Lecture 29:

Regulation of gene expression

IV. Eukaryotes (part 3)

Course 371

Lessons for life

AIMS

• Understand alternative ways of regulation of gene expression not related to transcription.

• Understand how alternative splicing regulates what exons get expressed and how this contribute to the variation in protein product in different cell types.

• Understand in general the regulation of gene expression by RNA interference.

Post-transcriptional regulation

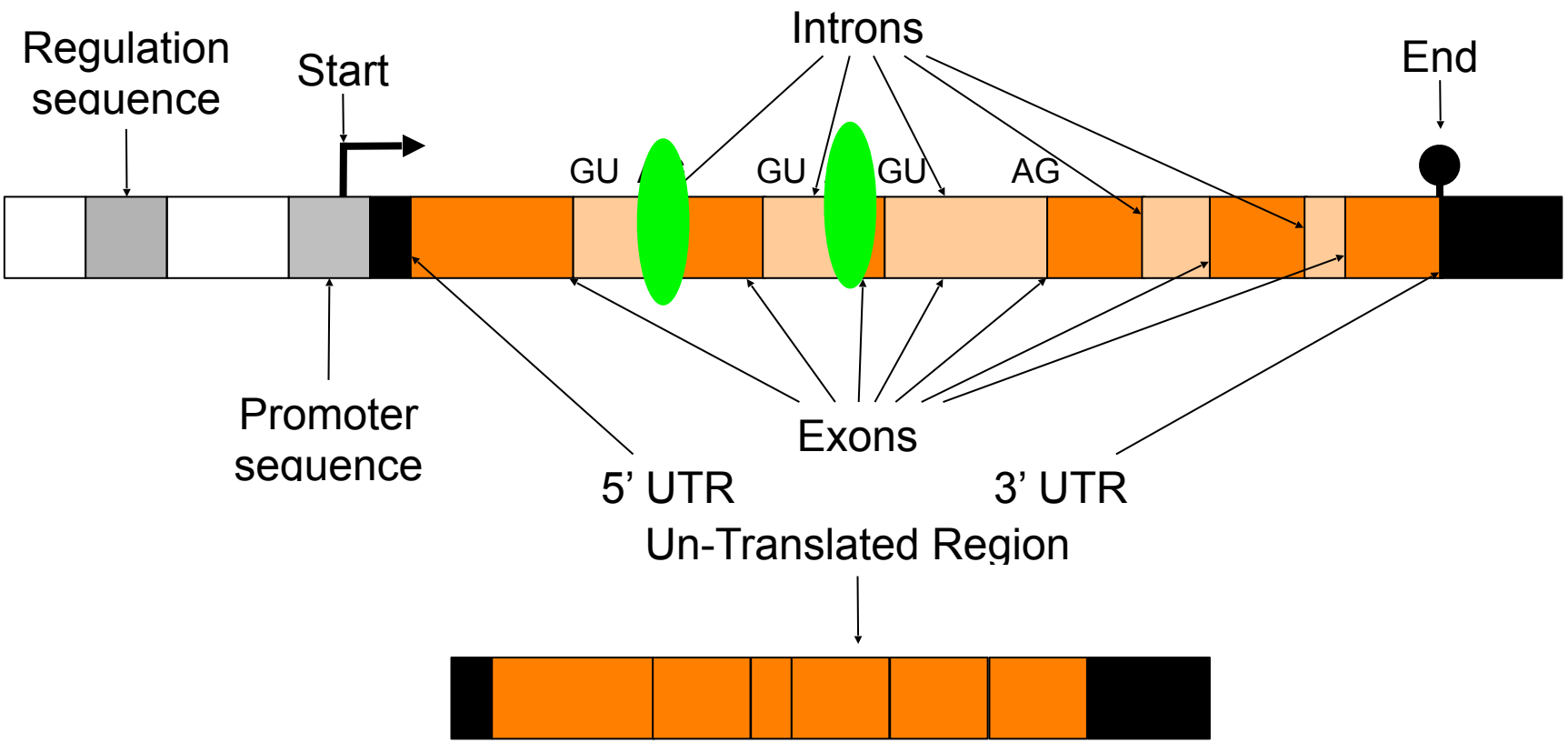
• Gene expression can occur **after** (post transcription) the transcription is completed.

• Regulation post transcription occurs less often than transcriptional control.

• There are many ways for the regulation of gene expression after transcription. We will focus on two ways:

- Regulation of alternative splicing
- RNA interference.

