containing the gene (3) has broken off and reattached somewhere else)





EMS -
chemical that causes defects in base pairing during replication, modifies T to pair with G or vice versa
X-Ray: double strand breakage, attempt at repair by cell can lead to inversions translocations, insertion, deletion, substitution (mic)

Once you’ve identified 1 or more mutations:
1- cross to true breeding WT and observe F1 for dominance, homo/hetero
2-observe F2 or F1 self: is mutation stably inherited, is mutation due to a single nuclear gene (3:1 ratio)
3- Cross new mutants with similar phenotypes to each other/similar mutants to see if they complement or are due to the same gene.

Summary of gene interactions

F_2 phenotypic ratios from a F_1 Dihybrid cross

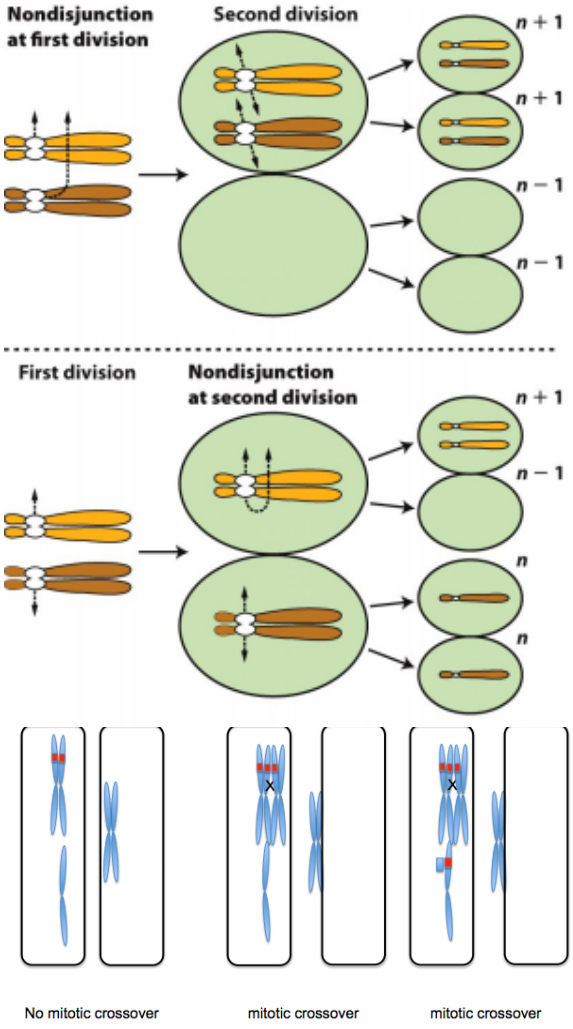
Gene interactions	A_ B_	A_ bb	aa B_	aa bb	F_2 Phenotypic ratio
None 4 distinct phenotypes	9	3	3	1	9 : 3 : 3 : 1
Complementary gene action A.K.A. Duplicate recessive One dominant allele of each gene necessary to produce phenotype	9	3	3	1	9 : 7
Recessive epistasis Homozygous recessive of one gene masks both alleles of another gene	9	3	3	1	9 : 3 : 4
Dominant epistasis I Dominant allele of one gene masks effects of both alleles of another gene	9	3	3	1	12 : 3 : 1
Dominant epistasis II Dominant allele of one gene masks effects of domiant allele of another gene	9	3	3	1	13 :3
Duplicate dominant	9	3	3	1	15 :1

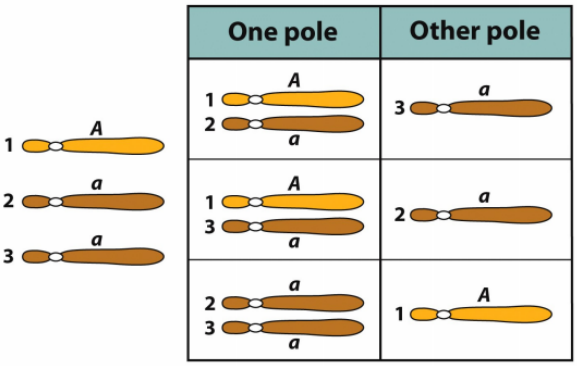
a deletion in intron: MRNA: processed transcript not affected b/c within an intron. Same sequence, same size, same abundance. **unless falls within a transcriptional regulatory sequence **Protein seq:** nn**Protein function:**nn **Deletion before UTR: MRNA:** Assuming this negatively affects the ability of RNA polymerase to bind, as it’s in the promoter, transcription will not occur. mRNA abundance decreases **Protein seq:** no protein **Deletion at acceptor splice site:MRNA:** Processed transcript will find the next available acceptor site therefore removing exons and introns and making a shorter transcript and shorter protein, likely a frame shift. **Protein Seq:** Altered amino acid sequence, could introduce early stop codon. **Protein function:** reduced/no function **Base misense mutation in exon: MRNA:** Changes mRNA sequence, but not size or abundance. **Protein Seq:** Single amino acid change in protein. **Protein Function:** Can’t predict what effect will have, but if radically different amino acid could change protein function dramatically. Small changes in important spots

