coreBio II - genetics: Wed. 23 Jan. 2018

hand in questions

Words to know

gene / alleles
homozygote / heterozygote
expressed
RNA molecule / transcription

asexual / sexual reproduction
haploid diploid gametes zygote

mutation: synonymous missense non-sense

Muller's morphs: amorphic, hypomorphic, hypermorphic
antimorphic, neomorphic

phenotype / wild type
genetic drift / founder effect / bottleneck

Ellis-van Creveld syndrome and the Amish

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Genetic studies often involve the cooperation of large numbers of affected persons and their families. The discovery of the gene that, when mutated, causes a form of dwarfism (Ellis-van Creveld syndrome) has been accelerated through a collaborative effort between geneticists and the Old Order Amish, of Lancaster County, Pennsylvania.

Aidan leads!

Exac Browser: EVC

Ellis-van Creveld syndrome and the Amish

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Originally described in 1940 (ref. 2) by paediatricians Richard Ellis and Simon Van Creveld, EvC syndrome is an autosomal recessive disorder, involving postaxial polydactyly of the hands (see figure), short stature with shortening especially of the forearms and lower legs and, in at least half of all cases, congenital heart malformation.

The mutation in the Amish of Lancaster County, Pennsylvania, in whom the disorder occurs at unprecedentedly high frequency, is predicted to cause aberrant splicing. It occurs in the fifth nucleotide of intron 13 of a novel gene, *EVC*, that is predicted to encode a protein containing a leucine zipper, three putative nuclear localization signals and a putative transmembrane domain.

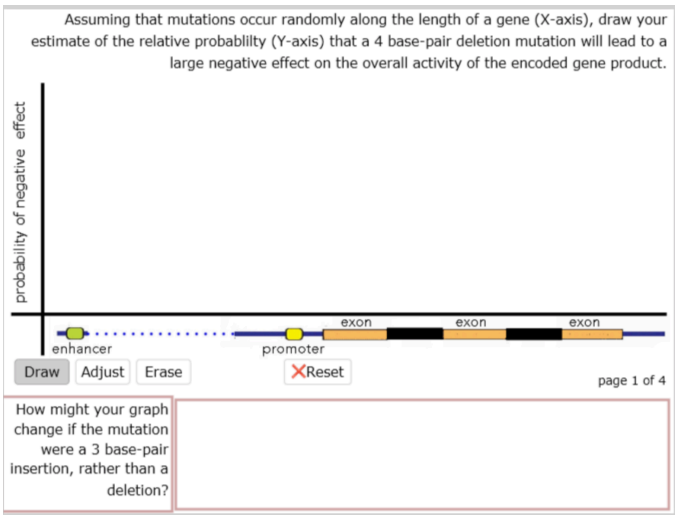
Exac Browser: EVC

Questions to answer and ponder:

