BIO495 Capstone

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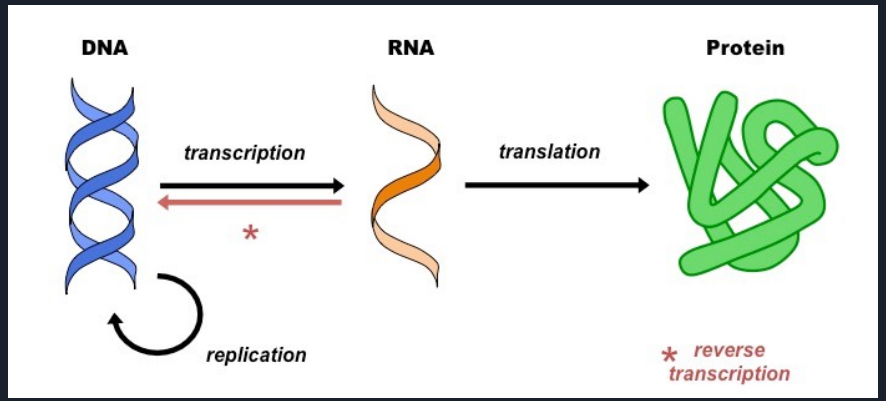
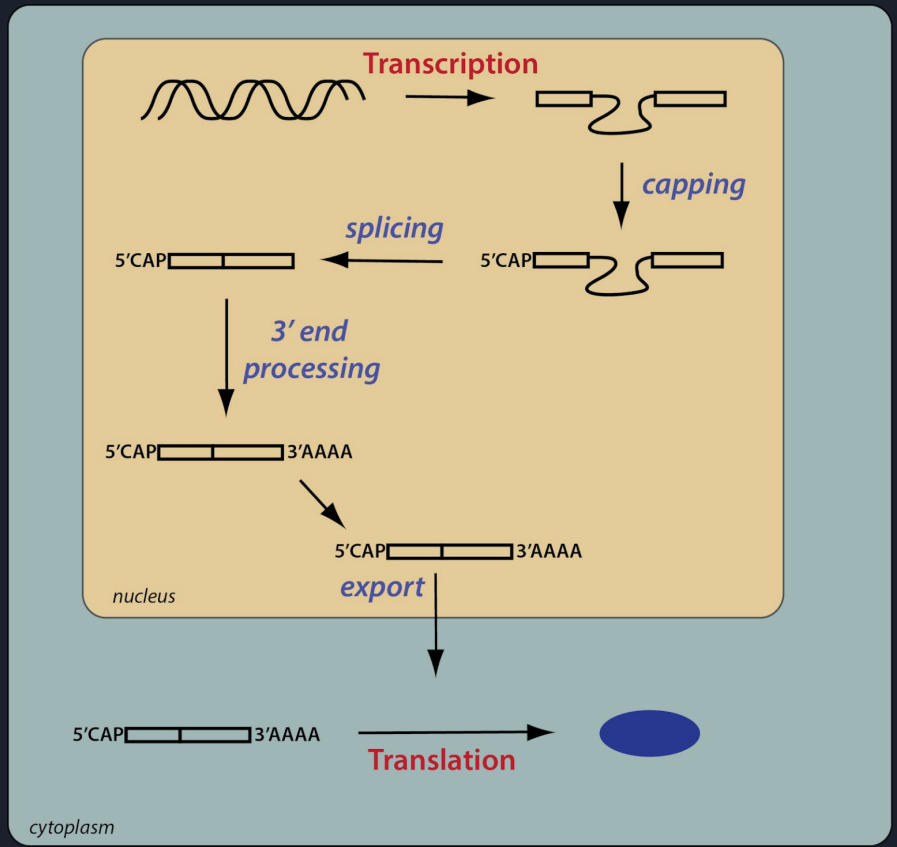
Central Dogma

