



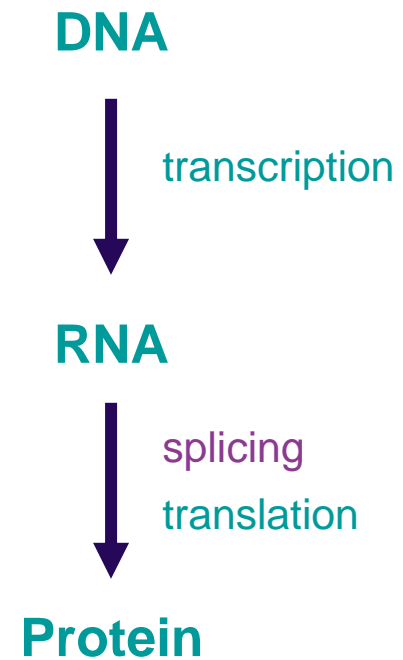
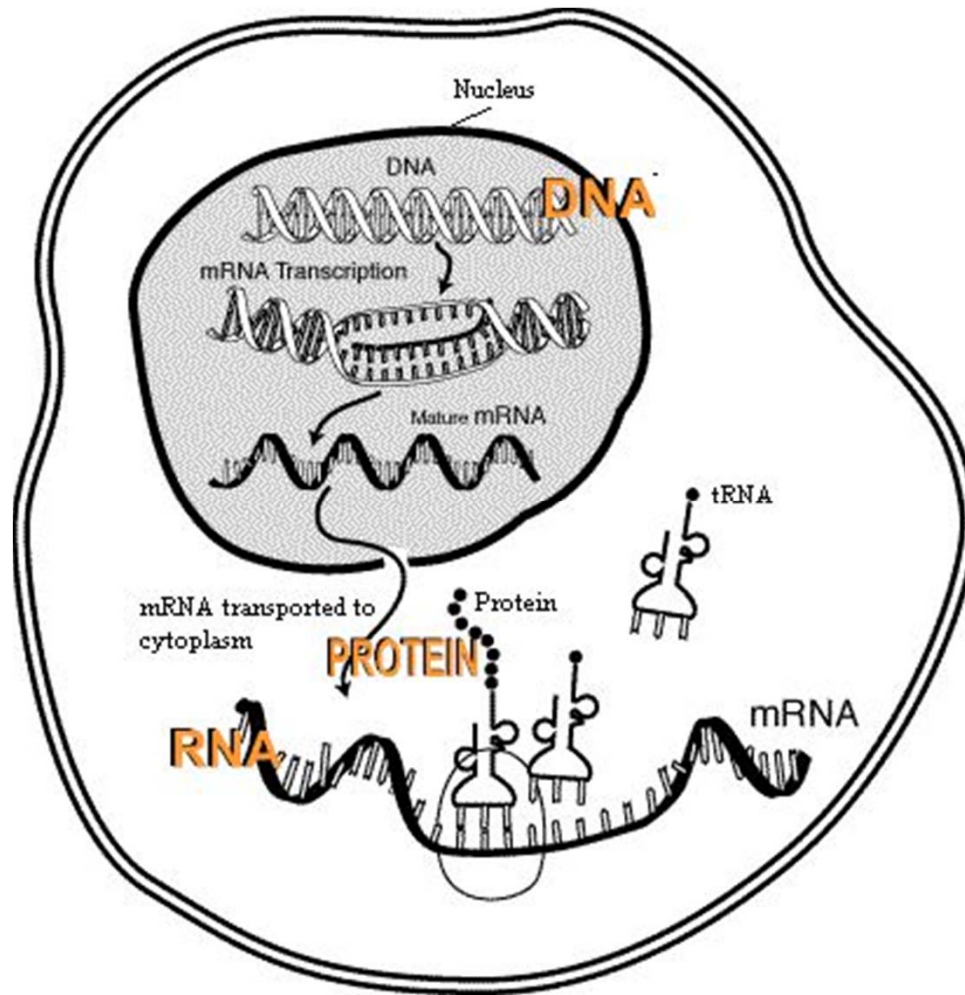
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## WHAT IS “SPLICING” AND WHY DOES IT MATTER FOR SMA?

