# Intro

January-06-14
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Dont need access code
m/c short answer lecture assignment 5% : about the course topics
- Labs start jan 13th Jance Tubman tubmanj@uwin
- Sign up on clew for a/b section tab on clew find out what section from sis ( JAN 8TH 5PM)
-

Why is it important in your lives
- Tech
- Understanding diseases
- Susceptibility to diseases (
- Everyone will know their genome ( can tell what drugs will work better etc)

Had a portion of genome sequenced 1 mill
actually around 3 billion ( 1 meter how much dna does each of your cells have ) / how much is info needed to survive it is in the single digits , not relative in terms of sequencing
- Much of the sequencing is more specific "hot spots" not general overall

What is DNA
Human genome project was completed in April 2003
- 20-25000
- Cost 3 billion $
- Under 10000 for 1 mill
- As technology advanced the price went down/ Moore's law : every new process can do double the amount of sequencing ( new tech)
- Incr in # of human genomes seq inver to cost of sequencing

Personalized medicine : your indiv genome seq. , $100 3-5 years , determine susceptibility, which drug will work for you and which will not, affect many people due to allergic reaction ( death due to drugs, how everyone responds to different drugs affect the outcome)
- 32 000 death/ year due to adverse affects of prescription drugs , wil l be used in doctors offices

Ethical questions ;
- What to do w info when some diseases dont have cures
- Psychological impacts on indiv and knowing that they could get a disease
- Impacts on

Other genome projects
- How many cell that your own 20-30 tril
- How many total cells In/on your body - 150 tril ( ex gut bacteria )
- Very few types of bacteria can be cultured
- Tech can id
- FOXP2 involved in speech development , same mutation found in chimps ( cannot speak)

- 2.7% of the genome is diff
- How do our cells know how to respond the different environmental signals

# Lecture 2

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History of Mol BIO

- Mutations how / why they occur , age ,
- One mutation can give rise to more
- They types of changes that occur can affect our lives

What we don't know

- Areas of the genome that do not have genes we don't know why , there is no selections to keep nucleotides in order
- Codes in genome are passed done to offspring , higher similarities

Amount of time that it takes has been reduced by a great number , also cheaper then they were before , revolutionary for medicine

- Other genomes : comparison of different mammals, animals etc
  - To see what difference influence the appearance , other physical characteristics
  - Ex dogs how they differ greatly
  - This principle can be applied to humans as well
- 5 Questions
  - What is gene : a segment of DNA that is heritable , that can be transcribed into RNA
  - What is an allele : alternative form of a gene / at a locus / if everyone had the same sequence there is only one allele for that gene but in most cases this is not the case
  - What is transcription: takes DNA as a template to produce a single RNA molecule , ( Enzymes involved know)
  - What is translation : ribosomes /conversion of nucleotides to amino acids
  - What is a single nucleotide polymorphism

At a certain spot where someone has A/T someone else might have G/C instead these make up the differences btw everyone SNIPS

- Retrovirus > reverse transcriptase HIV > AIDS
- Dna Replication < DNA polymerase dsDNA > ds DNA
- Transcription > RNA polymerase > ds NDA > ss rNA
- Reverse Transcirptase > ssRNA >ds DNA
- What is 1/2 of our genome is made of ( 3 billion letters) comes from viruses , they have had a very large impact on evolution

What is the definition of a gene : a sequence of dna that encodes a functional RNA molecule in protein coding genes the RNA in turn codes for protein

- Some genes encode ENA that is not translated into protein
- Ex : rRNA , tRNA, ( translation) , circular RNA , micro RNA, PIWI RNA ( development, which genes ar eon/off, sex cells) . Small inhibitory RNA , ( major role is to regulate )

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## TUESDAY JAN 14th

Dna is the genetic material n can transform cells

- 1928 griffith exp using pneumococcus : proved that virulence can be passed btw cells via dna transformation ( avirulent nonlethal) R type of bacteria could be converted to lethal S ( smooth) bac when cells are mixed FIGURE 1.3
- S/R strains how it happens
- Once the mice die they take the bacteria out extract it R> S bacteria , something in DNA that can convert R strain to S strain , toxin genes that are responsible for the toxicity
- DNA genetic material of viruses /hersey , chase exp ( 1952) / radioactive compounds to tag DNA and protein of viruses ( p32 , s35, phage T2 ) , sulfur containing sistine and mythyine ,/ infected bacteria and recovered viral progeny , easured radioactivity amounts /
    - Let them replicate , infect bacteria w viruses , measure where their radioacivitiy will go after infection
    - New viruses had high levels of p32 not s35
    - Dna genetic material of viruses
- Dna can be introduced into all cells
    - When dna is put into euk cells it is termed transfection which is the same as transformation into bacteria
    - Dna transforms at low eff
    - Need a way to select for cell that have taken up dna ( what do you have to put ) SELECTABLE MARKERS (using in the lab ) antibiotic resistance in bacteria ( allows the bacteria to grow normally in the presence of ampicillin
    - Prevent the antibiotic from licing the cell
    - If you add an enzyme
    - Synthetic cells craig dent 60 mins
- DNA structure
    - Has minor and major grooves
    - Know general structure A/T , G/C three bonds

- DNA supercoiling
    - Dna has built in tension base on the conformation , , can form diff shapes to re - leave some of the stress
    - Linear, relaxed supercoiled , difference btw the two
    - The only way to re-leave the tension is to cut , the problem , the supercoiling affects the # of bases and turn
    - Positive superC you twist the Dna in the same directio makes the bases come in closer together , // negative unwinding it m fewer base in the same distance , if you do it too much you are at risk separating the two strands
    - Denature when hydrogen bonds are broken , why is it important , cell evolves mechanism to counteract this
        - Replication , transcription when dna strands have to change configuration and separate
        - How does the cell do it ? : nick ( break is generate in order to relieve stress and after can be glued back together
        - Many enzymes participate , very fast rates // replication fork how it relieves stress
- Why do we have these enzymes, antiviral mechs , foreign dna detection , cut at a certain sequence , endonucleases, restriction enzymes isolated from bacteria
    - Used by bacteria primary antiviral mech
    - Dna ligase attach back ,

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Many molecular biology tech rely on hybridization

- Whole purpose is
- You can take a nucleic acid from 1 organism and compare it to another organism
- For it to work the probe used to hybridize they probe must but single stranded ,

- Degree of comp determines how well they hybridize
- You can manipulate parameters, high temp incr stringency , ( higher to temp higher degree of complentarity )
- Have to visualize this
    - Label it w radio IS
    - Emitting beta particles , where the hybridization is occurring you can detect it
    - Now alot of the probes are light emitting probes

- DNA mutation
    - Change in genomic DNA sequence
    - Diff btw the population , 99.7% is the same
    - Change in gene that affects te function , if the gene cannot do its func may have condition due to this
    - Where a specific gene is affected but the change allows the organism to survive
    - Most inherited genetic disease express as homo recessive , have the gene you are carrier
    - Spont mut . Mutagens : induced
    - If it occurs in germ it is passed on to the next generation
    - Cystic Fib: most common hereditary disease , ppl from Europe, 28 diff mutations in CFR gene
        - Depending on the mutation relation to severity
    - Liver cancer hereditary : in 95% of the cases = no , sometimes
        - Mutation that occur in somatic cells during our life times , they cannot be passed on
    - Mutation s can be detected and repaired in cells
        - If a cell detects muts it commits that cell to suicide path or apoptosis
        - gets rid of the cells
    - How the mutation affect the cell ,
        - Modify the mutation , bacteria small genome size , not much room , the ability for the cell to handle mutations ,
        - Hit w enviro pressure mutation gives them a selective advantage \
            - That's why bacteria can adapt so well/ quickly , picking up mutations is used to their advantage , ( genome size is small mutations have a greater affect on them )
            - Mutation and genome size related
        - Humans lots of space
        - Hetero selective advantage , carrier , wild type selective disadvantage and if you have two copies of gene no good
        - Some mutation in the heterozygous state can be a good thing
    - CCR5( CCR 5 delta 32 mut) > chemokine receptor 5 > immune response >
        - Delta sign means something is missing
        - Non functional and bunch of amino acids are missing
        - HIV resistant , euro origin uses T receptor
        - Black plague , if you have this as a homo zygote no affect , same with heterozygote you are protect from HIV / plague / aIDS
        - If you dont have the mutation you are susceptible to both
    - Beneficial Mutations
    - Questions
        - What has to occur in the pop for bene muts to be successful and become hereditable ?
            - Has to give and advantage selective pressure, heritable, examples given *

        - What are serious muts not generally observed in the populations ?
            - The ones that we know about , came from ancestors , came from the development , they dont cause serious inflictions , and the serious ones get weeded out if there are some present
            - Selected against in most cases
            - The % of abortions 60 %

        - The ones that go to term are only 40%
        - Development has a genetic program and selected against
        - Interaction btw the mother and placenta does not agree
- Types of mutations
- Base Analogs
- mutation reversion: can turn certain things back to OG , insertion/delete, deletions can'ts be reverted
    - Some muts dont have an affect sometimes they do
    - Forward mut : inactivate the gene , stores the inactive gee : backward mutation
    - Exact base reversal TRUE REVERSION
    - Second site reversion : base reversal somewhere else in the gene compensates for the initial mutation , store the function of the gene product
    - Suppressor muts : diff btw supr and second site is that it occurs in a different gene
        - Occurs in bacteria, only way to restore the gene ,
- Picture mutation hotspots , certain places more mutations /
- Genome differences
    - Expression of genes if diff in diff organs
    - 100-125 thousand proteins comprimise our proteome
- Genomes vary greatly in size , plants have more genomes than we do
    - Why do plants have more genes and what is about plants that they d

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Why do plants have more Dna and more genes than mammals ?

- Polyploidy
- They need more genes , they can't move around (like humans ) so they need them to adapt to the environment
- Some plants have smaller # of genes or larger number / genome size differs ( sunflowers. Poplar trees) cant move away from predators , immune system varies as compared to ours
- ---
- Viroids : def in
    - Becomes an organism once it comes in contact with host
    - Some pathogens dont have proteins> viroids > infect plants mostly
    - How are they pathogenic ? > sequence of that RNA molecule is directed towards certain genes > knocks out those genes= disease > RNA i mechanism
        - Ribozymes : inhibits rna trans
    - Viroids r made by the plants rna
    - Potato
    - Cadang cadang viroid > palm tree , formed as a sinlge transcript . Mutate a couple of the nucleotides reduces the virulence of the viroids * sequence is IMPORTANT in this case
    - Infectious particle is a piece of rna
        - Comes in through cuts and breaks in the plant
    - Prions : no dna /rna , they do infect mammals
        - Glycoprotein made in the brain has a specific duty , maintains protein integrity
        - PrP
        - PrP^c : normal and degraded by proteases in the cell
        - PrP^sc : resistant to degradation
        - PrP^c > PrP^sc cause disease
        - Caused in most cases by mutations >

- # CHAPTER 2
    - Genes codes for proteins
        - A chromo contains
    - A very long stretch of dna that contain many genes
    - Clusters in certain spots , blank distance , cluster etc
    - Each gene processed = code four letter tell us where genes are n are not
        - What parts the chromosome went under changes ,
    - Alleles
    - Locus
        - Recombination /
    - Sometimes you dont get 1 copy from each parent ,
    - compared genomes sequences for ppl of diff populations ( europe. Africa, asia etc) 27 ppl
    - CNV s: copy number variations ( >1000bp)
        - Insertions, duplication, deletions // larger chunks // when you look at a populations of genome < 1447 CNV account for 12% of genome ( 360 megabases )
    - What does this mean ?
        - Health/genome
        - For some genes we may inherit more or less genes from on parent ( genomic copy number )
        - Vary in the # of genes that we get from our parents
    - PMP22 copy # impact on disease m hoe severe it is // higher risk of getting the disease
        - Doesn't happen often , if they did pop up would during meiosis
    - Some genes we have many copies ,
        - Different racial ancestry you have more genes of certain types and others you have less
    - why do we have extra copies
        - Focus on diet // you eat what is available // diet can select for high amylase gene ( AMY1) copy number
        - Selection affecting copy number
    - What is gene / what is a allele, what is CNV, what is an SNP
    - Does the cell have control to turn of the gene is an extra copy is obtained *Q

        - If its lethal they may get rid of it
        - Or turn down the expression of the gene
    - One gene - one enzyme hypothesis slide LAST
        Carrier protection
        Homozygote , het
    - Null mutant : nothing being made
        - Sometimes lethal = death of organism

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Multiple alleles

- Changes that occur are passed down , mating within pop , mixing of alleles and they spread out in the pop
- The one that has the highest % is the "normal" allele / usually one allele that stands out in most cases
- Ex eye color in fruit fly
    - Wild type normal ( red) W+
    - White eye ( no pigment) Wi
    - Hetero is the red ( dominant) W+Wi
    - Homo is white ( recessive ) WiWi
- Some genes have more than one type of wild type
    - Polymorphism : whole bunch of diff alleles at the locus but none are considered as the wild type ( <1%)
    - Ex ABO blood type group locus on chromo 9 , produces an antigen ,
    - A allele
    - B allele
    - o allele : if O is a mutation how did it become a common blood type
        - Can give your blood to everyone bc doesn't have antigens
        - Rh factor
    - AB uni acceptor , O is uni donator
- Protein production : translation
    - Only one strand of dna serves to produce Rna template via transcription
    - Genetic code as codons
    - Gene includes a series of codons and read starting >termination point 5'-3' direction
    - Codons as non-overlapping
- Transitional Mutations
    - Insertions . Deletions into the dna can lead o amino acid changes in the protein
    - Frame shift mut : severe effects
    - Acridines : chemical dyes) that induce structural distortions in dna - leads to frame shift muts
    - If the insertions or deletions are in group of 3 occur , it as less severe impact
- Rna has the same seq as the coding strand
- Which strand does rna polymerase read to transcribe the rna the template strand the bottom strand > why?
- RNA produced from 3'>5' / polarity has to line up as well /
- Complete mRNA contains 5' untranslated (UTR) called leader / shipped>translated > the sequence up stream doesnt go through that
- mRNA also contains 3' UTR called trailer / stability of the RNA can be dependent on the how long it is
- Other genes who's UTR's are very short ,d
- Bacterial transcription /translation occurs at the same time Why ? No nucleus to separate the genetic material
- Euks transcription takes place in nucleus / the translation in cytoplasm , mrna transport from nucleus > cyto
- Can't screw up splicing bc you shift the frame BAD
- CIS/ TRANS
    - Cis-acting : acts on its own molecule ( usually DNA) attached
    - Trans- acting : can function on other molecules ( protein or rna ) move
    - All gene products ( proteins and rna ) can act in trans
    - Diffusible in the cell and can act on other molecules
    - binding sites on the same dna molecule are cis -acting
        - Tata box , binds a protein that turns gene off
    - Can also be used to describe complementation of mutations
- Affects on transcription
    - Promoter / gene x / > transcription = gene x RNA

    - Promoters require binding of proteins produced from different genes to be activated
- Promoters cis acting , bc they are linked to what they are acting one
- In control
- Red proteins are acting in trans b/c moving coming from somewhere else
- Gene can become inactivated , you can have mutation to prevent binding , ( lac operon, lacz MICro)
    - Gene can be inactivated by a mutation in the cis acting dna element that control the gene expression or in another gene that acts in trans to regulate the protein
- Diagram : microbiology notes on lactose / glucose / lac operon and inhibitors

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Work on bacteria and viruses in the 1970's and 1980's let to development of recombinant
- Foreign dna could be manipulated and transferred into other organisms ( ey human dna > functions in bacteria )
    - If you give the bacteria a human sequence it will translate still / it doesnt know
- Allowed for humans to be isolated and the proteins produced in bacteria
    - Insulin approved in 1982 for diabetes treatment( produced in bacteria )
        - Before it was taken from pigs / problem the human and pig insulin gene were 2 amino acids off/ when you injected it over and over again you started to make antibodies / less side effects now
    - Epogen : human erythropoetin ( produced in mammalian cell culture by Amgen )
        - This hormone
        - What happens in bacteria cell and not ours : cDNA copy is put into the reading frame / there are post translating modifications that ocurr during process ( golgi) transform the protein, the bacteria does not do this ( red blood cell production )

TNF - your body is under going inflammatory response , good if your sick , not if your not , goes after your cells otherwise
Embrel : helps with inflammation / joints ( famous golfer uses it )
Initial drugs made in mice , when injected into human antibodies were produced . So they had th fix it they modify it so that anti bodies // they become less effect over the year b/c your body startt to produced antibodies even after you change it w human aspect

News
- Purple tomatoes , purple is produced due to high levels of anthocyanins , engineered them to produce a higher level of flavanoid , turned skin purple / transcription factors that have been turned on / gene from a snapdragon
- Tumor prone mice fed extracts of these tomatoes lived 30% longer than mice fed regular tomatoes / Why ? The high level of antioxidants helped ,

Celery , break , rub on hand put out in to sun, turns red, anti pathogenic
- Fluorescent proteins genetically engineered except for the green one ( taken from jelly fish )
- Gave scientist a tool to monitor where protein go in real time , before you had to kill the cell but now you just image the cell and you are able to see
- Transgenic pets

Terminology
- Cloning vector

Type of dna vectors
- Plamid
- Phage : virus that infects bacteria/ coming back in medicine
- Cosmid
- Artificial chromosomes
- Depends on the size of the dna fragment in use

YAC
- Yeast rgin of replication
- Bacteria selectable marker, yeast selectable
- Can be moved in and out of bacteria nd yeast
- Telomeres , so when they translate it , it becomes linear ,
- Why were YAC important : why are they better than plasmids
    - You cna cut the dna and then piece it together at the end ( 1 million bp ) total is 10 million bp
    - Incre in computing power ,
- Whereas plasmids the pieces are smaller 10 kb more work ( 10 million bp )
- Clone into plasmids

- Dnase

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Chapter 4 - interrupted gene
Euk egen structure

- Pre-mrna contains exons and introns
  - Nucleus , machinery present transcribes gene / pre-mrna b/c its not fully processed
  - In euks genes there are regions that code and do not encode protiens ( do not code introns )
  - Splicing
  - B4 transport into cytoplams / complicated process / mult protein complex, cuts , splices , and attached it back
    - Mistakes can cause a shift in reading frame
    - Dont know the signals that tel them to splice certain ones and not others
    - 5'and 3' regions in UTR's
    - Exon order does not change btw dna and pre-mrna
      - There is change btw pre-mrna and rna , some exons dnt make it to the mature rna , but the positions done change
- Humans 20,000 genes
  - Majority of which encode proteins , >100 000 diff proteins are expressed in our bodies
  - Alternative splicing , pre-mrna haas introns /exons , splisome decides at a approp time it will take out certain exons and splice them together differently // produces additional proteins that are different in the amino acid sequence
  - Certain exons are removed before premrna > rna the positions never change
    - If you remove 5 you dont get if you have 3.5.8.10 > dont get 3,10,8 > 3,8,10
  - Diagram
    - Exons contain protein subunits that contain functions , they perform certain functions in more than one gene
  - Diagram 2 the order of exons does not change btw dna/rna
    - Any mistakes in the seq can throw of the reading frame can cause the protein to no function properly
    - Insulin : cant use bacteria b/c they dont express it / you express it into cDNA > then it turns it into
      - If you every want to express you use cDNA bc the exons/introns arent expressed
- How to determine where introns are in the gene ?
  - You can get the cDNA and compare it to the genomic dna becasue the cDNA doesnt have introns
  1. Compare the sequence of genomic DNA with mRNA ( cDNA)
     i. More variation in the in sequences
     - How does an organism know when the introns and exons occur
  2. Restriction enzyme digests (maps ) of genomic vs cNA revealed extra dna
- REStriction enzyme mapping + diagram
  - Cut genomic dna and cDNA ( from mrNA) with restriction enzymes and compare dna dna fragment lengths
- Intron position conserved
  - In related genes btw diff species
  - Introns seq hasvaried over time / b/c seq and size has changed / due to mutation and it is not important to survival of the organsim it get spliced out every time / the exons is the important part
  - The length varies but position is conserved
  - Alpha beta globin genes : in mammals frogs and birds the introns occurs in the same position but different lengths
- Diagram globin genes vary in intron length
  - Lengths for exons vary but , more tightly resitricted as apposed to introns / no selection on introns
  - Easier to pick up mutations b/c it does affect them that much
- How do you knwo where the intron and exons are
  - There are particular sequences that splicosomes know > splicing sites > highly conserved sequence that tell them where to splice it out
- Intron structure
  - Mutation within intron may be silent
  - Sometimes mutation can be very bad > at splicing sites > wont be able to splice properly
  - Can have affect on protein function
  - Types of mutations it produced > frame shift bad
  - Ribosomes starts reading it b/c doesnt know > frame shift mutation can cause big problems
  - Evolutionarily doesn't make sense > 15% of humans disease are caused by inefficient splicing or mistakes in splicing
  - In euk introns are longer than exons > lack of selection on the them makes them longer
  - Majority of our genes are comprised of introns
  - Some euk like yeasts have very few introns
  - You can have mutation in the middle of introns that wont make a large impact ( negative impact)
  - Splice sight mutations BAD
- Progeria
  - Usually die around 20 and cells are around 100
  - Very rare disease , give insight into aging . Causes premature and rapid aging of cells
  - 1/ 8 mill births
  - Most die around 15
  - Cells age , cant repair as much , when your sick ittakes longer to recover > rapid decline > accelerated pace
  - Lamin A . Single mutation in the protein causes the disease
  - LAMIN A mutation change C-G to C-T transition
    - Its gly608gly mutation : changes GGC codon to a GGU codon
    - Done have to know detail of this slide
    - Exon become an intron , turns it into a splice site / forms an exact duplicate of splice site ,

Exon shuffling (later) : evolutionary mechanism that genomes use to incre diversity of genes

deletes 50 amino acids from the protein
        - Forms a mutated version of lamin A = progeria
        - Nuclear membrane in these individual is messed up = progeria
        - Know > RSY there is a prptease that cleaves the Lamin A but the mutation causes the cleavage site to be deleted
- Progeria treatments
    - Block the farnesylation , but you blockage what happens in the other cells too
    - Farnesyltransferase inhibitors ( FTI's)
        - The normal phenotype of the nuclear membranes comes back a bit

# Week 5

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Slicing can cause problems
Intron have gotten larger

Diagram grids
- Dna is conserved in exons
- Two genes , they were same and then duplicated and took on dif functionsn
  Dia

Exon seq are more conserved btw species than introns in related genes
- Exons can be said to the building blocks of genes
- Genes arise from duplication of genes
  - This is how you get the diversity of genes that we have
  - They were lsight changes , that did this ( inserted an exon )
  - Or added another exons to itself , if it was successful it was passed on
- Some genes are composed of exons that are related to other exons from other genes
- Other exons are unrelated
  - They all give rise to proteins with sim/diff functions
  - Ones that are sim has sim exons . b.c sim functions
- Evolutionary selective pressure is against mutations in exons but not in introns
- Exons encode functional proteins
- Introns evolve more rapidly

Half of genes have more than 10 introns
- Mammalian genes are split into very many pieces (exons ) 50% human genes have >10 introns
- As complexity increases the length increases ( or varies as well )

Genes have a wide range of sizes

Most introns are spilceosomal DONT REALLY NEED TO KNOW

- Exon length is same ( w little variation )
- Just b/c you have large gene doesnt mean you code for large protein
- Higher euk have longer introns
- The avg gene is about 5x the length of mrna

Yeast flies , human
- In exon in humans are smaller as compared to yeast , flies
- Introns can vary in length

Overlapping genes- same reading frame??
- What happens when a gene uses more than one reading frame ?
- Occurs in many viruses and some mitochondrial cells
- Produces
- Two readins frames are note the same proteins coming off of them are different
- So when you have smaller genome you are able to increase your diversity ( the type of genes you have )

Alternative splicing
- Troponin T : muscle protein that produces aplha and beta form the same gene
  - Called protein isoforms
- WDR1 - protein involved in cell structure and shape
- Wild type : 606 amino acids - 15 exons
- Wdr 1delta 35- 466 amino acids ( lacks exons 3,4,5)
  Same amino acids and carboxy ends : reading frame is not altered
- Estimated that 50% of all alternate spliced mRNA 's have altered reading frames
  - Bus they still produce functional protein its just a different protien
  - Give the cell an opportunity to generate new genes/cells

Orientation

How do genes evolve ?

- Did genes orginate as interrupted with introns or uninterrupted
- Which one is correct ?
- Intro sink Mutation sink > suck mutations
- Introns provide a space for exon shuffling , swapping during evolution
- Led to more combinations of exons and protein functions

Diagram

- Random translocation

# Week 6 After midterm Thursday Feb 13th -

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Psuedogenes : it looks like a gene ( has codes and sequences , but its not functional

- We knew that they existed in our genome
- We have come to learn that they are much more numerous than we thought
- Genetic fossils of our genome
- At sometime they may have been functional
- Become nonfunctional over the course fo evolutionn
- They de not encode protein> not functional
- Debate on whther the produce rna , usually they dont
- The reason why the dont work anymore is that they have picked up mutations that have stopped it
- Usually related to similar genes ( they may have been duplicated , and picked up muts and then was shut down)
- Some still have exons /introns but do not express rna
- HOW? They picke dup muts in regulatory places in the gene , so thats why they are not expressed ( coding part hasn't been effected) // no selection for mutations
    - Muts in the promoter regions
    - Beta globin has many Pseudogene
- All organisms have them

Diagram figure 8.23

- Typical gene with 3 exons , normal wild type genomic copy , promoters. Splice site etc
- If you take that gene and duplicate and picks up mutations it can turn into the gene at the bottom , promoter regions, splice sites can be taken out
- Eventually the structure of the gene starts to disappear , can't tell that its gene , doesnt look its coding anything
- There is no selection for it b/c duplicate for another one picks muts
- Psuedogene disappears

Figure 8.24

- We share over 1200 Pseudogene btw chimps
- Mice only 6 ,
- Where have they gone > disappeared

Olfactory receptor genes

- Olfactory receptors have many pseudogenes
- They have been duplicated and amplified over and over
- The # of pseudogenes in species is dependent on need for sense for smell
- Mice : 1200 active receptors / 300 pseudogenes
- Human : 700 active receptors/ 800 pseudo
- As humans evolved the # of olfactory pseudo have incr

Olfactory receptor genes

- Evolved color vision , the gene # decr
- Where as old world didn't have ti so their levels of

Chapter 5

- How are our genomes related to other human like species : we contain some of their gene
- How is this possible : they mated,
- Highest freq of Neanderthal genes > Beijing china
    - 2.7 %
- Why is N dna still in our genome : they was something that the N had that really helped us out
    - When we move have the potential to transmit disease that the new pop hasn't seen before
    - Some of the N genes in our genome codes for immune response and genes
    - there were enviro condition that N found themselves in that gave an advantage to their offspring
    - In some areas of the word that have high N %, could affect your fertility

Genome Mapping

- Physical arrangement of all genes in the genome on chromo
- You can pick out every single gene across the chromo
- Low res : recomb freq
- Restriction map : measure the dist btw the sights of cleavage ( medium res )
- Dna seq map :
- Most our genomes are pretty much the same
- Assignment *

Genome variation

SNP's and disease

- Most snp are in non gene coding regions
- Important to know where it is
    - Apolopoprotein E (Apo E) : role in Alzheimer 's disease , maybe heart disease
    - In the human pop there are 3 alleles , on chromo 19 ,
        - E2: cys cys
        - E3 : single nucleotide change cys arg
        - E4: mutation arg arg
    - Which one is wild type ? Which are snp's
        - Which ever one is ____ is wild type

Mutations within alleles leads to different dna sequences which causes different restriction enzyme sites

- RFLP's :
- Changes where its cut

Diagram figure 5.1

Figure 5.2

- If you cut w different enzymes it give you a diff banding pattern

Genetic mapping with rflp's and snps

Figure 5.4

Importance of rflp

---

Where have you come from ?

- National geographic : geographic project
- Trying to map human migration
- Based on snp data analysis :

# Tuesday - Feb 25th -

February-25-14
11:34 AM

Finishing Chapter 5/6
Every person has a unique collection of RFLP's and SNP's

- Diff combinations of alleles
    - Haplotype : min genotype sequencing
    - Look for gene that are associated with diseases and response to drugs
        - Can look at to determine how they may respond , before they experience - side effects

Where have you come from ?

- You have your Y ( male ) from father
- Have mitochondrial dna from mom

Egyptian Pharaohs

- Who were their ancestors IGENEA

Diagram

Genome Sequences:

- Non- rep seq : wont find anything the same
- Mod rep seq: multiple copies throughout the gene
- Highly rep seq : generally very short , usually found in clusters
    - Take out the seq and find out the ones you have )(STR's ) very unlikely that two ppl have the same STR's

Diagram

Synteny :

- Order of genes is the same just occur on different chromosomes
- Homology btw the gene order in different species

Diagram
Syntenic blocks very in length

- All the genes are in the same order
- Homology
- Chunks of the chro have been recombined
- Most of the chromo show the same order

Diagram

Organelle genomes :

- Mitochondrial genomes are smaller , depending on cell type you have 10-100
- Chloroplast genomes are larger ,
- Most mtDNA contains some introns except for higher euks
- Lower euk have alot more introns ( mito)
- They used to be bacteria, went down to 35 genes , where did the dna go ?
    - It came out of the mito and went into the nucleus

Diagram figure 5.13

Human mt DNA

- Used to measure evolutionary time ( mtDNA) , goes under 2% mutation rate per millions years
- By comparing mtDNA you can make relationships / evolutionary timeline
- Yeast , larger mtDNA
- Nuclear code yeast do not introns

- Same genes as yeast except yeast have introns
- Why? At some point it picked up the intron or the yeast lost them

Diagram

- Yeast one has introns > introns in red > there are a lot of them

Chloroplast Genomes

- Large ,

# Tuesday Feb 25th

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Chapter 6 : genome seq and gene numbers

Diagram

- Intr parasite , pathogenic , needs a host cell to survive , uses itss machinery to replicate
- Does not encode everything that it needs to survive the host provides them , smallest genome

Figure 6.1

- 1500 genes needed to be self replicating and being able to survive by yourself
- Know the number of cels that it takes to be each different type

Figure 6.11

- Only % is exons , why is so large when there is only a small amount of exons
- Viral fossils from transposons , left in our genome

Species evovle more complex protein function

- Organisms > more complex > more genes> incr complexity
- When did cells start to communicate
    - Cell com w each other all the time , signalling , binding , secreting etc
    - All the the
    - When did the communication start
    - Started from the very beginning > video 0

# Thursday Feb 27th

February-27-14
2:37 PM

Quorum Sensing- picture
- Only 10% are shared
- Major roles in human disease
    - You develop your own bacteria and you have developed a relationship btw the bacteria and you
- If you control the levels of bacteria in your gut they have other affects
    - Chemicals > blood > transmitted all over your body
- Take a drug that prevents binding > they stop producing their toxins
    - Chemical are very affective
    - Problem they are not very stable

Britain could create the first 3 parent baby through IVF
- The affect it has on atp production
- Get rid of mito and take nucleus and put in w other egg , sperm
- Mother's nuclear dna and other genes from

Essential genes
- Some genes are essential for development of organism
- Bad if you get rid of that single gene
- Bacteria have few thousand genes 1/2 are essential
- Mammals have 10% the are essential
- It has to do alot w gene family , protect us by having sim gene . With sim function so if one gets knocked out another one can step up and take over the function
- Redundancy and gene family : genes may have other related gens that compensate when one gene is eliminated
    - Found in all cell , especially higher cells euk
    - Protects organisms from deleterious genes
    - Can provide functional information for related genes

Figure 6.16 and figure 6.17
- # of essential genes in yeast and worm
- The type of genes and the functions
- They affect all cell structure function > yest
- In worms they knocked out alot and it didnt have n affect

How can you tell whether two genes whether the function of two genes are functionally related
- Synthetic lethal : deletions in two genes that produce lethality together but no on their own
- If gene A is knocked the cell is viable
- If gene B is knocked out while A is intact and the cell is viable >good
- Knock them out at the same times > cell dies
    - Not ess genes , when they are knocked out together = esse

Cell contains two genes ( a/b)
- Function of the products of genes > sim > in the same type of packet
- One mut had
- Implies functional redundancy btw certain genes exist

Protein protein picture

Cool picture

Levels of gene expression
- Some care expressed at smaller levels
- Alot of those genes are ness enzymes that needed for our cells to live
- Rest around called house keeping genes

Human Y Chro

- Human sex chromosomes ( x/y) have evolved from common autosomes
- Some animals have diff types o sex chromosomes
- There 65-70 genes on the y
- The x chromo contain alot of genes
- Primaryly
- Y chromo
    - Made up of bunch of different type of sequences
    - X deg : muts
    - Amp seg :
    - All three come together = y chro

/figure 6.15

Video

# Tuesday March 4th

March-04-14
11:29 AM

- Personalized genomics and medicine
  - Didn't have access to information
  - What the company can do with info and what it has to do w your health is debatable
  - You figure out if you are carrier ,
  - Haplotypes : combination of x/y chrom. Snp's
    - Tells you where your family is from
  - SNP analysis :
  - What will you be able to get very soon ?
    - Exome seq , all your exons of all your genes that are expressed
    - A lot less than genome seq
    - But gives you all the seq of genes expressed
  - It may be required to obtain it
    - Iceland : everyone dna is sequenced
      - They have used this to id genes involved in diseases
  - Epigenetic marker information :doesn;t change the seq but changes the structure ( which groups are o and off) <methyl groups>
    - Not just seq of a,g,t,c
    - You can change the seq without even touching them
    - Put chemical group onto the seq and change what they do
    - You can pass those changes onto the next gener.
      - How diseases are cause , how we pass on what we are exposed to

- Personalized / human disease , halo, snp analysis
  - Want to know if your carrier
  - Disease risk factors ,
    - Number are based on scientific literature
  - Prob.
  - Scaring ppl

- What does the information give you
  - Make reason ppl in er is due to rxn b/c interaction or reactions to medicine
  - Either you metabolize it to fast or too slow
  - Fluorouracil - cancer chemotherapy drug : if you r body cant metabolize it makes your blood toxic
  - It starts it kill your normal cells DPDY
  - Homo you cant get it out your system
  - Hetero - cant get enough
  - If you dont have the mutation

- Your ancestry
  - Haplogroup info / male you get two type of info paternal/maternal
  - Women only get maternal line , only from mitochondrial

- How do you get your dna information
  - Spit saliva into a tube

- His breakdown
  - Lactose : the mut so that we break it down kept high

# Thursday march 6th

March-06-14
2:28 AM

-

# Tuesday March 11th

March-30-14
11:45 AM

# Thursday March 13th

March-13-14
2:30 PM

Telomere Function :

1. Protect chrom ends from being degraded
2. Allows the telomere

Figure 9.32

- Green are telomeres
- The dna is everywhere , centromerese are everywhere
- All the telomeres are being tied up by the specific spot where chromosomes come together
- Don't how it regulated

Telomeres do not completely replicate at ends of chromosomes

- Replicatio fork
- Has a leading and lagging strand synthesis
- In order to go from the 3' 5' end needs hydroxyl ( rna primer )
- At the end , on the leading strand
- The lagging strand is not a problem its going to keep going until it end s
- Rna primer at the end disappears at the end
    - End becomes shorter every time it goes through dna replication

Telomerase

- Ribonucleoprotien enzyme
    - Has a rna component and protein component
    - Only other is ribosomes
- Contains rna template
    - It is complementary to the telomerase
- These two genes are turned on in the steps for - ovarian cancer , and also present in many other cancers
    - Turn them on so that thy can keep their chromosomes at a length that is favourable for replication

Mechanisms of Action

- Binding : template rna binds to chromosome free end
    - Acts as reverse transcirptase and make dna
- Polymerization
- Translocation

Figure 9.33

Telomerase are essential for survival and are implicated in disease

- Cells that lose their telomeras exhibit senescence
    - They are dividing **
    - They dont die , they are not regenerating
    - Eventually the cell will die out
- Chromosomes are degraded and mutation freq starts to increase
    - If left long enough and telomerse are chewed long enough the structure of the dna is weakened
    - System has to evolved in order to counteract this
- Once you r past your childbearing years you dont have much telomerase left over
    - Passed on your genetic material
- Dont want high telomerase levels when your in 40's / 50's
    - Cancer
- New treatments are targeting telomerase

Telomeres and centromes n the human evolution

- Chromosome are in the same seq ,btw us and ancestors
- The problem is that they have one more pair of chromsomes that we do

# Tuesday March 18

March-18-14
2:46 PM

Histone Mod

Figure 10 .18
- Brought into form the core nucleosome
- Acteyl group are chopped off

How is chromatin structure regulated during dna replication
- Unwinding : what stress does it put on the molecule ?

10.36
- Where the dna i being unwound
- Nucleosomes are removed very quickly

Model of nucleosome assembly
- If you are in the nuclues you r dna b4 dna replication it is all wound up
- Your doubling your dna and you need double the number of nucleosomes

10. 17
- Form a core

10.38
- Black lines are dna
- Caf 1 bring the new dna
- This dna as its being unwound, it has to relieve torsional stress
- Process is very fast
- What dna seq actually bind to these nucleotides
    - Are they random
    - Or are there determine by the seq
- Its a bit of both

Do nucleosomes occur at specific dna seq
- Boundary limits where hetero and uchromo goes

Nucleosomes during transcription
- When rna transcription occur they cannot get excess to dna , they nucleosomes must be removed

- Dnase hypersensitive sites
- There are specific sites that always cut
- Why as they sensitive , they are fee-e=re of structure / nucleooes
- Hypersen are found in promoters site

The SV40
Chromatin insulators
- figure 10.50
    - The enhancer activates the promoter

- 10.51
    - Serves as a barrier
    - Hetero creepage
    - Saves the uchromo region ( the nucleosomes are closer together )

Drosophila Insulators
- Essential for expression

- Insulators are called SCS 's
- They dont bind tightly

10.52
- SCS sit at junction points
- There is some protein that bind to the sides that protects the seq

Slide/ white/ yellow

Video
- Helicase

On Thursday epigentics
- Def**
- Def smaller terms the roles that they play
- Two we are talking about the meth,

Affects, what effects them , how they come about , how does our understanding affect the field
-

# Thursday March 20th

March-20-14
2:32 PM

Epigenetics
Chapter 29 covers a little about this stuff

Figure 29.11
- Dosage compensation : different expression of alleles ,
- Happens all the time in F , with X chromo, different set is expressed
- Coat color is determined by X chromo in some animals
- Supresses the entire x chromo and not the other results in the cat picture
-

Imprinting
- Methylation ***
- Certain genes are differentially methylated , depending on who you get the allele from ( mother or father )
- not meth from father will always be expressed
- Meth = gene is inactive
- Survival of the embryo is dependant on the imprinting
- Clusters
- 80 genes imprinted in humans , list is growing
- Genes that imprinted important to maintain the imprinting , if you lose the imprint > bad
- If it depends on what maternal or paternal gene you get ??
    - How is the imprinting maintained

Figure 29.23
- Reps two alleles of the same gene
- Maternal is methylated > inactive
- Paternal non meth> active
- Embryo ca be F/M
- Methylation pattern is reset every generation
- Male , one is meth , when male produces sperm , hapoid sperm , re- sets
- Re - setting is important
- Maternal meth - alway be off > female resets the > meth
- Paternal

IGF II , Receptor
- Cell membrane receptors
- Produced by IGF-II\
- Missed
  Fathers is always expressed, mother is never expressed ( IGF II)
  IGF receptor gene is always off from your paternal alleles and the mother allele is always off
- This brings up : if your a female you need this ( dont want a 15 pounds baby )
- Evolutionary : you want your offspring to survive , size of fetus
- Thought that the genes that you are born with ( imprinting ) does not change
    - We know now that it can change

Imprinting control region
- Cis acting
- Clusters
- Icr meth inactivates the H19 , allows the igf II to remain active
- Meth , imprinting can de-activate genes , in maternal vs paternal state

New areas of epigenetic research
- Certain indiv in starvation condition passed on negative health effect onto their kids and grandkids
- Trangenerational epigenetics
- Change the imprinting by meth

- Ex:
- Sensitive period of exposure :
- Women your egg are already formed when you are born ( in the womb ) your sensitive during pregnancy and more so during the last trimester
- 9/11 women who were prego , then and monitored their coritsol levels , in the last trimester larger affect , anxiety etc they was a correlation btw the events and environment , exposure
- Can change their imprinting levels

Impact of epigenetic regulation on human disease
- Depending on who you get the deletion from determine the disease

Identical twins do not share diseases
- Height s genetic
- Environment can alter the imprinting and meth pattern

Impact of epigenetic regulation on human disease
- Valproic acid : showed to be a histone modulator , leads the acteylation of histones that leads to the activation of some genes
- It starts up genes that have been shut down
- If you lose imprinting ,it can lead to a number of cancers >

Effect of early traumatic stress on suicide rate and depression
- Potential link

Understanding the epigenome is the next frontier of molecular biology and pharmacology

## CHAPTER 19 TRANSCRIPTION

- When does a cell know to turn that particular gene on
- Promoters
- All genes have promoters that regulate the amount of rna being made
- Enzyme has to unwind the dna b/c it only use one strand the dna
- Transcription start site : rna polymerase binds there
- Terminator seq
- Pro / euk

Euk rna polymerase
- We have 3 rna polymerases
- Rna polymerase 1: transcribes rRNa
- Rna polymerase 2: transcribes mRna
- Rna polymerase 3: transcribes tRNA and small RNA's
- How does it know to transcribe what it does ?
    - Promoters bind to transcription factors
    - All the polymerases interact with specific transcription factors

Figure 19.1
Figure 19.2
Transcription bubble
Figure 19.3
- Transciption bubble, dna melting to clone the bubble
- Enzyme st onto of the bubble and starts making the template ( rna ?)
- After it passes it detaches and spit out the back the enzyme,
- Yellow strip is the rna that is spit out ,
- Rna gets longer , enxyme falls of the dna when reaches the terminate factor
    - In introns they have to take out exons etc

Figure 19.5
- Mouth catalytic site
- Moving left to right dna is unwound and rewound

- Histone are being take off throughout the process and repositioned after

Transcription Stages
- 4 defs

Figure 19.6 ^ related to defs

# Tuesday March 25th

March-25-14
2:28 PM

Handle changes in gene expression by mod -ing

Transcription "stalling "

- The initation phase the most important > when does it know to go /
- Rna poly unwinds the dna using enzyme
- I fthe conditions are nto right , the pool to nulceotides that it uses at rna for the template starnd are limiting
- The rna has a senseing sys that allows it to abort or slow down transcription
- Detects damange in the dna it wont be able to use it properly
- The rna can stop back tract , cut the rna off and generate a new 3" ends and start again , has repair abilities
- Once everything is fixed it can start again
    - How is the rna polymerase > unwinding, transcription, rewinding , template strand

Rna polymerase enzyme

- Very large complex of protein with channels running through it
- Once the intial part hits the rudder separates from the dna and go out the top of the complex
- There is an intake hole , that sucks all the nucleotides into the central part of the enzyme > uses it

Figure 19.8

- Yellow / red are starnds of the dna . Fed through the central part
- Template R , having rna placed complentary to it
- The other starad goes up and around the complex , dont want it the way during transcitption
- Rna put in and eventually get kicked out

Figure 19.26

- Enzymes L>R
- The dna comes into the jaws of the enzyme
- Coding strand is dark blue , light blue is the template one
- In the central core is pool of nucleitides that make the rna strand , as the rna is pushed out it hits the rudder
- This where the RNA / DNA hybrid separate
- Dna unwinds and reform when the enzyme is going by
- Rna is placed complementary to the nucleo and then is coming out the back
- Thing that is not shown histones , they have to be kicked of and then reformed when the enzyme comes back around

Bacterial RNA polymerase

- There are difference btw EUK and PRO transcription !!! Know ****
- Very different from ours , there main major differences
- It has a single ( we have 3)
- 2-5000 ( presents some problems caus ewe knwo the bacterial genome are very copact , very little non0unique seq , how do the rna poly's knwo what to transcribe
    - The second problem there are a bunch of mRNA genes , there is only one polymerase
- The major component : holoenzyme > 5 subunits 5 diff protein from 5 diff genes
    - Core enzyme ( aplha beta x2 ) + sigma factor () major players
        - Catalytic center where it does att activity
        - Alpha > structure
        - Sigma : key factor
            - Essential for the bacterial to recongnize specific promoters at different time s
            - There are a bunch of different sigma factors
            - When bound to the core enzyme allows then to reco promoters
            - Our cells dont have sigma factors
            - Rifa :

Figure 19.7

- Dont have the know each of these genes \KNOW ALPHA BETA ONES **********

Only the holoenzyme can initiate transcription
- Contains core enzyme and sigma factors ( aplha beta )
- Not required for elongation ( sigma factor )
- Sigma only needed for transcription
- Core enzyme needed for elongation but not transcription
- Without sigma cant determine where the promoter is
    - When sigma binds to the core enzyme it change the conformation of the whole comples now that it can actually lock into the _____
- Sigma control specificity ,
-

Figure 19.10
- Sigma binds to rna poly to form holoenzyme it can see the promoter seqences
-

Transcriptional imitation
Bacterial promoters
- Very conserved
- bacteria promoter is 40 nucleotides long
- Transcription start point, tata box
- Tata box is so conserved b/c rna poly recognize its
- Secondary seq >-35 seq
- If the 16/19 is deleted the promoter will not work , you kill promoter : positioning of the seq is important and conserved

Three major promoter sequences

Rna polymerase bind to the bases -50 .+20
- 19.22

Promoter Mutations

Figure 19.13
- Bar is nulceotides form +20-50 that where it binds sigma stretches ot out
- Binds to closed conformation , then melts to open conformation
- Sigma factors use tot get it started

Dna super coiling
- Problem the dna has to be unwound
- Assist the rna polymerase to do these processes

How are different genes regulated in bacteria ?
- Big ones reco vast majority of promoters
- The seq dont look like tata box seq ?
    - That the seq in promoters that are reco by holoenzyme that contain sigma
    - Sigma 32 what does it do ? What type of genes does it transcribe : contains alot of C/G has an extra hyrdogen bond, what si easier to break ( close to open conformation ) sigma 7 ( more A/T ) easier to break less hydrogen bonds
    - Types of genes that have these promoters ? : the purpose of the genes when do they get activated when the cell are under heat shock ,
        - If you raise the temp a bit they have a survival mechanism that prodoces heat shock proteins
        - Subject bacterial to heat stress , sigma 32 binds to promoter with help og core enzyme , easier to break the bonds apart , transcibes the genes and translated
        - the cell is not under heat stress you dont wan these promoters to be turned on
        - Fail safe mech > heat shock sigma factor only under heat conditions
            - They have very diff seq , reco by holoenzyme

Figure 119.36
Heat shock

- Competes with the core enzyme
  The sigma cascade
- Evolutionary response
  - Uses sigma factor to control when genes are turned on /off > ,middle , last phase patterns of expression
- Allows it to go through its lifecycle without having to compete

Figure 19.39

- Attaches to 1st promoter makes gp28, outcompetes
-

# Thursday March 27th

March-30-14
11:47 AM

# Tuesday April 1st

April-01-14
11:44 AM

Chapter 28

- Diff promoters ad how they recognize
- Even when basal factors are there doesnt mean that they are on
- Chromatin is methyl it wont allow the factors to bind

Figure 28.1

- Basal factors that __ onto the core promoter
- Enhancer seq

Types of transcription factors

- Act : different type of transcription factors that are general found in enhance seq , interact to turn on genes ( bind to dna )
- Coacts: link basal and acts
-

Transcriptional activators

Figure 28.8

- Connecting separate the binding /activating domains and allows for movement

Figure 28.8
Some acts do not contain act domains

- You have an act and another gene that encodes and coact that provides a link btw the two

How do these acts work ?

Figure 28.10

- Most histones are gone
- When polymerase binds it must have free access to the dna

Transcriptional activator types

- They are based on the final structure of the proteins > names 5

Zinc finger

- Loops to form finger like structure and held together by zinc

Steroid recep

Homeodomain

What do homeobox activators do if mutated ?

- Messes up the binding points

Figure 28.14

-

Leucine Zippers
Figure 28.16

- Positively charge interact with dna

Chromatin has to change structure in order to be able to interact
Dynamic model

Chromatin remodeling
Figure 28.20

- Conserve all the way through
- Don need to know any of them on the picture

How are 14 contacts between the histones and DNA broken
Promoter activation : same as slide
Figure 28.29

Final Exam
- Not cumulative
- 4,5,6,9,1,19,20,28,29 ( imprinting and 30 ( weeks 6-12)
- 70/80 m/c + SA 20/25 marks

THURSDAY APRIL 10TH 3:30 PM toldo 100,102,104

# Assignment

April-03-14
10:34 PM

Gene :
FTO fat mass and obesity assoc

Chromosomal position ": 16q
# of exons 9

Function of the gene
The exact function of this gene is not known.
FTO gene exact function is not known. It is a nuclear protein of AlkB which associated with non-haem iron and 2-oxoglutarate-dependent oxygenase superfamily. FTO is a protein coding gene, it may play a role in body mass index , obesity risk, type 2 diabetes and it may also play a role in nervous and cardiovascular system.

Which genes on either side
At position16q11.2 gene myosin light chain kinase 3 and at position16q21 gene autocrine motility factor receptor, E3 ubiquitin protein ligase

Citation
Olza et al.: Influence of FTO variants on obesity, inflammation and cardiovascular disease risk biomarkers in Spanish children: a case–control multicentre study. BMC Medical Genetics 2013 14:123.

Cdna
ATGAAGCGCACCCCGACTGCCGAGGAACGAGAGCGCGAAGCTAAGAAACTGAGGCTTCTTGAAGAGCTTG
AAGACACTTGGCTCCCTTATCTGACCCCCAAAGATGATGAATTCTATCAGCAGTGGCAGCTGAAATATCC
TAAACTAATTCTCCGAGAAGCCAGCAGTGTATCTGAGGAGCTCCATAAAGAGGTTCAAGAAGCCTTTCTC
ACACTGCACAAGCATGGCTGCTTATTTCGGGACCTGGTTAGGATCCAAGGCAAAGATCTGCTCACTCCGG
TATCTCGCATCCTCATTGGTAATCCAGGCTGCACCTACAAGTACCTGAACACCAGGCTCTTTACGGTCCC
CTGGCCAGTGAAAGGGTCTAATATAAAACACACCGAGGCTGAAATAGCCGCTGCTTGTGAGACCTTCCTC
AAGCTCAATGACTACCTGCAGATAGAAACCATCCAGGCTTTGGAAGAACTTGCTGCCAAAGAGAAGGCTA
ATGAGGATGCTGTGCCATTGTGTATGTCTGCAGATTTCCCCAGGGTTGGGATGGGTTCATCCTACAACGG
ACAAGATGAAGTGGACATTAAGAGCAGAGCAGCATACAACGTAACTTTGCTGAATTTCATGGATCCTCAG
AAAATGCCATACCTGAAAGAGGAACCTTATTTTGGCATGGGGAAAATGGCAGTGAGCTGGCATCATGATG
AAAATCTGGTGGACAGGTCAGCGGTGGCAGTGTACAGTTATAGCTGTGAAGGCCCTGAAGAGGAAAGTGA
GGATGACTCTCATCTCGAAGGCAGGGATCCTGATATTTGGCATGTTGGTTTTAAGATCTCATGGGACATA
GAGACACCTGGTTTGGCGATACCCCTTCACCAAGGAGACTGCTATTTCATGCTTGATGATCTCAATGCCA
CCCACCAACACTGTGTTTTGGCCGGTTCACAACCTCGGTTTAGTTCCACCCACCGAGTGGCAGAGTGCTC
AACAGGAACCTTGGATTATATTTTACAACGCTGTCAGTTGGCTCTGCAGAATGTCTGTGACGATGTGGAC
AATGATGATGTCTCTTTGAAATCCTTTGAGCCTGCAGTTTTGAAACAAGGAGAAGAAATTCATAATGAGG
TCGAGTTTGAGTGGCTGAGGCAGTTTTGGTTTCAAGGCAATCGATACAGAAAGTGCACTGACTGGTGGTG
TCAACCCATGGCTCAACTGGAAGCACTGTGGAAGAAGATGGAGGGTGTGACAAATGCTGTGCTTCATGAA
GTTAAAAGAGAGGGGCTCCCCGTGGAACAAAGGAATGAAATCTTGACTGCCATCCTTGCCTCGCTCACTG
CACGCCAGAACCTGAGGAGAGAATGGCATGCCAGGTGCCAGTCACGAATTGCCCGAACATTACCTGCTGA
TCAGAAGCCAGAATGTCGGCCATACTGGGAAAAGGATGATGCTTCGATGCCTCTGCCGTTTGACCTCACA
GACATCGTTTCAGAACTCAGAGGTCAGCTTCTGGAAGCAAAACCCTAG

Olza et al.2013. Influence of FTO variants on obesity, inflammation and cardiovascular disease risk biomarkers in Spanish children:case control multicentre study. BMC Medical Genetics. Vol:14, 123.

At position16q11.2 gene myosin light chain kinase 3 and at position16q21 gene autocrine motility factor receptor, E3 ubiquitin protein ligase