CONCEPT: POST TRANSCRIPTIONAL REGULATION

RNA Processing, Translation, and Degradation

● Regulation of mRNA after transcription is a major way to control gene expression

□ RNA processing includes alternative splicing, preparation for nuclear export, and RNA editing

- Improperly processed mRNAs are not exported and translated

□ RNA translation can be controlled

- Phosphorylation of eIFs (bind to 3' mRNA to promote translation) can globally inhibit cellular translation

- Phosphorylated eIF cannot exchange GDP for GTP and therefore can't promote translation

- **Translational repressors** are proteins that control translation of specific mRNAs

□ mRNA degradation rates vary and are one way to regulate gene expression

- Shorter poly(A) tails are less stable than longer tails

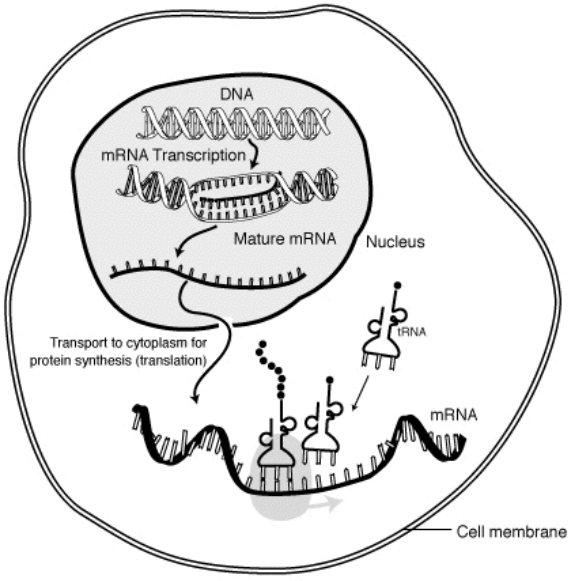
- **Exosomes** degrade mRNA from 3' to 5' via exonucleases

- **P bodies** are nuclear mRNA processing bodies that degrade mRNA from 5' to 3'

- **Nonsense mediated decay** degrades improperly spliced mRNA that lack proper protein coding regions

- When stop codon is in wrong place

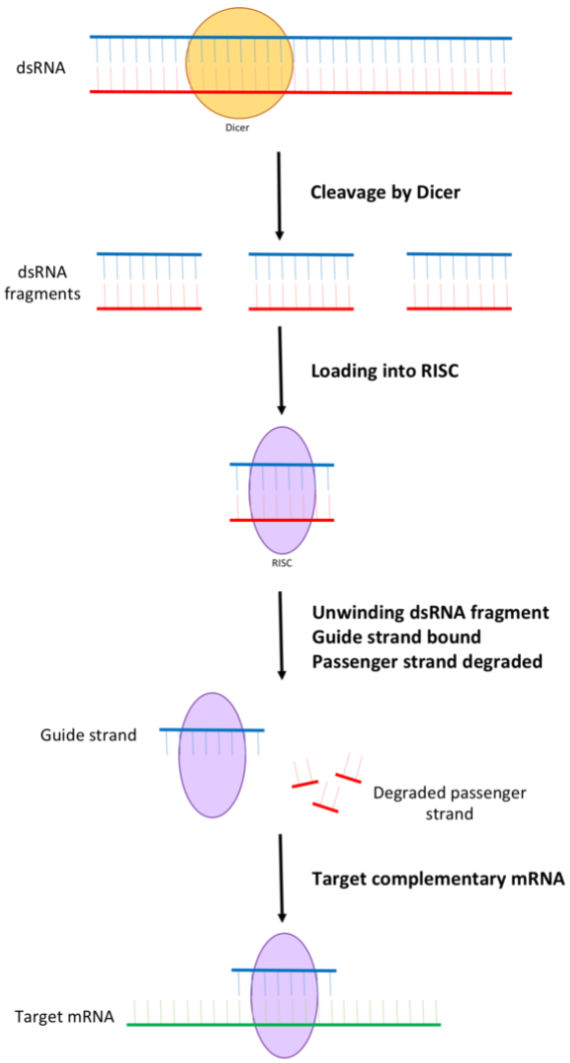
EXAMPLE: RNA processing, translation, and degradation can control gene expression