Post-transcriptional control – alternative splicing



mRNA with all exons included and introns are spliced

Post-transcriptional control – alternative splicing

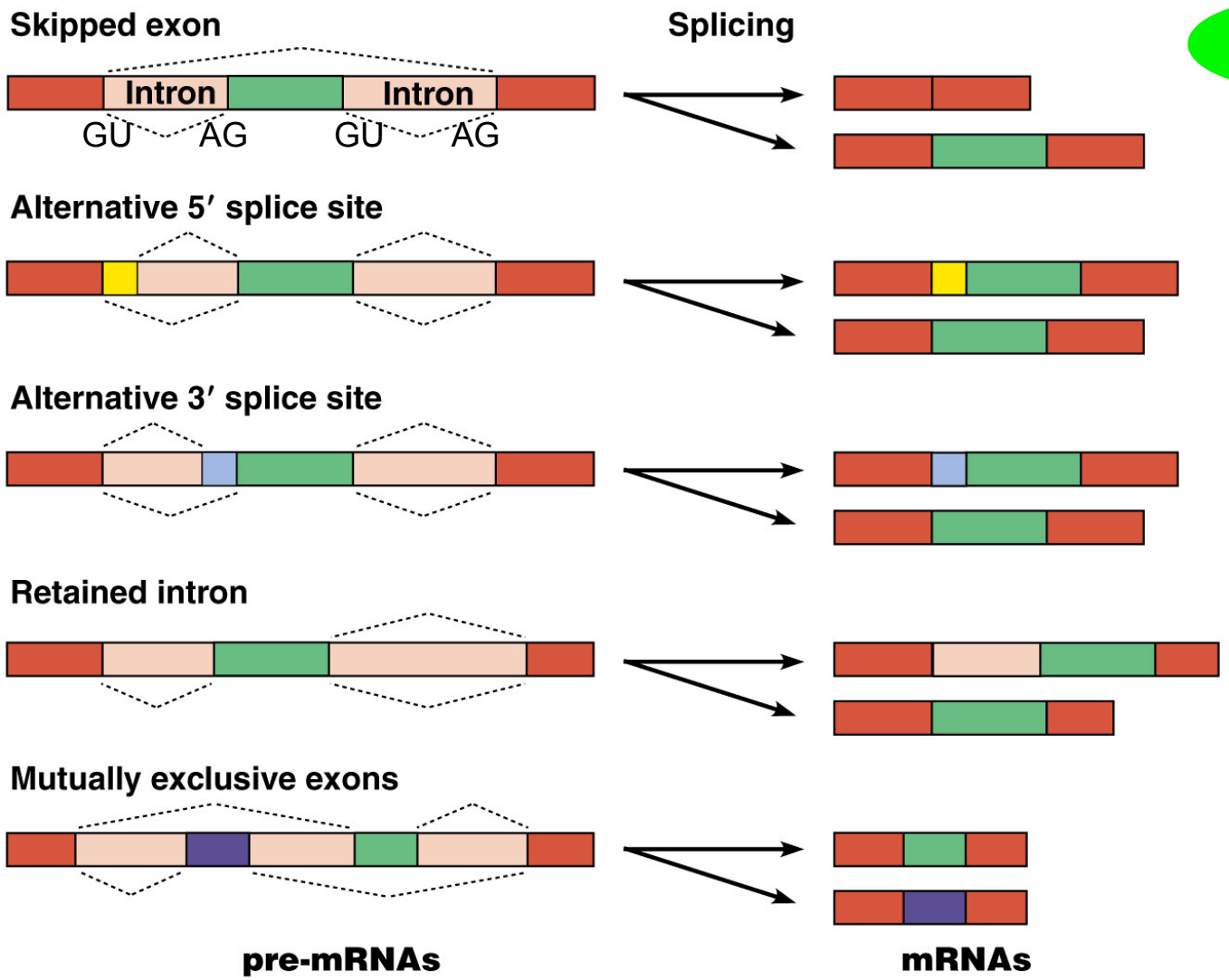
Can the resulting mRNA contain different exons in different cell types?

Post-transcriptional control – alternative splicing

Where does splicing take place?

Post-transcriptional control – alternative splicing

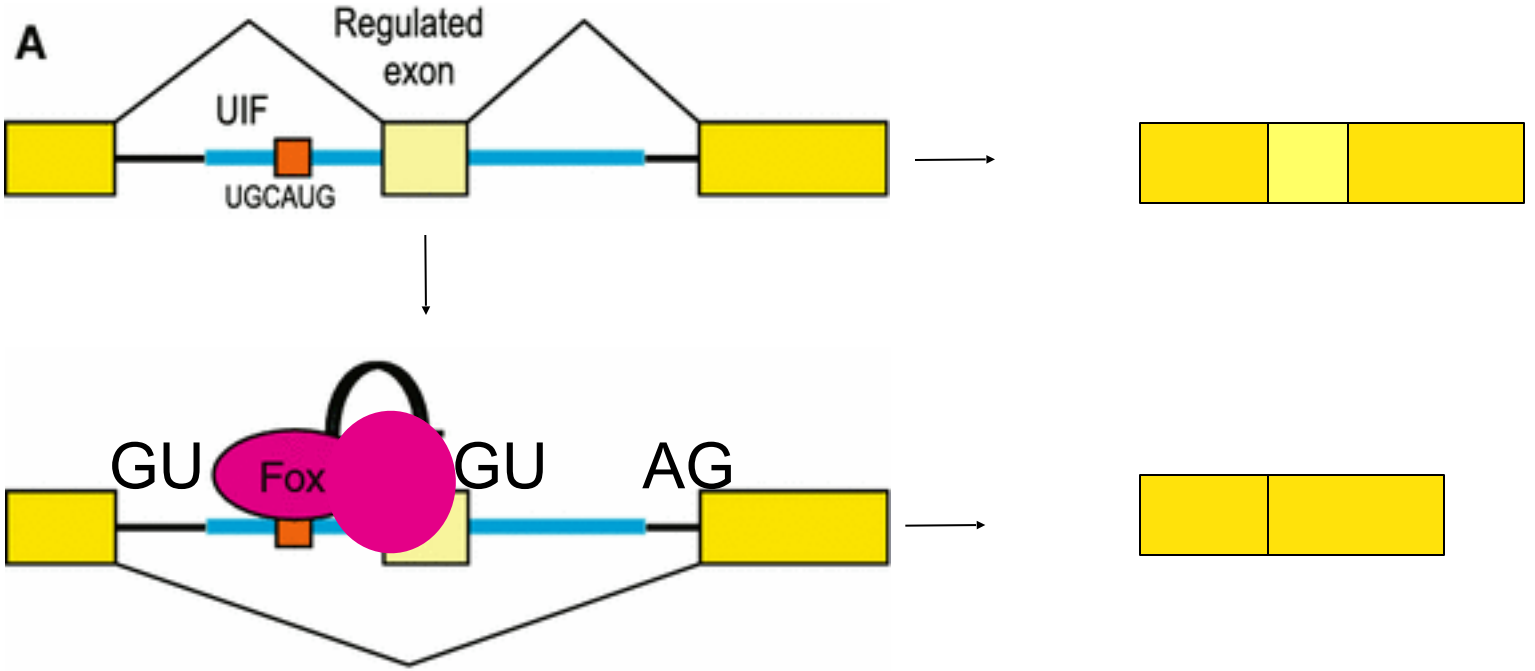
Various ways to obtain different transcripts



Post-transcriptional control – alternative splicing

•An RNA motif is present in one of the introns where an RNA binding protein binds causes the **<u>exclusion</u>** of one of the exons (repressor of splicing).