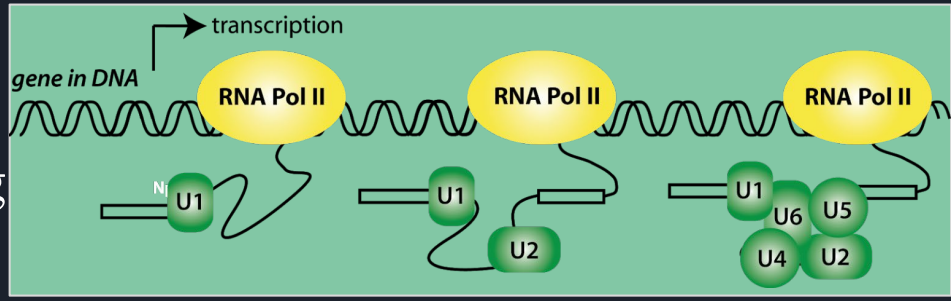




Coupling

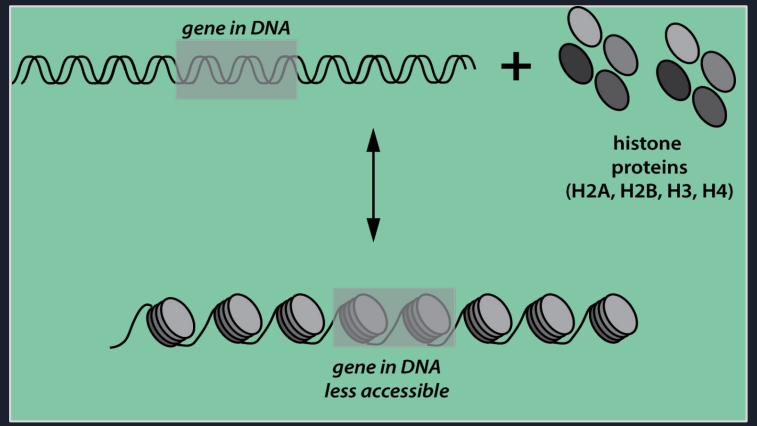
- Cellular processes occur concurrently
  - Ex. Cotranscriptional Splicing
- Coupling is the biological concept that independent cellular processes are linked using similar cellular resources in order to allow for more efficient utilization of energy
  - Enzymes often have multiple roles in different cellular processes
- Analogous to buying a multitool for multiple purposes versus buying seperate tools for each job

An Example of Coupling: Cotranscriptional Splicing



- Though often described sequentially, transcription and RNA splicing occur at the same time
  - Splicing machinery is known to load onto the growing pre-mRNA strand before the termination of transcription
- The Carboxyl Terminal Domain (CTD) of RNA Polymerase II (the main driver of transcription) is known to recruit splicing machinery
- This is a well known phenomenon; however, our lab was interesting in studying how **chromatin modification** (a precursor to transcription) and **3' end processing** could also be coupled to RNA splicing in this way.

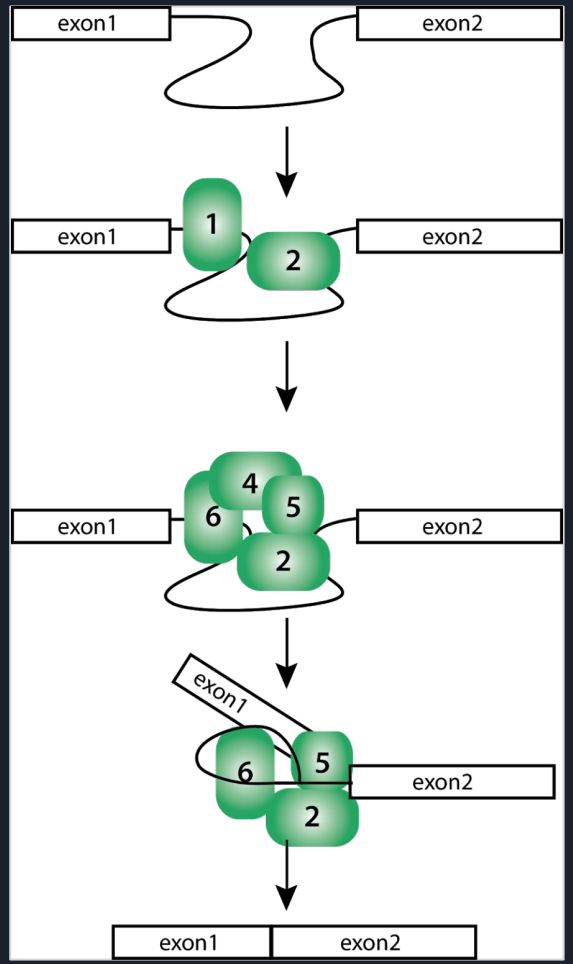
Chromatin Modification



- For transcription to occur, DNA must be accessible for RNA Polymerase II to bind and transcribe DNA into mRNA
- 2 classes of proteins that achieve this
  - Chromatin Remodeling Proteins - physically removes histones from DNA
  - Chromatin Modifying Proteins - chemically modifies amino acid residues to change the bonds of DNA to the histones
    - Subtypes include histone acetlyases (Nua4 Complex), methylases and phosphorylases.