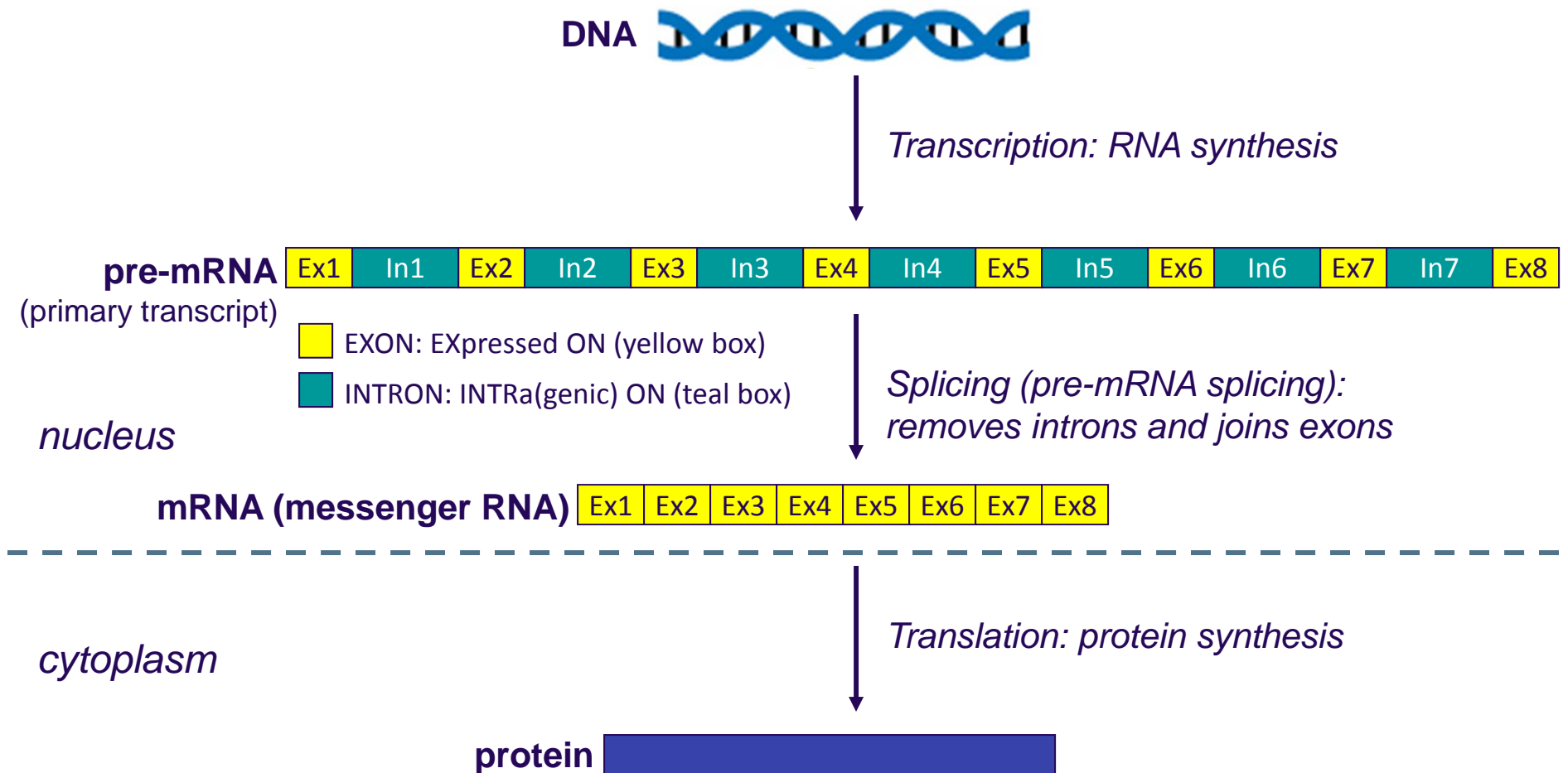


# RNA IS AN INTERMEDIATE STEP BETWEEN DNA AND PROTEIN

Diagram of a cell



# SPLICING IS THE PROCESS THAT REMOVES SEGMENTS (INTRONS) FROM PRIMARY RNA TRANSCRIPTS



# THE MAJORITY OF PRE-MRNAS ARE PROCESSED BY SPLICING

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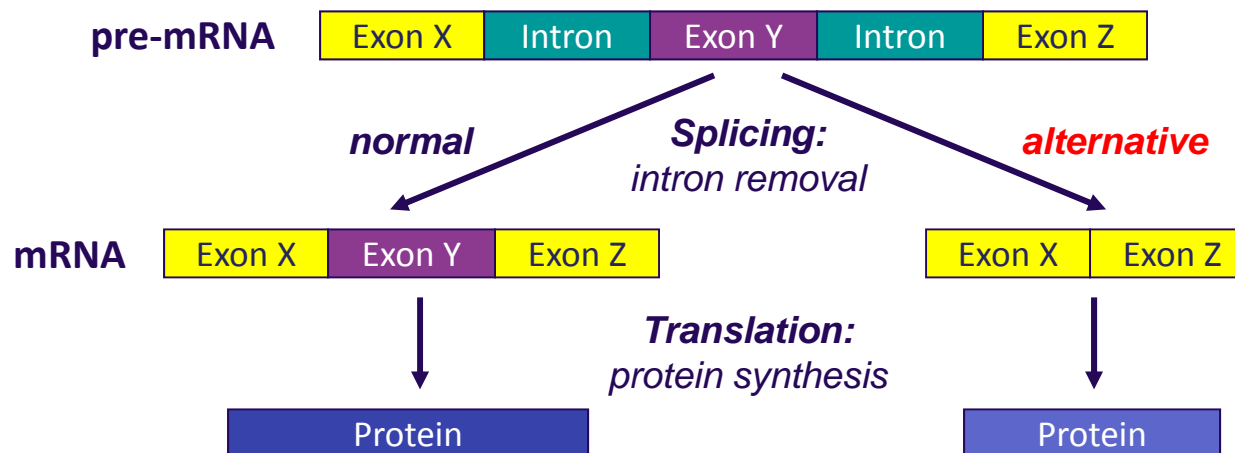
- Splicing\* is carried out by the spliceosome
- The spliceosome recognizes specific sequences in pre-mRNA
  - If the recognition sequences are mutated, it could result in expression of abnormal proteins
- Splicing is a complex and energy consuming process
- Why do we need splicing?