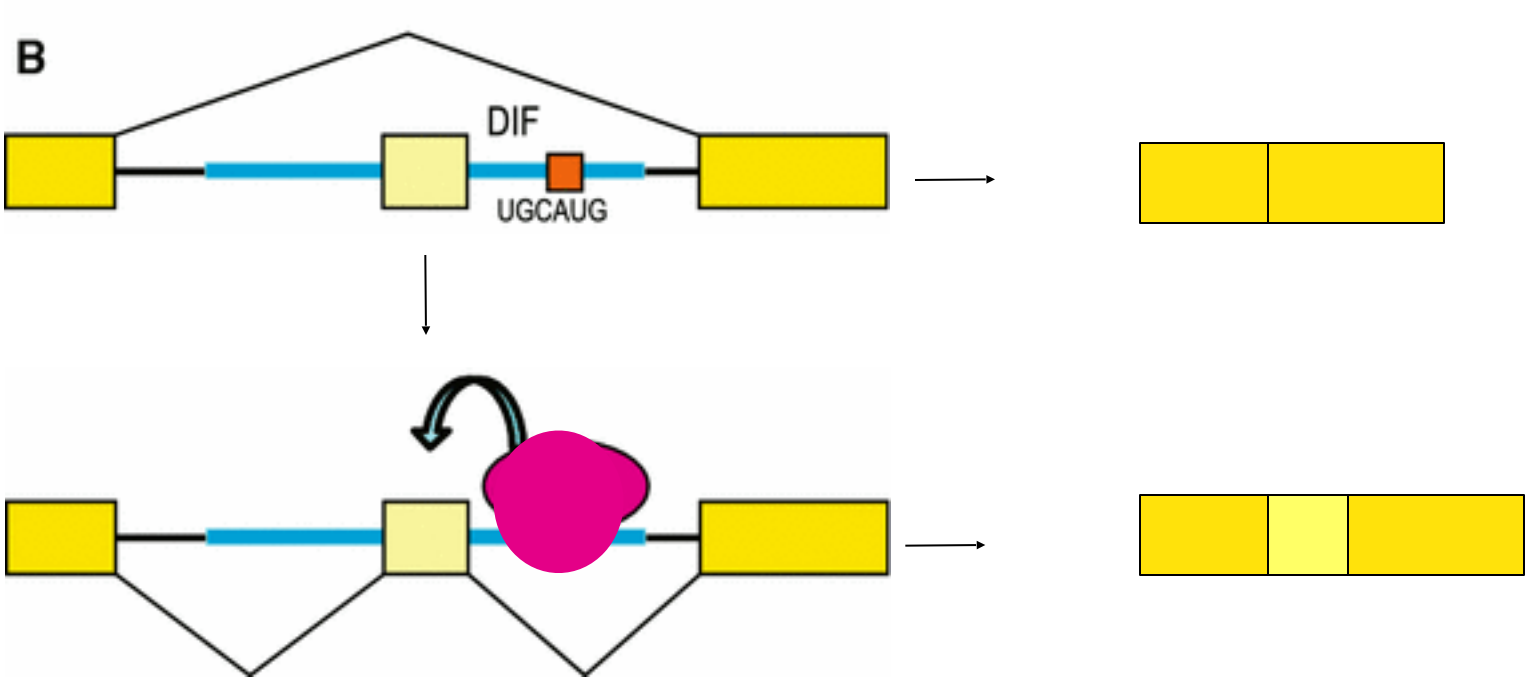
•**Repressing the splicing of an exons by <u>splicing inhibitor</u> factor.**



Post-transcriptional control – alternative splicing

•An RNA motif is present in one of the introns where an RNA binding protein binds causes the **<u>inclusion</u>** of one of the exons (repressor of splicing).

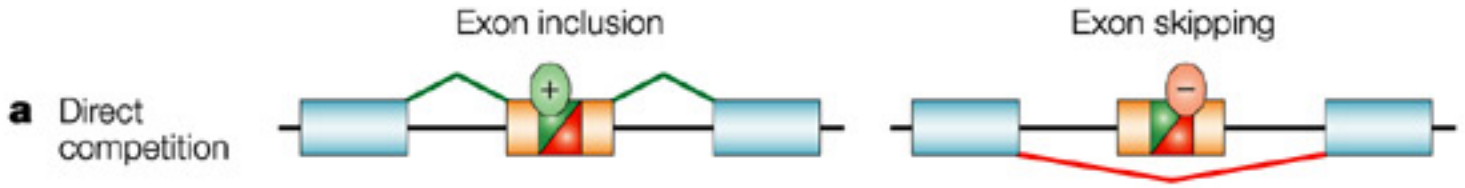
•**Activating the splicing of an exons by splicing <u>stimulator</u> factor.**



Post-transcriptional control – alternative splicing

• Splicing inhibitor and stimulator factors can compete for the same binding site.

Where do splicing inhibitors and regulators come from?



Post-transcriptional control – RNA interference

- **RNA interference**: is silencing gene expression using small RNA molecules.
- **Gene silencing**: preventing the expression of genes.
- If we consider expressing a gene is talking, gene silencing is asking the cell not to say a word.

Post-transcriptional control – RNA interference

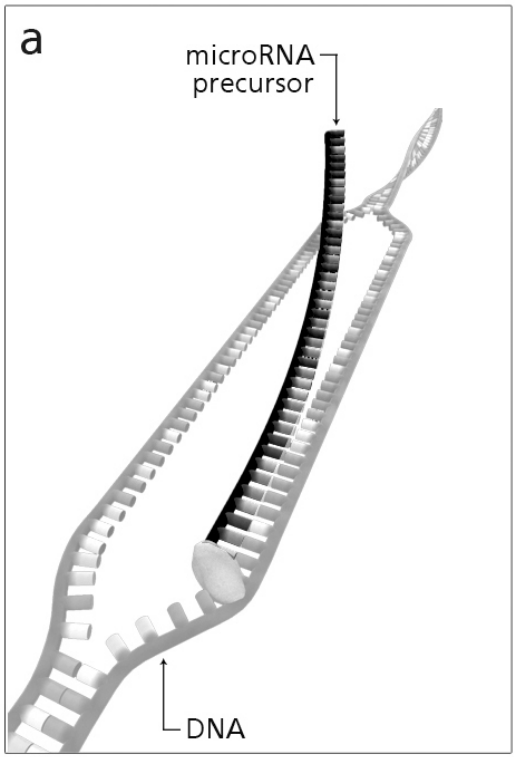
- Gene silencing by RNA interference is achieved by:
  - Using microRNAs (miRNAs)
  - Using short interfering RNAs (siRNAs)

Where do miRNAs and siRNAs come from?

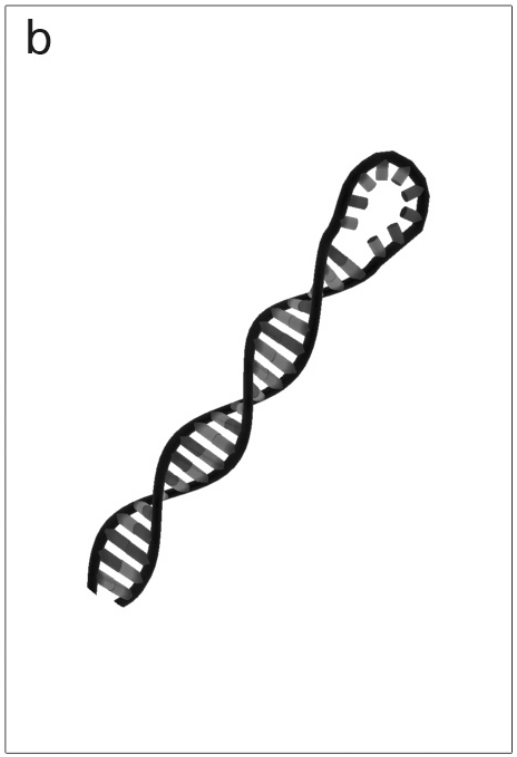
Post-transcriptional control – RNA interference

- miRNA and siRNA are represented by **noncoding genes**.
- **What are noncoding genes?**
- miRNA genes get transcribed into a linear RNA in the nucleus.
- Linear RNA of microRNA folds to make double stranded RNA (dsRNA).
- miRNA then is processed in the nucleus into small molecules.

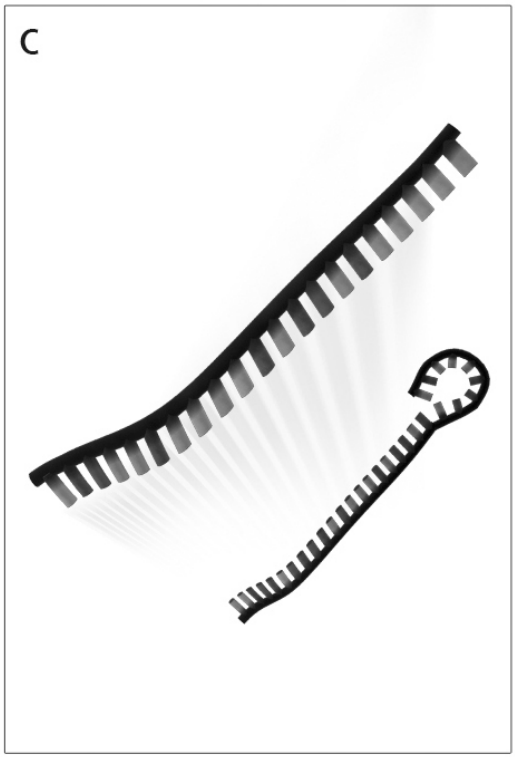
Post-transcriptional control – RNA interference



MicroRNA Precursor
Transcribed from DNA



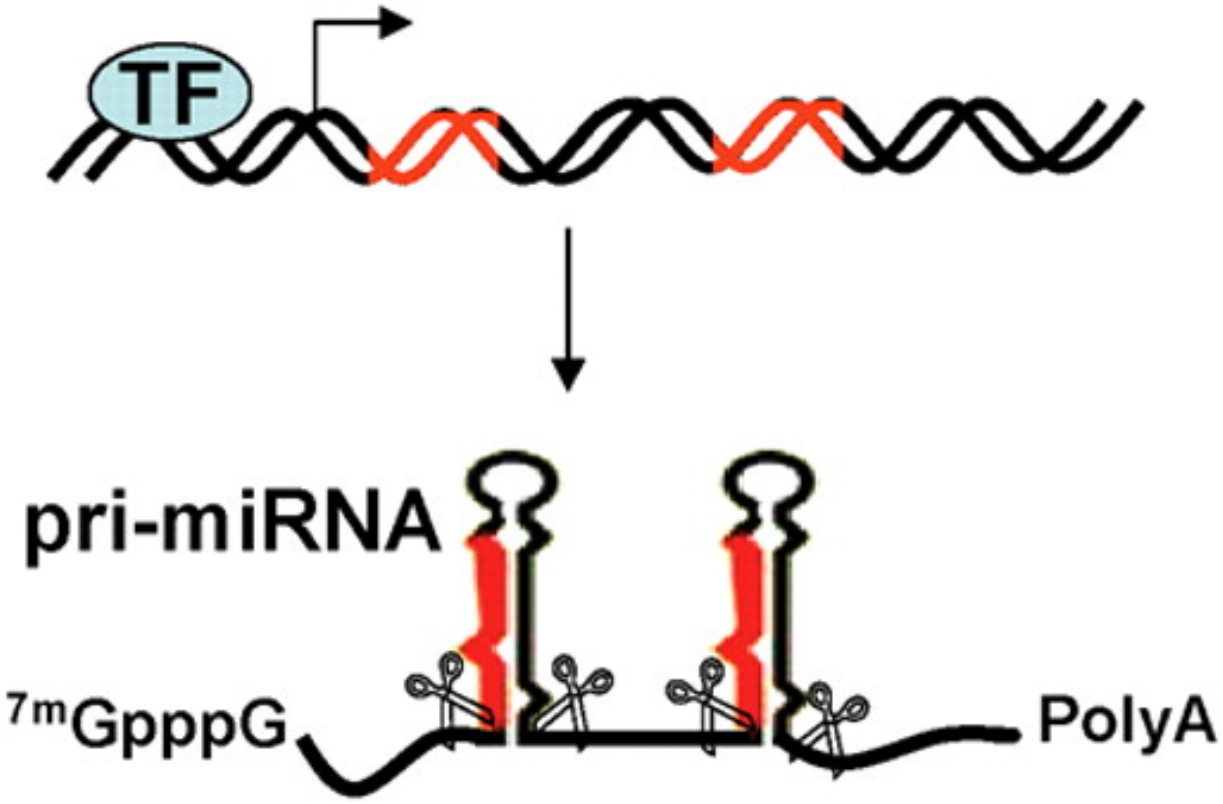
Hairpin Shaped Precursor



MicroRNA is Cut Out
from the Hairpin

Post-transcriptional control – RNA interference

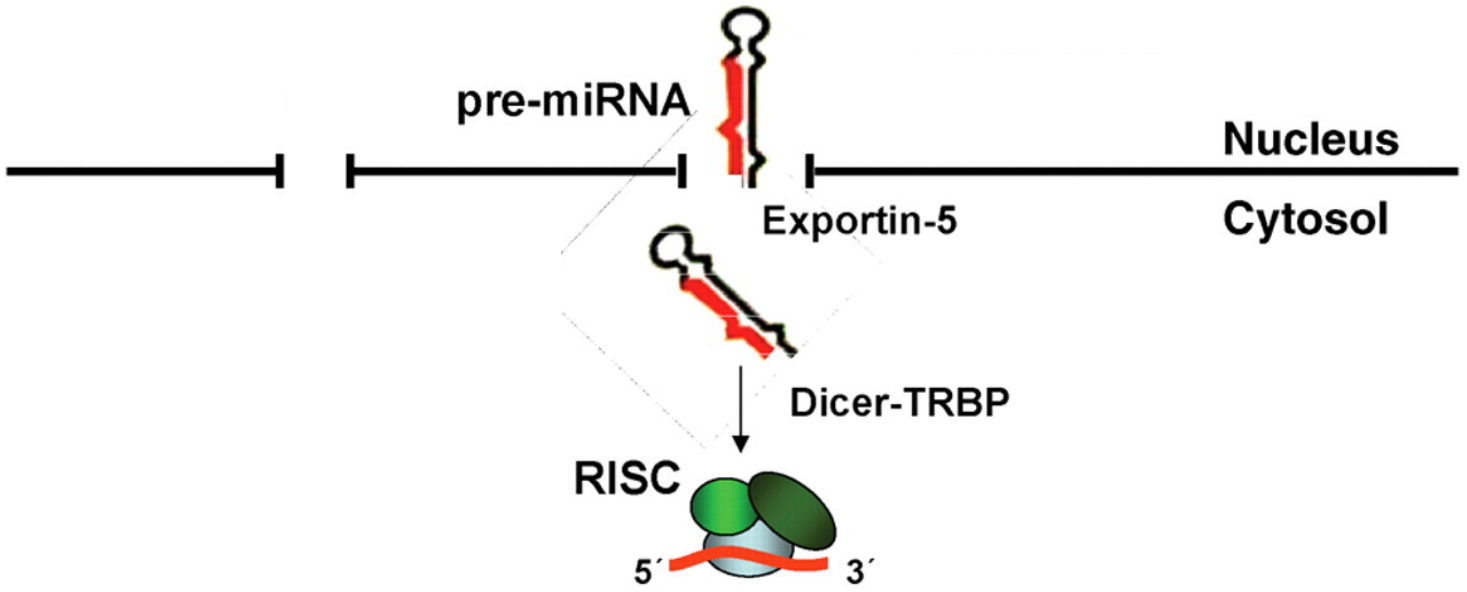
- The mRNA of miRNA gets cut into fragments using specific RNA nucleases.
- This takes place in the nucleus.



Post-transcriptional control – RNA interference

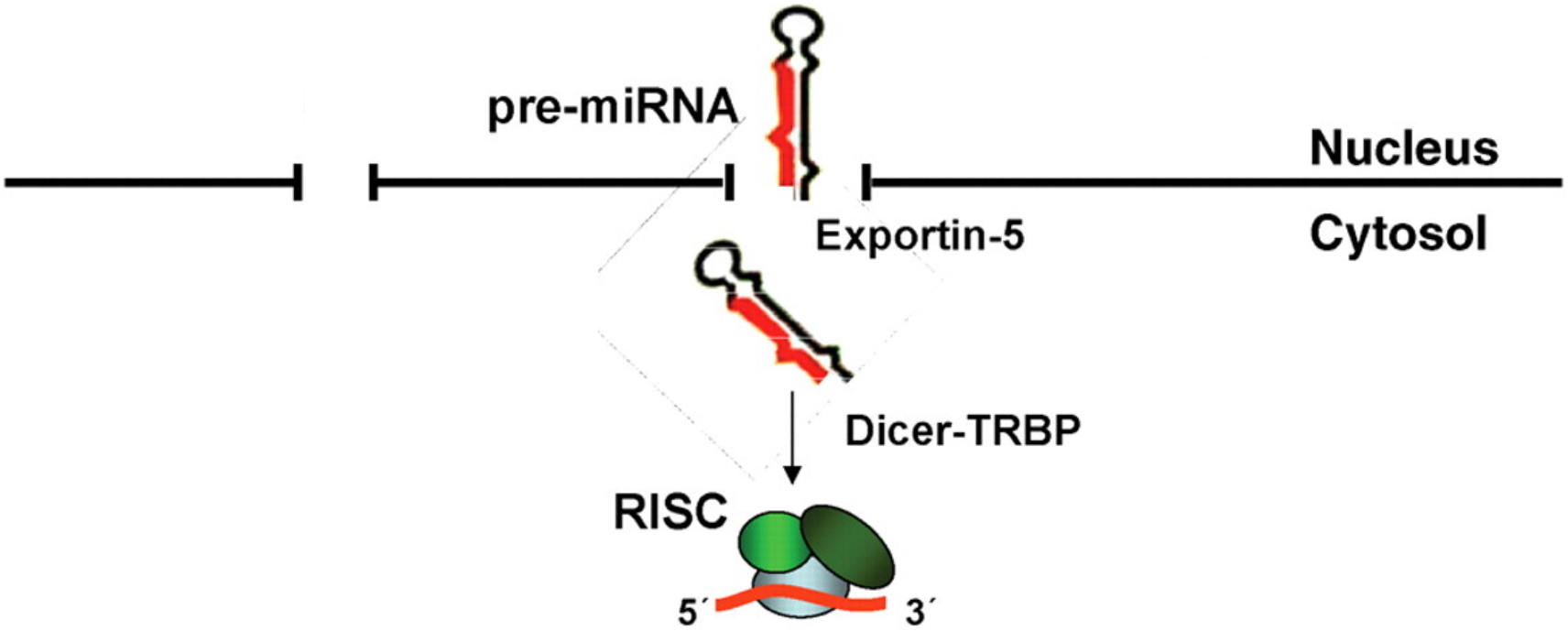
- Double stranded miRNA gets exported to the cytoplasm.
- **Why?**

- Double stranded miRNA gets processed into a single stranded miRNA in the cytoplasm.