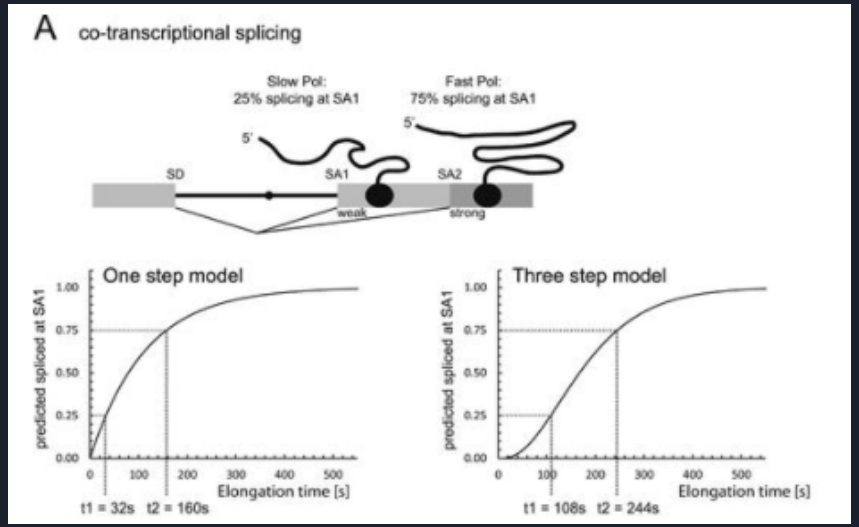
Splicing

- Splicing- the process of removing non-coding introns of pre-mRNA and retaining coding exons
  - Occurs cotranscriptionally
  - Alternative Splicing- mRNAs can be spliced in different ways by selectively retaining or removing introns to create different protein products.
- Accomplished through splicing factors associated in a complex known as the spliceosome:
  - The main drivers- the snRNPs (U1, U2, U4/U5/U6
  - Helped by helicases (Prp28, Prp40, NTC)