  - Provides a mechanism for generating different proteins from one pre-mRNA (alternative splicing - see next slide)

*\*Splicing and pre-mRNA splicing are the same; the terms are used interchangeably*



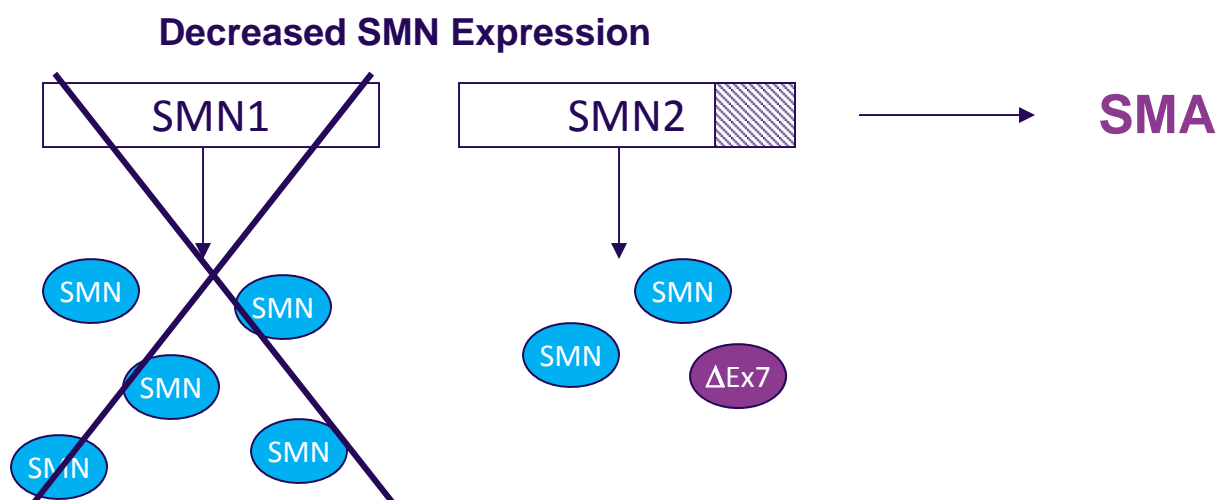
# ALTERNATIVE SPLICING

- Alternative splicing is the process by which a single primary transcript (pre-mRNA) yields different mRNAs
  - Different mRNAs are translated into different proteins
- Nearly all genes are alternatively spliced
- Significance:
  - Protein variants produced by alternative splicing can have diverse properties and functions
  - Fewer genes can produce more proteins, making the genome more efficient
  - Provides fine tuning for gene expression
- An essential aspect of normal biology