Post-transcriptional control – RNA interference

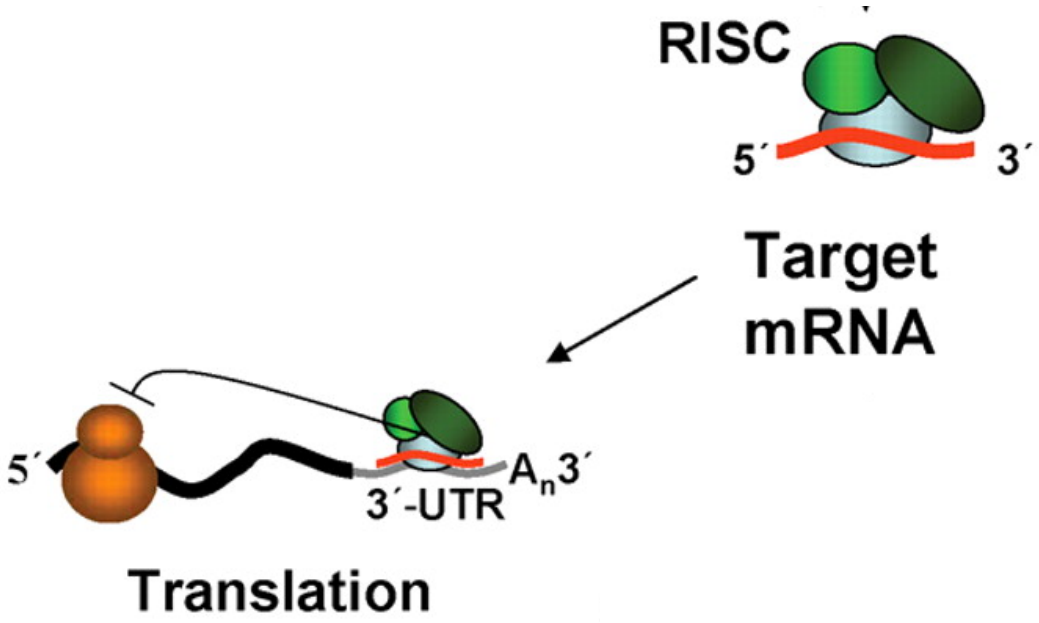
- Single stranded miRNA binds to a protein complex to form the machinery of RNA interference.



Where does RNA interference take place?

How does the miRNA + proteins regulate gene expression?

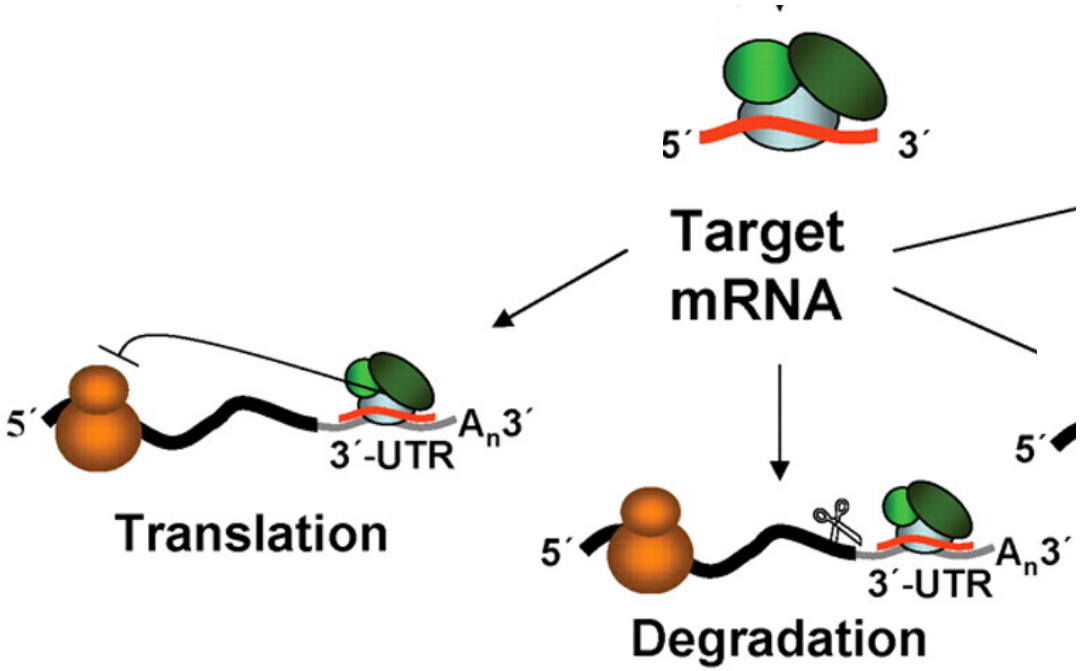
1.**The inhibition of translation of targeted mRNA:** miRNA + proteins binds to the 3' UTR of a mRNA of a gene and inhibits the translation.



2. **Signaling the degradation of mRNA:**

- miRNA + proteins binds to the 3' UTR of a mRNA of a gene and cleave the mRNA.

- Cutting the mRNA sends a signal for its degradation.