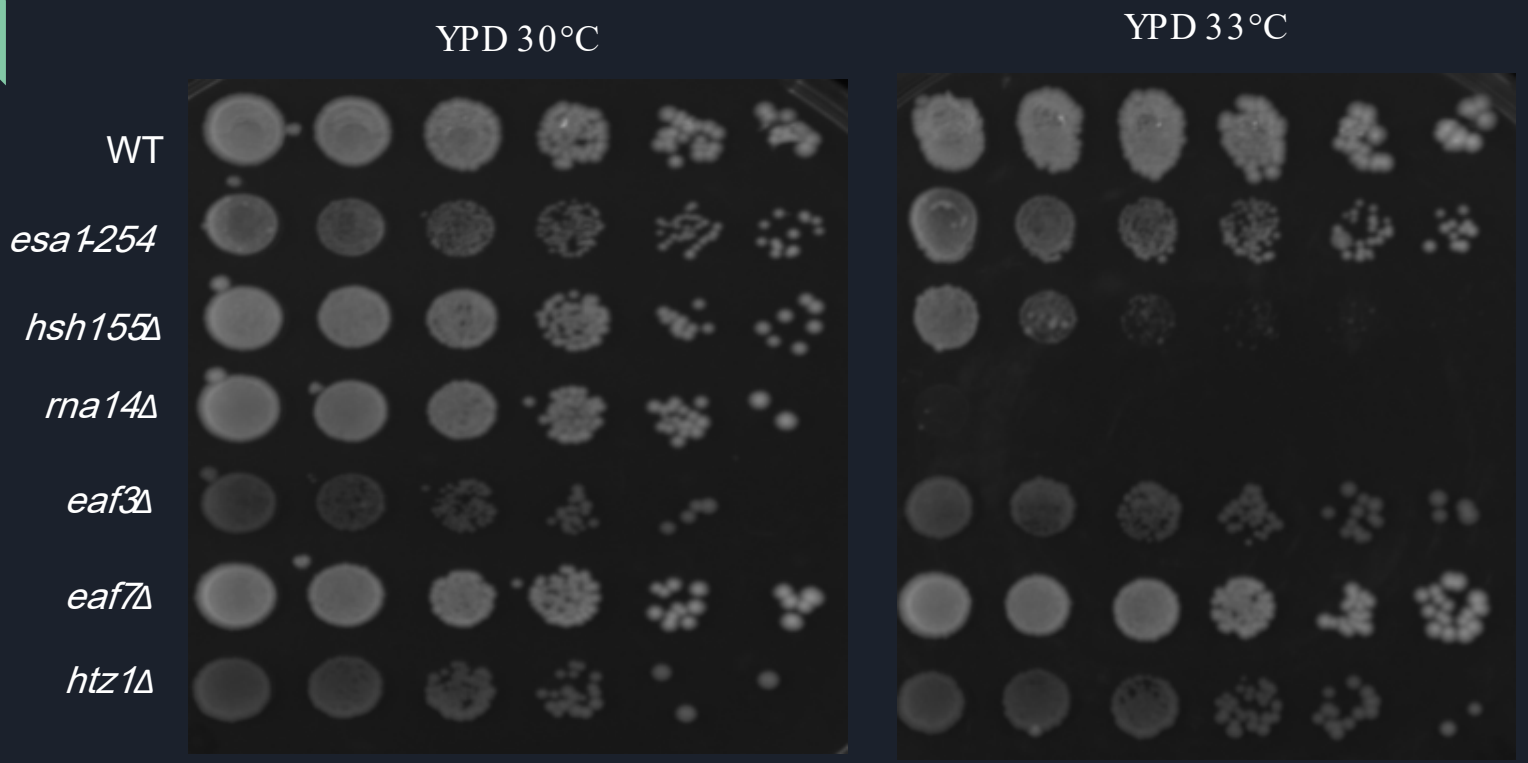


The Models on the Effects on Splicing

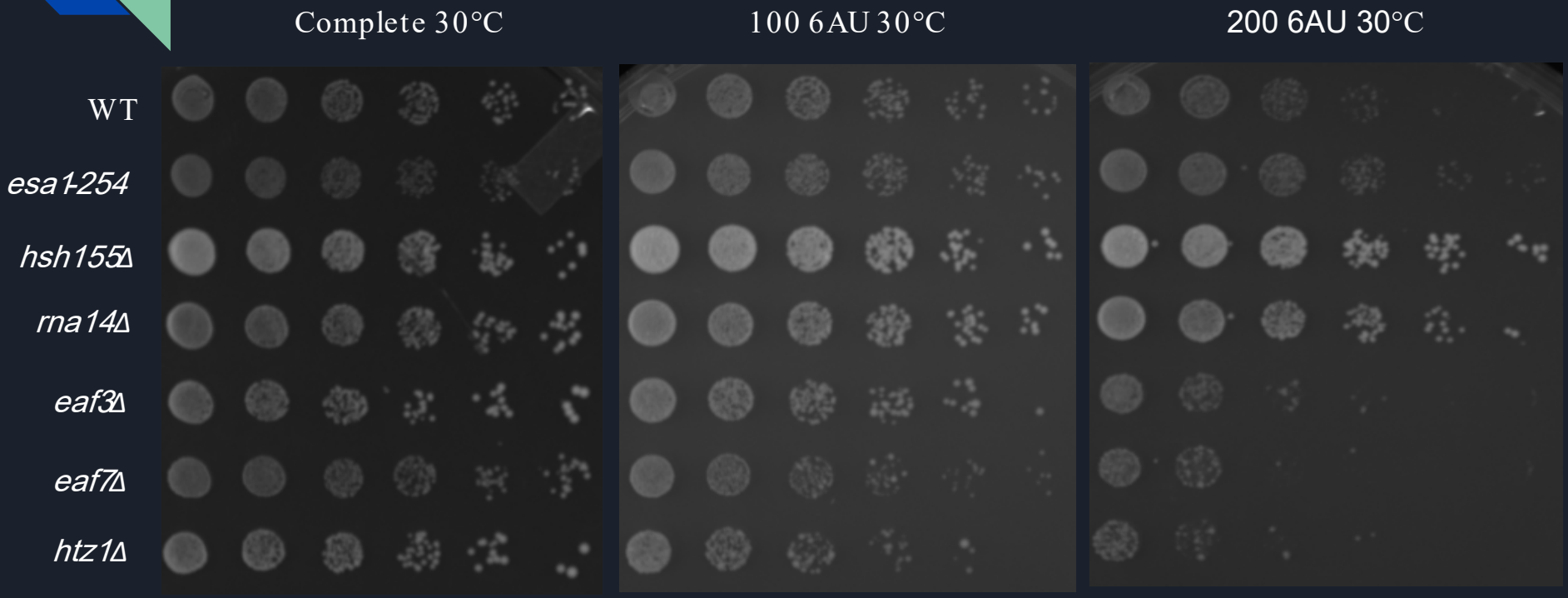
- There are two models that couple how the qualities of transcriptions can affect the effectiveness of splicing
  a. Kinetic Model - the speed of transcription (the speed at which RNA Pol II moves) changes splicing
     - Faster transcription reduces the quality of splicing
     - Slower transcription increases the quality of splicing
  b. Recruitment Model - proteins involved in transcription actively recruit proteins involved in splicing