178. How are transcription and translation similar, how are they different?

179. Within a gene, what signals and signal binding proteins are involved in gene expression? make a diagram.

180. How would having two copies of a gene (in a diploid cell) alter the behavior the cell?

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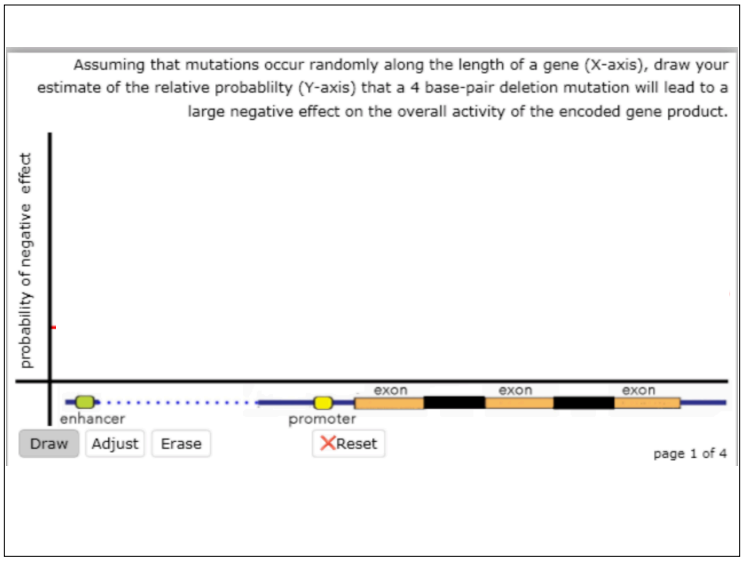
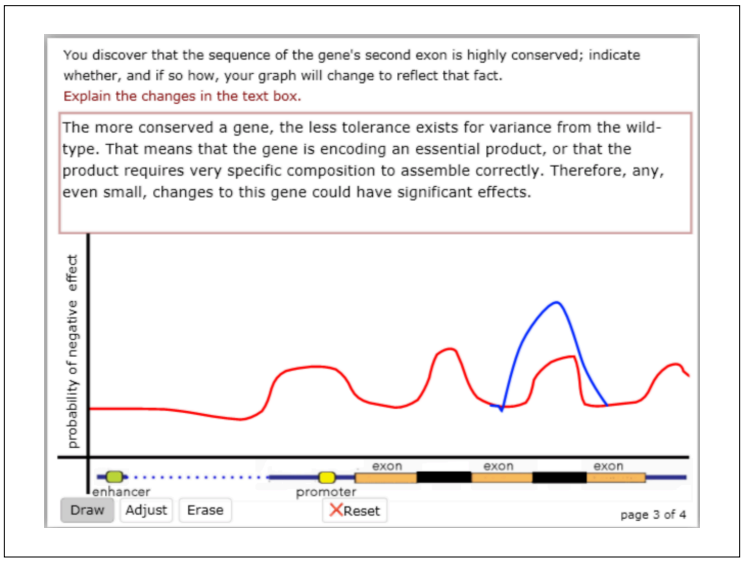
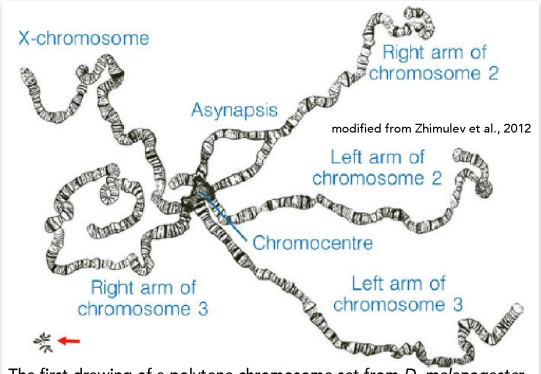

Assuming that mutations occur randomly along the length of a gene (X-axis), draw your estimate of the relative probablilty (Y-axis) that a 4 base-pair deletion mutation will lead to a large negative effect on the overall activity of the encoded gene product.
probability of negative effect
enhancer
promoter
exon
exon
exon
Draw
Adjust
Erase
Reset
page 1 of 4


You discover that the sequence of the gene's second exon is highly conserved; indicate whether, and if so how, your graph will change to reflect that fact.
Explain the changes in the text box.
The more conserved a gene, the less tolerance exists for variance from the wild-type. That means that the gene is encoding an essential product, or that the product requires very specific composition to assemble correctly. Therefore, any, even small, changes to this gene could have significant effects.
probability of negative effect
enhancer
promoter
exon
exon
exon
Draw
Adjust
Erase
Reset
page 3 of 4

Questions to answer and ponder:

181. Based on your understanding of DNA, draw out (schematically) the relationship between a specific allele and the phenotypic traits it is associated with.
182. Why might the mutation of gene not be associated with any one specific phenotypic trait?



The first drawing of a polytene chromosome set from *D. melanogaster* made under light microscopy by T. Painter in 1934. The chromosomes have been spread by squasking them on a microscope slide. Each parental chromosome is tightly paired with its homolog, and there are regions where two homologous chromosomes are separated (asynapsis). All the chromosomes are linked together by the pericentromeric regionto create a single "chromosome center"/\. In the lower left corner, mitotic chromosomes (indicated by arrows) from ovarian tissue are shown at the same magnification, demonstrating the giant size and transveral banding in polyploid polytene chromosomes.

Questions to answer and ponder:

183. Draw out the relationship between gene - RNA - polypeptide, and describe the effects of missense, non-sense, and intron-exon junction mutations on gene expression.
184. How does the position within a gene of any of the mutations mentioned above influence their effects on the function of the gene's product?
185. Why is the MyoD mutation (mentioned above) neomorphic? What would you call it, if the mutated MyoD protein blocked the binding of wild type MyoD to its target DNA sequences?
186. Describe how a DNA change (missense, non-sense, junction mutation) produce Muller's morphs.
187. Describe how a neomorphic mutation alters the behavior of transcription factor and an enzyme.

Questions to answer and ponder:

-A *Drosophila* polytene chromosome can have over 1000 DN molecules (strands). How, do you imagine, does the banding patte observed in Drosophila polytene chromosomes relate to the gene on the chromosome?

-How does the polyploid nature of these chromosomes mak visualizing chromosomal duplications and deletions possible? Wh are its limits, do you think?

next: