Lecture 2

Genome & their regulation

- Phenotype - something that changes the physical attributes of an organism (eye color, etc)
  - Biochemical assays - something that changes some physical properties that are used for performing a specific assay
- Junk DNA - DNA that is not in the coding region, not everything that doesn't code for protein or is immediately adjacent to the coding region that is specifically involved in transcription does not necessarily have an affect on genes.
- Chromatin structure has an enormous effect on transcription level, proteins that bind to repetitive DNA govern where the 3d structure of genes reside in the nucleus.
  - therefore genes that have to be accessible to TF end up accessible TF and due to chromatin structure those that are in lineage that the gene is no longer expressed they end up sequestered and are no longer available to TF.
- Every enzyme reaction in a cell or organism is catalyzed by an enzyme, otherwise they would not be energetically favorable enough or would occur slowly, resulting in nothing happen
  - every enzyme has to be produced from a gene made into mRNA then translated into protein. The protein is processed as the RNA is processed and are regulated by time, development and cell type
  - Micro-arrays - snap shots of the gene expression level of the whole genome at once.
- TFs control whether transcription occurs
  - TFs regulate at what point RNA transcription is at in cell development
  - role of TF can be many folds different
    - TF are complexes of 12 to 15 proteins, can be dimers, tetramer, pentamer, etc
      - factor usually means the functional unit.
        - factor implies a biological function
        - some factors directly bind to DNA sequences that are parts of genes, some are adjacent to the coding region, some can be in the introns, some can be 1000 bases either before or after the gene coding region ends.
  - regulatory regions can act at distance quite far apart from where the coding region is.
  - some TFs bind DNA to sequences, others bind to other factors to recruit them. Still others act to the RNA polymerase itself.
  - differentiated cells exist because only that cell type makes that unique TF and no other cell makes that factor
  - in general, transcription of a gene requires a combination of many different TF binding to many different transcription sequences some of these factors are common in all genes, and others maybe unique

- Not like a binary switch (not like an on or off switch)
- Hallmark of regulation is that the level of proteins varies enormously in cells. Some protein in cells are present at minute amounts (hormones, etc), other proteins are structural and involved in protein synthesis, actin, or things that make the cell membrane. Levels can be as much as 4% of the total protein in the cell.
- Level of protein usually mimic the amount of RNA that encode that protein, so the level of RNA vary over a million fold.
- Level of RNA produced is controlled at the level of initiation not at the level of elongation.
- strong promoter = high level of RNA in cell making abundant protein made
- normal role is to have initiation occur sporadically, even the cell that needs it, the RNA produced is very low and when translated very low level of protein translated
- Transport of mRNA out of nucleus
  - control at how efficiently the RNA can get out of the cell
  - often art of that control is RNA splicing
- RNA splicing
  - Removal of the non-coding regions of the RNA to form a RNA that has a complete open reading frame.
  - not all sequences end up in the mRNA
  - occurs only with any internal sequence, thereby joining the other two ends (cut out an internal sequence having the two other ends join, not splicing if the ends are cut)
  - delete intron = gene not regulating correctly
- variant of splicing = alternative splicing
  - The same as primary RNA transcript can be spliced to generate a different set of exons (in one form a sequence may be considered an intron and the other may be an exons).
  - In alternative splicing, what controls if an exon is removed?
    - splicing factors that either mask splice junctions or make novel junctions more desirable. Alternative splicing is very specifically controlled so there is no accident it uses unique splicing factors.
  - 60% of cell undergo alternative splicing
  - can make a splice junction attractive or not
  - multiple RNA from same region
  - some of the exon are common and others are different,
  - can be unique to a certain cell type (alcohol dehydrogenase), and can have all forms made in the same cell produced by alternative splicing.
- in the majority of splicing the gene will produce one mature RNA even though it under went splicing, it would always connect the same way so that you would get that gene

- mRNA stability - often special proteins tag mRNA to either keep the stability of the RNA or tag the RNA for degradation.
- Translation
  - regulation occurs at RNA level, can also be in oocyte
  - siRNA play a role to modulate translation, matter of what level of translation occur
- Protein stability - change in activity or stability of protein in cell
- Protein modification
- chromatin structure affect transcription --> siRNA controls activation or deactivation
- Chromatin - DNA of genome + folding protein
- Abnormal regulation

- Eukaryotic gene
  - nucleotide written from 5' end
    - always goes from 5' to 3' in an anti-parallel fashion.
    - not all genes encode protein
      - rRNA - is not encoded as protein, and function in catalysis
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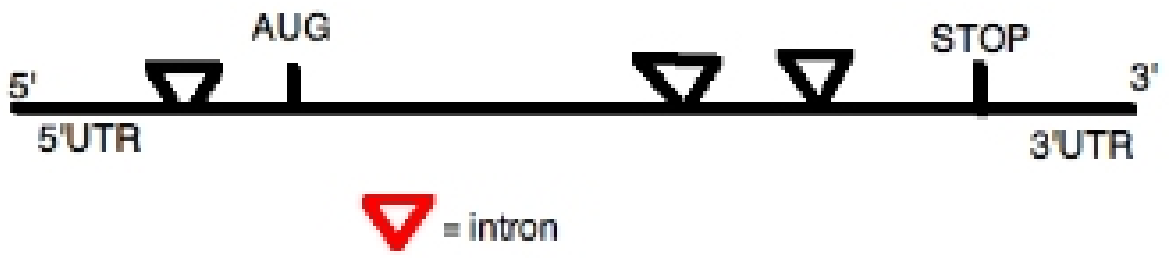

      - only transcriptional eukaryote RNA have 5' methyl g cap
        - methyl g cap + poly a - involved in transcription
        - initiation + translation occur with the joining of the RNA that has these regions
        - 3'UTR region - region that have stability sequence
        - 10 nucleotide from AUG --> ribosome binding site --> not there ribosome cannot start without ribosome binding site
  - Intron deleted and exon kept
    - intron removed at mRNA level, but introns found in both DNA and RNA
    - can have introns in non-coding region
    - anything that gets removed is considered introns
  - enormous introns can affect translation
    - coding region is AUG to stop codon
  - Reading frame doesn't start until AUG and ends at stop
  - RNA=AUG, DNA=ATG