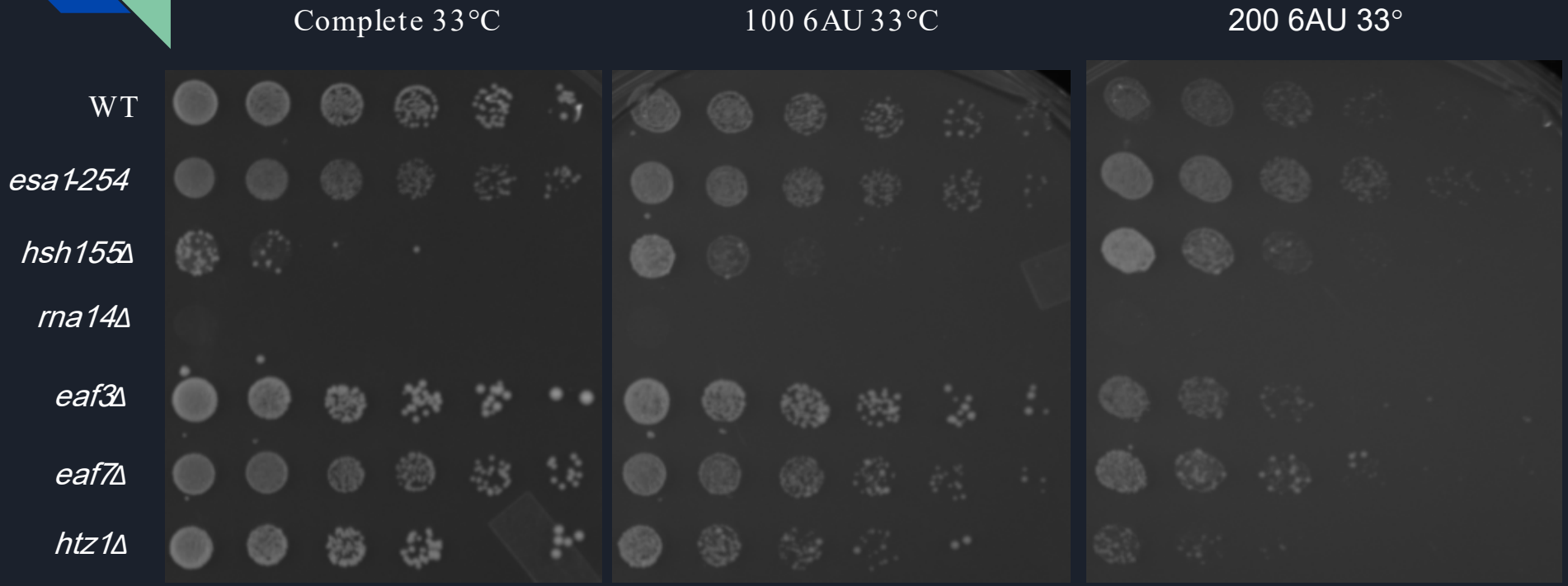
Single Mutant Qualitative Growth Assays



Elongation Restrictions on Single Mutants



Elongation Restrictions on Single Mutants



esa1-254 Mutants on Meiotic Genes