Control of Gene Expression in Eukaryotes

Introduction
- Huge topic - just choose a few choice examples

Control of translation
- In some cases, possible to control
- **Egg cells** have a huge amount of mRNA present, but only translated after fertilisation
- Mammalian RBCs have no nucleus, but they do have globin mRNA, the translation of which is regulated by haem
- No point making globin if there's no haem to go with it
- The "haem controlled inhibitor" is a kinase, active at low haem concs and inactive at high haem concs
- It phosphorylates the initiation factor eIF2 blocking initiation of translation

Control of transcriptional modification
- For example, alternative splicing permits tissue or developmental specific changes in gene expression (e.g.: ALPHA-tropomyosin)
- Controlling the stability of mRNA also allows us to regulate the number of times a given mRNA transcript is translated
  - For example, the milk protein **prolactin** increases the half-life of **cesein mRNA** for <3 hr to >24hr
- It has become clear that the expression of many genes is controlled by small RNA molecules. Some features are becoming clear
  - By virtue of their ability to base pair, these small RNAs can target specific sequences for control
  - Examples of small RNA
    - RNAi
    - MicroRNA
    - Viral infection
  - Effects
    - These can bind flat onto the mRNA, causing degradation
    - These can bind onto RNA forming a "loop", inhibiting translation
    - these can **silence genes (DNA)** - mostly in **plants**
  - For example, microRNAs are thought to inhibit effective mRNA translation o target genes through imperfect base-pairing with the 3' untranslated region of traget mRNAs

Control of transcription - transcription factors
- These bind to specific sites on DNA and either activate or repress transcription
- Sometimes, they're *very* far away from the gene they control
- In such a case, they control the sequence by "bending" the DNA and coming into contact with the relevant sequence
- **Silencers** also exist performing the opposite function
- A good example is seen in the steroid response element family
  - This are lipid soluble and so permeate straight through the membrane
  - They then do their job once inside!
- Mouse mammary tumour virus
  - Transcription is induced in response to glucocorticoid hormone (mebrane permeable)
  - Receptor (localised in nucleus) which binds to the hormone, and whose affinity to DNA is greatly increased
- Control of 5S rRNA transcription by polIII
  - Transcription factor TFIIIA can bind to RNA transcript AND gene itself
  - If RNA transcript is in excess, it "mops up" the factor, and none is left to bind to DNA to stimulate transcription
- Helix-turn-helix motifs are also common here (just like in proks)
- The "**zinc finger**" motif is most common
  - C2H2 zinc finger has a loop of 12 amino acids anchored by two cys and two his residues that tetrahedrally co-ordinate a zinc ion
  - Also contains an alpha helix that sticks out like a finger into one of the DNA groves
  - The DNA-binding is mediated through specific side chain interactions between the alpha helix and the major groove base pairs
- So is the "leucine zipper" motif
  - Contain a hydrophobic leucine residue at every seventh position
  - These lie in an ALPHA-helical region an the regular repeat forms a hydrophobic surface on one side of the alpha-helix
  - Two of these can therefore dimerise
  - These also contain a basic DNA-binding domain N-terminal to the leucine zipper
  - These effectively form a **clamp** around the DNA