Regulation of Gene Expression in Eukaryotes
Opportunities for the control of gene expression in the eukaryotic cell
Gene Expression

• Spatial – not every gene product needed in every cell type
• Temporal – Different genes expressed at different times
  – Environmental stimuli
  – Hormones
  – Especially seen in development- formation of tissues and organs
Regulation

- RNA processing
  - 5’ cap
  - Poly A tail
  - Intron removal

- In eukaryotes, more level of regulation than prokaryotes due to complex organelles
Cytoplasmic control

- mRNA stability:
  - Long vs. short lived mRNAs
  - Long- many rounds protein synthesis from one mRNA
  - Short – rapidly degraded, needs more transcription to replenish (half-life)
- Rapid mRNA degradation may be desirable
- Half-life problem with making a drug, too
mRNA stability

• Poly A tails – can add stability
• Longer tails stabilize message more
• E.g., histone mRNAs no poly A tails; message very short lived
Induction of transcription

• Not found as often in eukaryotes as in prokaryotes
• Induction can work by:
  – Temperature
  – Light
  – hormones
Induction of transcription

- Temperature
  - Synthesize heat shock proteins (HSPs)
  - Transcriptional regulation – stress of high heat signals HSPs to be transcribed
  - Studied in *Drosophila*- but occurs in humans also
Induction of transcription

• Light
  – RBC (ribulose 1,5 bisphosphate carboxylase)
  – Plants must absorb light energy
  – RBC produced when plants are exposed to light
    (see Northern blot in figure)- remember what is a
    Northern blot?)
Induction of transcription

- Hormones
  - Secreted, circulate through body, make contact with target cell and regulate transcription
  - Called signal molecules
  - 2 classes of hormones that activate transcription
    - Steroid hormones
    - Peptide hormones
Steroid hormones

- Small, lipid molecules derived from cholesterol
- Easily pass through cell membranes
- Examples
  - Estrogen
  - Progesterone
  - Testosterone
  - Glucocorticoids
Steroid hormones

- HRE’s- hormone response elements – mediate hormone induced gene expression
- Number of HRE’s dictate strength of response (work cooperatively)
Peptide hormones

• Linear chain of amino acids
• Examples
  – Insulin
  – Growth hormone
  – prolactin
Peptide hormones

• Cannot pass through cell membrane easily, so convey signals through membrane bound receptors

• Signal transduction – hormone binds receptor on cell surface, signal gets internalized, then cascade of events begin
Molecular control

- Transcription factors – accessory proteins for eukaryotic gene expression
- Basal transcription factors
  - Each binds to a sequence near promoter
  - Facilitates alignment of RNA polymerase
Special transcription factors

• Bind to enhancers
• Promotor specific (HRE’s for e.g.)
• Properties of enhancers:
  – Can act over several thousand bp
  – Function independent of orientation
  – Function independent of position – upstream, downstream, etc. (different than promoters- close to gene and only one orientation)
• Yellow gene in *Drosophila*
• Tissue specific enhancers for pigmentation for each body part
• Mosaic patterns- alterations in yellow gene transcription in some body parts but not others
• Also see SV40 enhancer (simian virus 40) –
How do enhancers work?

• Influence activity of proteins that bind promoters
• RNA pol and basal transcription factors
• Physical contact with other proteins?
  – Enhancer and promotor regions brought together by DNA folding
Transcription factors

• 2 chemical domains
  – DNA binding
  – Transcriptional activation
• Can be separate or overlapping
• Physical interaction also quite possible
Transcription factor motifs

- Zinc finger – DNA binding
- Helix-turn-helix - DNA binding (COOH required)
- Leucine zipper - binding
- Helix-loop-helix – helical regions allow for dimerization
  - Homo and hetero dimers
Gene expression and chromosomes

- DNA needs to be accessible to RNA pol for transcription initiation
- Place on chromosome may affect this
- So, gene exp influenced by chromosomal structure
- E.g., lampbrush chromosomes
Is transcribed DNA more “open”? 

• Used DNase I treatments
• Groudine and Weintraub – showed transcriptionally active DNA more easily degraded by DNase I than untranscribed DNA (more “open” to nuclease digestion)
• Have DNase I hypersensitivity sites – near promoters and enhancers
Whole chromosomes: activation and inactivation

• Equalizing activity of X chromosomes in XX versus XY organisms

• Recall mechanisms:
  – Humans, inactivate one X chromosomes in females
  – In *Drosophila*, male X makes double the gene product
X compensation

- Inactivation, hyperactivation, hypoactivation
- What is molecular mechanism of dosage compensation?
  - Specific factor(s) bind to X- regulate its gene expression above all other regulatory elements
Dosage Compensation – example of X in humans

- XIC- X inactivation center – makes XIST (X inactive specific transcript) - 17kb mRNA with no ORF- so likely does not encode a protein
- RNA is the functional product of the gene
- Found only in nucleus and not associated with active
Opportunities for the control of gene expression in the eukaryotic cell