RNA Interference

- Various types of regulatory RNAs can control gene expression
  - □ **Small interfering RNA (siRNA)** is one form of RNA mediated inhibition evolved to protect cells from viruses
    1. siRNAs are double stranded RNA that enter cells via foreign objects
    2. The enzyme **dicer** cleaves siRNAs into small fragments
    3. The **RNA induced silencing complex (RISC)** binds these fragments and degrades one strand
    4. The single stranded siRNA can bind to a complementary mRNA – which is then degraded by RISC
       - **Argonaute** is the catalytic component of RISC that cleaves the mRNA

EXAMPLE: siRNA mediated mRNA degradation

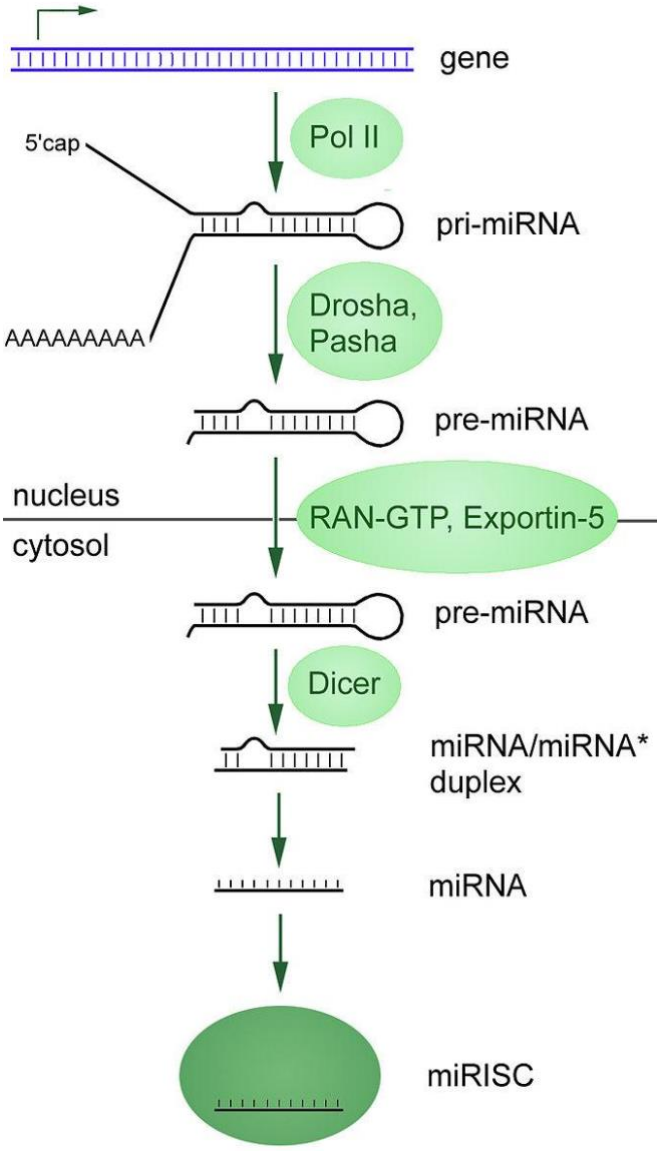


□ **Micro RNA (miRNA)** is a second form of RNA mediated inhibition that is encoded by the genome

1. miRNAs are single stranded RNAs created through transcription (~22 nucleotides long)
2. After transcription, miRNAs form *hairpins* or loops based on complementary RNA sequences
3. **DROSHA** cleaves the loops and the free miRNA associates with RISC
4. The processed miRNA binds to a 3' UTR end of mRNA and inhibits expression via RISC degradation