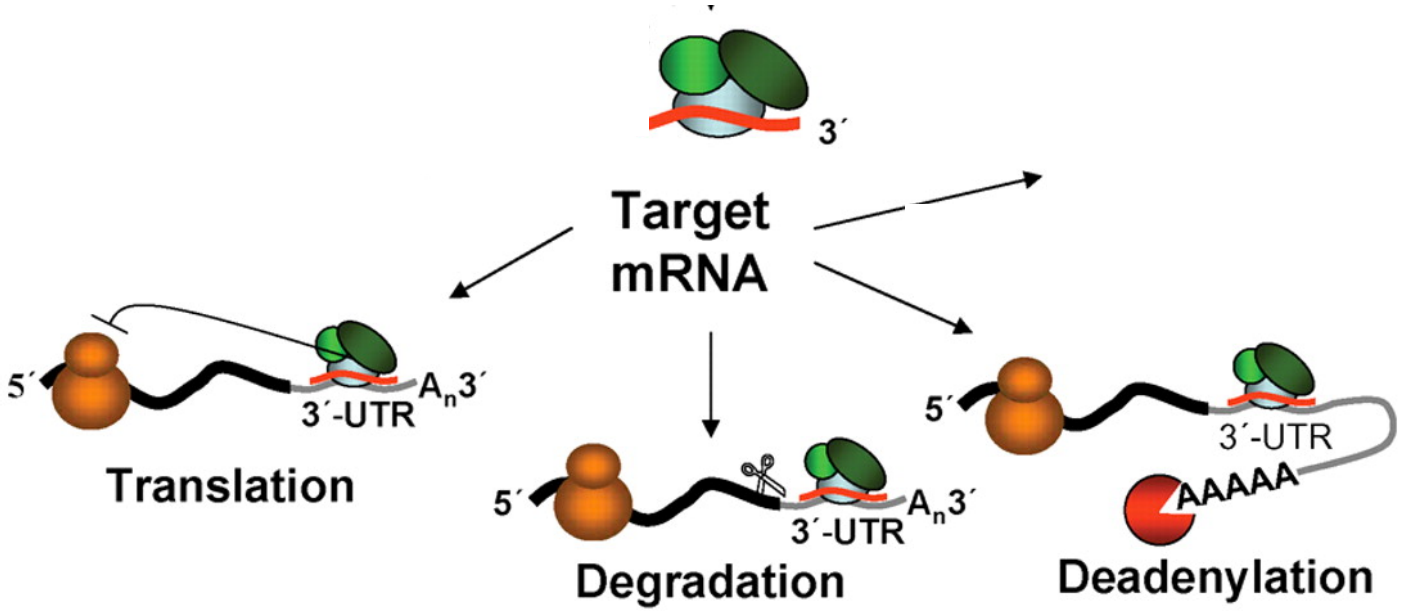


Posttranscriptional control – RNA interference

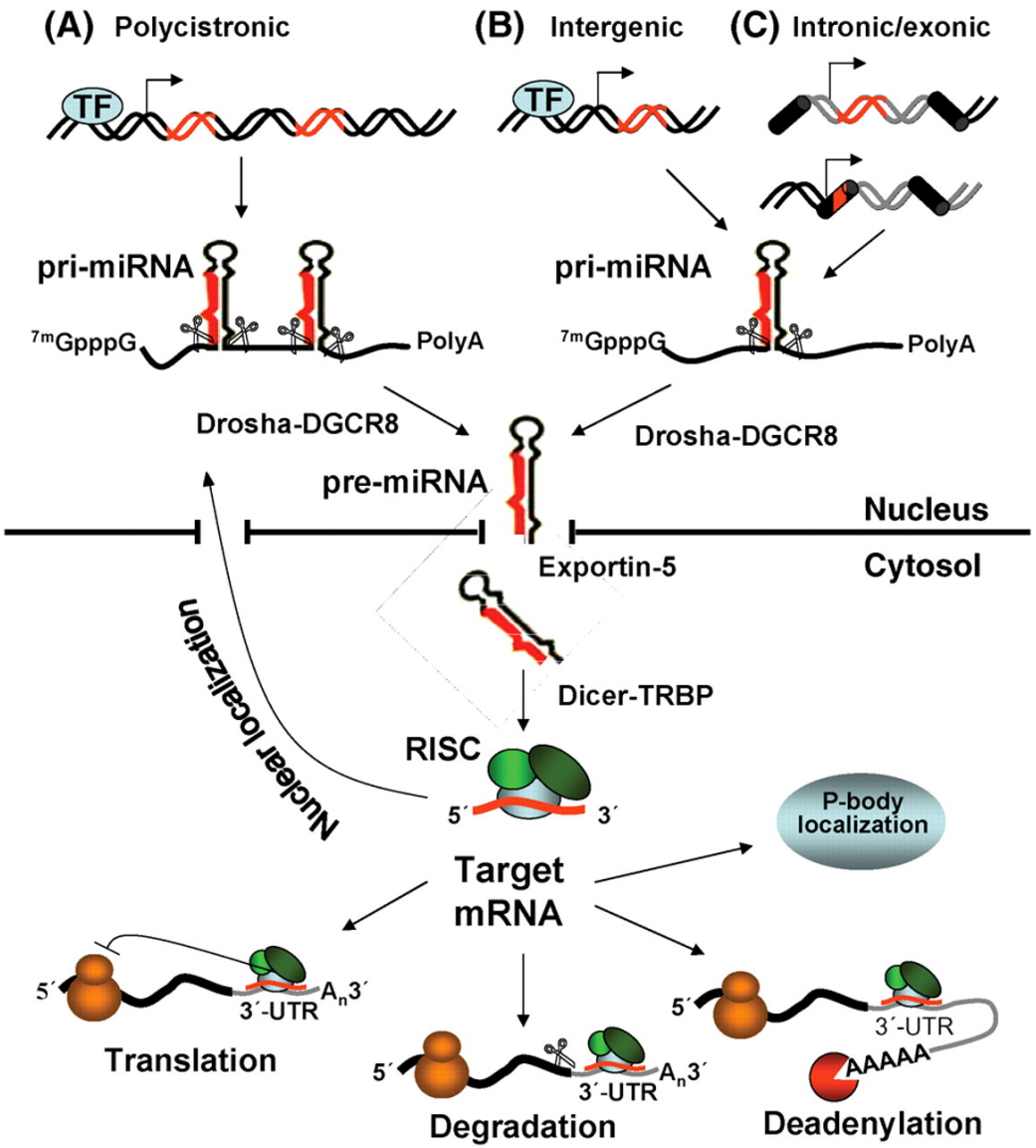
3. **Signaling the removal of the polyA tail:**

- miRNA + proteins binds to the 3' UTR of a mRNA of a gene and recruits exonucleases to remove the polyA tail.

- Removing the polyA tail may lead to the degradation of mRNA or inhibit translation.