H**ow many mutations ('hits') does it take to make a cell more likely to become cancerous?**

If the target is a gene that, when mutated, results in more cell division?Oncogene: One hit.An activating mutation will be dominant, so only one is needed. Activating mutations are very rare. A loss-of-function mutation will be recessive, so both alleles must be knocked out. But many different mutations can destroy function, so these types of mutations may be more common.

If the target is a gene that normally suppresses cell growth? Tumor Suppressor: Two hits. A loss-of-function mutation will be recessive, so both alleles must be knocked out. But many different mutations can destroy function, so these types of mutations may be more common. 1. **Oncogene**. Dominant mutation. eg. in a gene (proto-oncogene) encoding a positive regulator of cell division. A dominant mutation alters the positive regulator such that it functions too well thus promoting cell division too much. 2**. Tumor-suppressor gene**. Recessive mutation. eg. In a gene encoding a negative regulator of cell division. A recessive loss-of-function mutation when homozygous results in a non-functional negative regulator. Thus cell division proceeds unregulated.





	AB	ab	Ab	aB
ab	AaBb	aabb	Aabb	aaBb

#1	X'	Y
X'	X'X'	X'Y
X	X'X	XY

#2	X'	Y
X'	X'X'	X'Y
X'	X'X'	X'Y

Bbcc x bbCc

	bC	bC	bc	bc
Bc	BbCc	BbCc	Bbcc	Bbcc
Bc	BbCc	BbCc	Bbcc	Bbcc
bc	bbCc	bbCc	bbcc	bbcc
bc	bbCc	bbCc	bbcc	bbcc

cross Rb rB rb X X X (X) rb X Y

bivalent univalent

20mu

1st pairing (1/3 of total) R b / r B and r b (need common denominator and normalize each for 1/3 of total)

				Phenotype
4/10 Rb	1/2 rb	4/20 Rrbb	4/60 Rrbb	red
	1/2 Ø	4/20 Rb	4/60 Rb	red
4/10 rB	1/2 rb	4/20 rrBb	4/60 rrBb	blue
	1/2 Ø	4/20 rB	4/60 rB	blue
1/10 RB	1/2 rb	1/20 RrBb	1/60 RrBb	purple
	1/2 Ø	1/20 RB	1/60 RB	purple
1/10 rb	1/2 rb	1/20 rrbb	1/60 rrbb	white
	1/2 Ø	1/20 rb	1/60 rb	white

2nd pairing (1/3 of total) R b / r b and r B

1/2 Rb	1/2 rB	1/4 RrBb	5/60 RrBb	purple
	1/2 Ø	1/4 Rb	5/60 Rb	red
1/2 rb	1/2 rB	1/4 rrBb	5/60 rrBb	blue
	1/2 Ø	1/4 rb	5/60 rb	white

3rd pairing (1/3 of total) r B / r b and R b

1/2 rB	1/2 Rb	1/4 RrBb	5/60 RrBb	purple
	1/2 Ø	1/4 rB	5/60 rB	blue
1/2 rb	1/2 Rb	1/4 Rrbb	5/60 Rrbb	red
	1/2 Ø	1/4 rb	5/60 rb	white

total = 60/60

Summary

purple	12/60 = 2/10	**20%**
red	18/60 = 3/10	**30%**
blue	18/60 = 3/10	**30%**
white	12/60 = 2/10	**20%**

Aneuploidy: Addition or loss of an individual chromosome (within a diploid individual). (eg: 2n+1, 2n-1, XO, XXY) Euploidy: Changes to the number of chromosome sets eg. triploidy (eg: diploid = 2n, triploid=3n, tetraploid=4n)