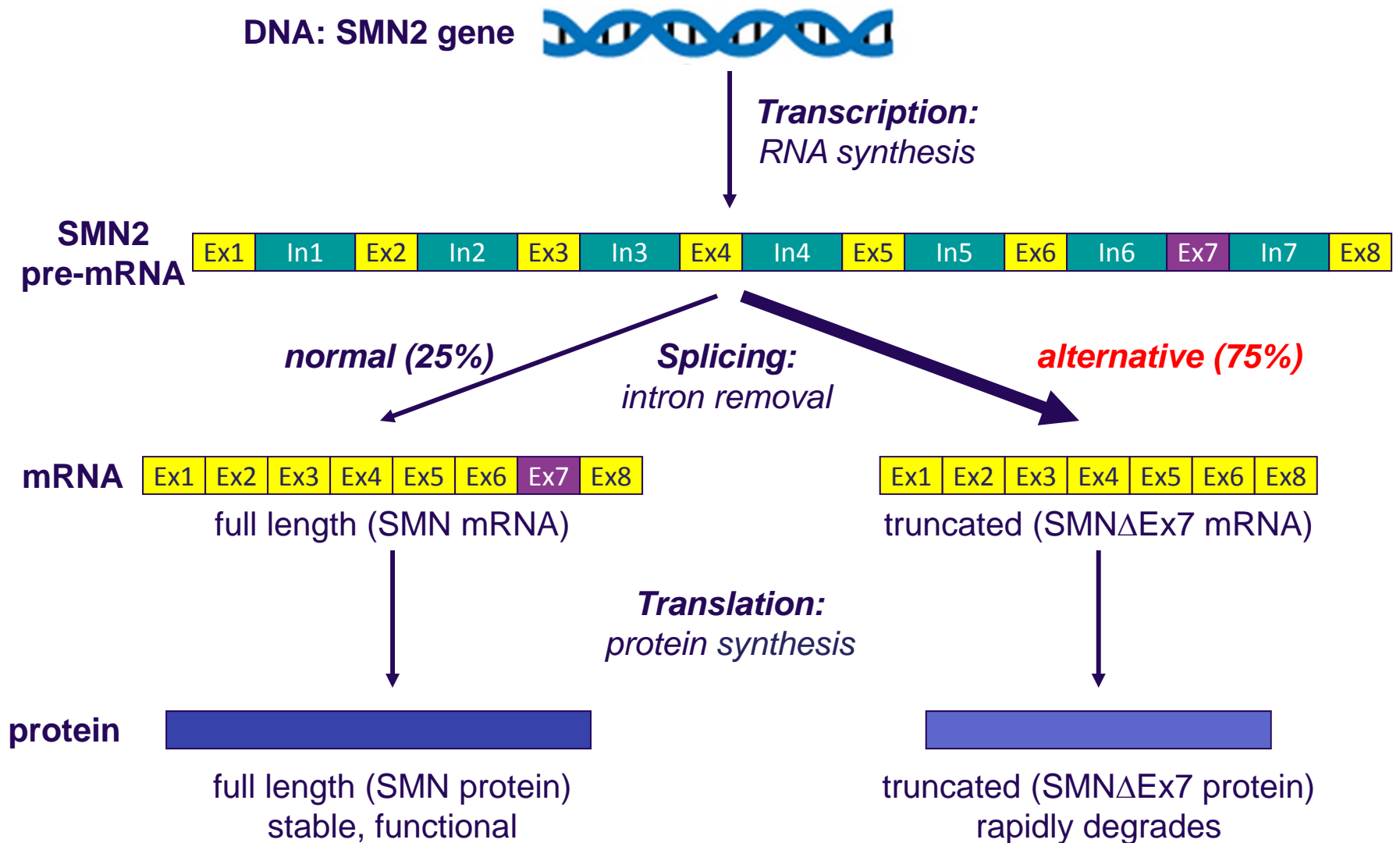


# ALTERNATIVE SPLICING PLAYS AN IMPORTANT ROLE IN SMA

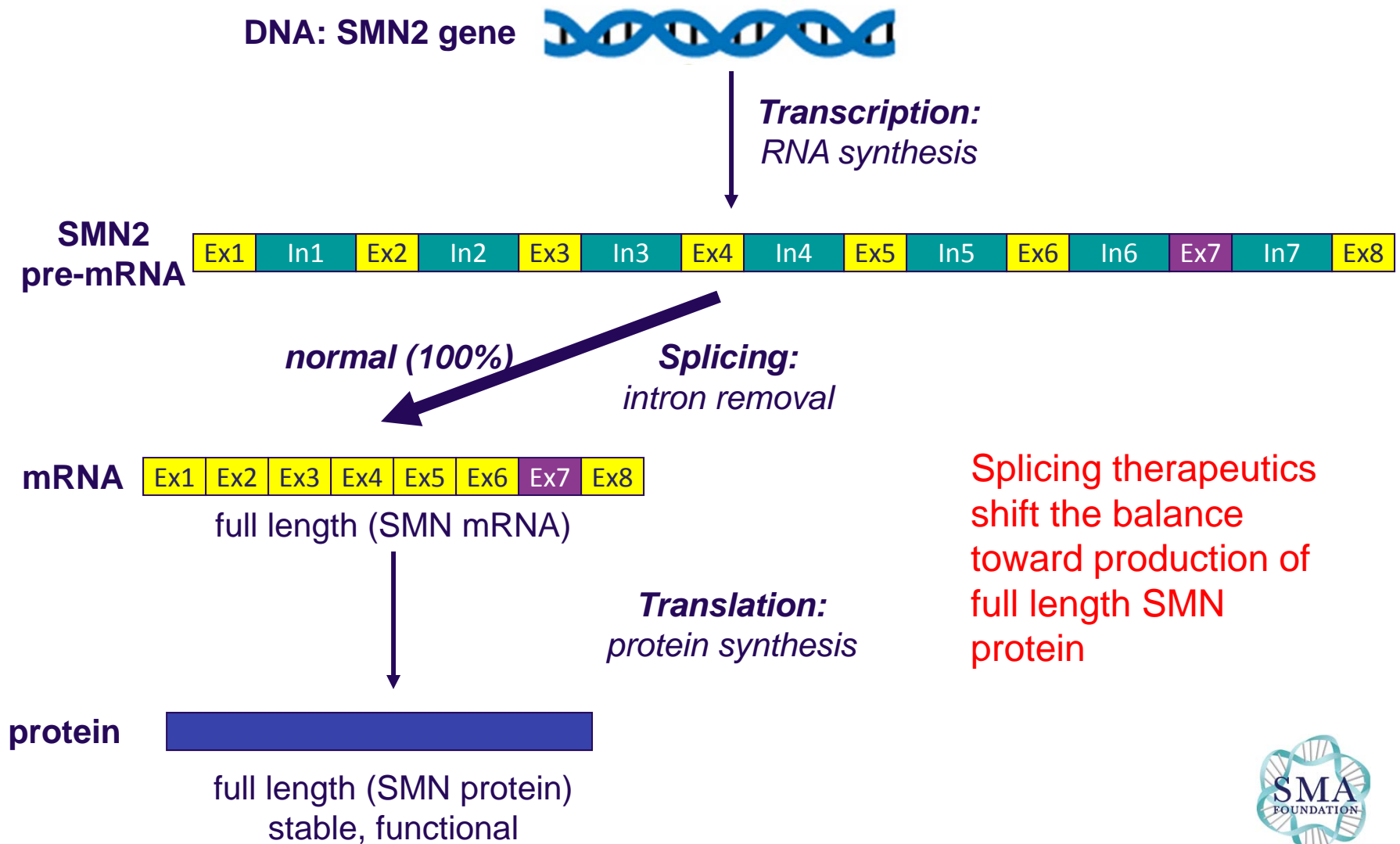
- Mutations or deletions in the SMN1 gene lead to low levels of SMN protein and cause SMA
- There is a “backup” version of the SMN1 gene called SMN2
  - SMN1 and SMN2 genes are >99% identical
  - Nearly all SMN1 mRNA is translated into normal, full-length SMN protein
  - SMN2 is alternatively spliced and makes two proteins
    - Low levels of normal, full-length SMN protein
    - An unstable, truncated protein called SMN $\Delta$ Ex7



# ALTERNATIVE SPLICING OF SMN2 PRODUCES MOSTLY AN UNSTABLE, LESS FUNCTIONAL VERSION OF SMN



# “SPLICING” THERAPEUTIC APPROACHES FOR SMA AIM TO CHANGE THE ALTERNATIVE SPLICING OF SMN2





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TO LEARN MORE ABOUT SPLICING AND ITS ROLE IN SMA,  
PLEASE VISIT [www.learnaboutsma.org/science/](http://www.learnaboutsma.org/science/)