- Each miRNA can regulated ~200 mRNAs

EXAMPLE: miRNA processing and complex formation with RISC



□ Other noncoding RNAs regulate gene expression

- **Piwi-interacting RNA (piRNAs)** suppress movement of transposons

- **Long noncoding RNAs** are 200+ nucleotides in length and regulate gene expression

Protein Regulation

● Regulation of mRNA after transcription is a major method of controlling gene expression

□ Protein modifications can inhibit or activate protein _____

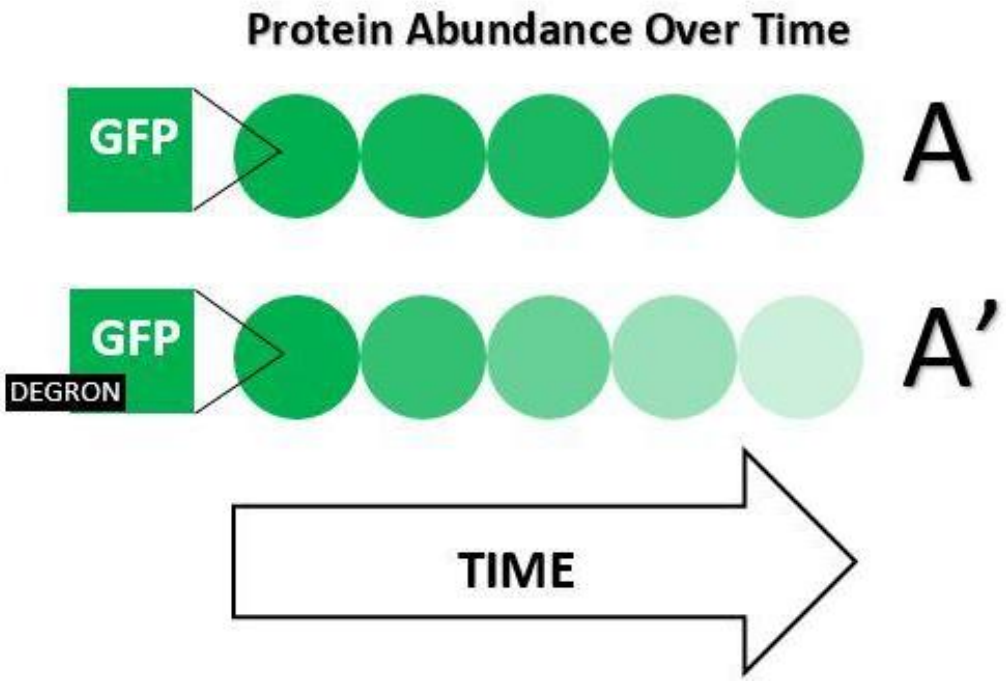
- Examples include: Protein phosphorylation, dephosphorylation and cleavage

□ Protein degradation controls a proteins function

- Ubiquitin labeling - proteasome destruction and lysosomal destruction

- **Degrons** are protein regions that control a protein's destruction

EXAMPLE: Presence of degron reduces protein presence over time



PRACTICE

1. Choose all of the following post-transcriptional regulators of gene expression.

a. Micro RNAs

b. siRNAs

c. RNA Polymerase Degradation

d. Exosomes

2. True or False: When the siRNA interacts with RISC for the first time it is single stranded.

a. True

b. False

3. What is the name of the enzyme that cleaves the miRNA in the nucleus before it travels to the cytoplasm to exert its effects?

a. RISC
b. Argonaut
c. DROSHA
d. RNA Polymerase

4. What is the name of the region on a protein that controls its degradation over time?

a. Degradation sequences
b. Ubiquitin
c. Ubiquitin binding site
d. Degron

5. True or False: All non-coding RNAs are responsible for regulating gene expression.

a. True

b. False