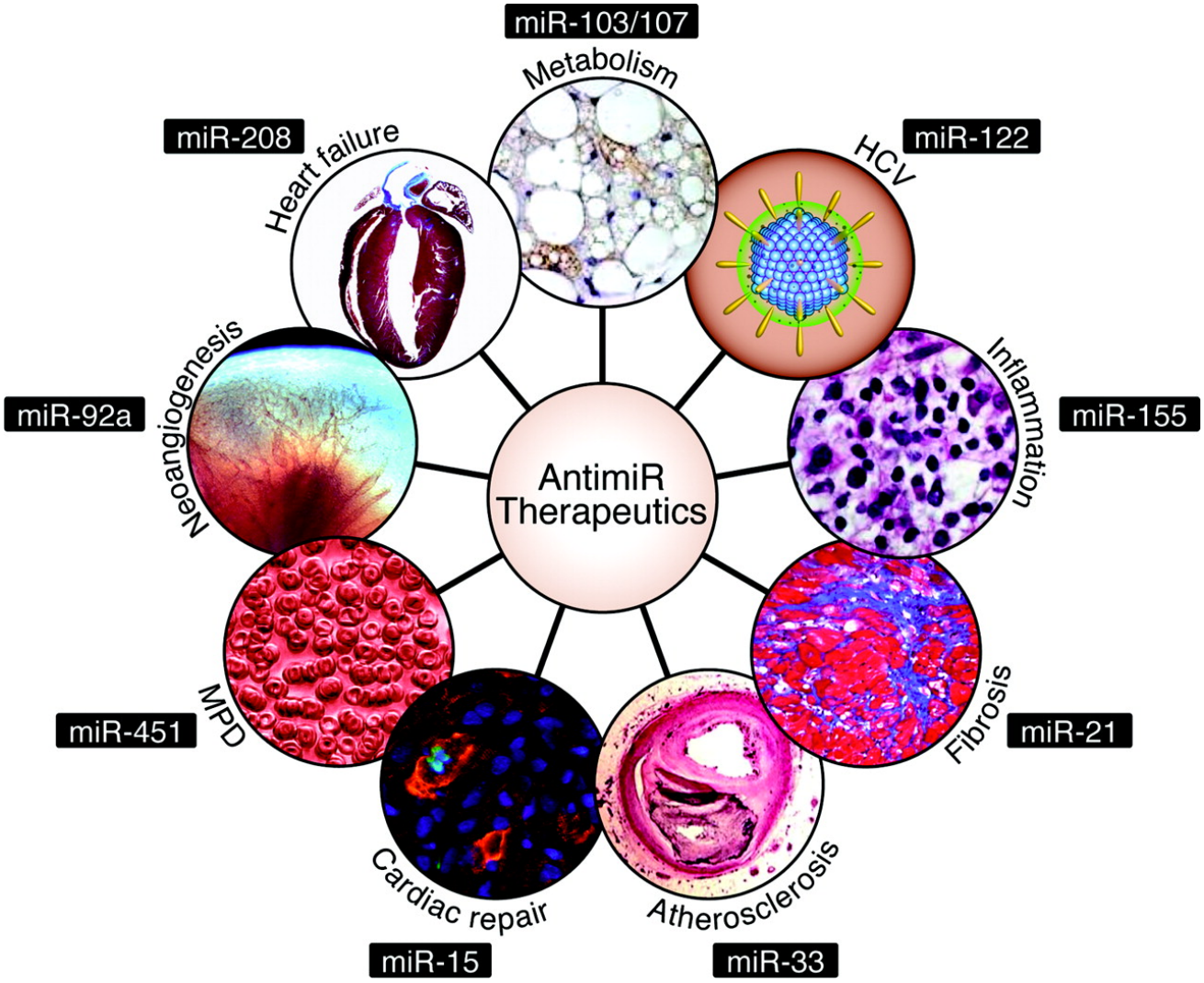


Post-transcriptional control – RNA interference



Post-transcriptional control – RNA interference

RNA interference can be used for gene therapy



To know

MicroRNA

Alternative 3’ splice site

Exon skipping

miRNA

Alternative splicing

Splicing inhibitor factor

Gene silencing

Short interfering RNA

Splicing stimulator factor

siRNA

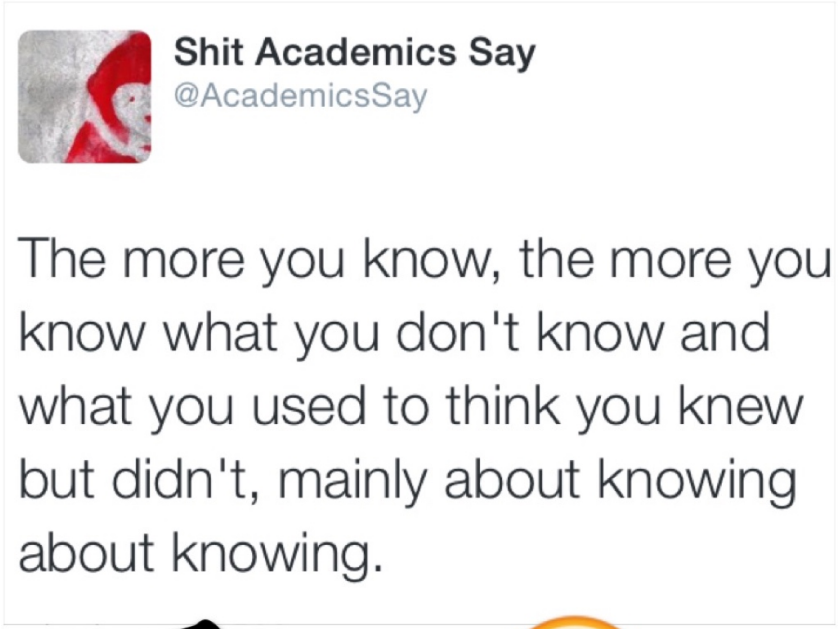
RNA interference

Alternative 5’ splice site

Expectations

- You know how alternative splicing results in different patterns of gene expression.
- You know where in the eukaryotic cell alternative splicing takes place.
- You know the process of RNA interference as a gene expression regulation mechanism.
- You know where RNAi takes place in a eukaryotic cell.

For a smile


Shit Academics Say
@AcademicsSay
The more you know, the more you know what you don't know and what you used to think you knew but didn't, mainly about knowing about knowing.
True