

Splicing

Overview: Post-transcriptional Modifications

Transcription is a process where a DNA template strand is used to guide the creation of an mRNA transcript that is complementary and antiparallel. In eukaryotes, this mRNA strand is called pre-mRNA because it is the precursor to what will be used for translation. The pre-mRNA contains both exons and introns and lacks a cap and tail.

Post-transcriptional modifications are the changes that turn this piece of RNA into a usable strand for translation. A guanine cap is placed on the 5' end and a poly-A tail is placed on the 3' end. Introns also must be spliced out before the mRNA is used for translation. Only after the mRNA has undergone splicing and a cap and tail are added can it be used. This new mRNA that is used for translation is called a mature mRNA transcript.

Splicing:

Splicing is the process of removing parts of the mRNA. Introns cannot be used for translation, so they must be cut out. Specific sequences in the mRNA act as indicators for where splicing should occur. Once the introns are cut out, then all of the exons are annealed together.

Alternative Splicing:

While splicing occurs for every eukaryotic mRNA transcript, not all transcripts undergo alternative splicing. Alternative splicing is a special type of splicing where all introns and some exons are cut out of an mRNA transcript. The remaining exons must be annealed in the same order they were originally in. The order of the remaining exons cannot be rearranged.

Below is an example of what this can look like. In this example, all introns are cut out and the exons named exon 2 and exon 3 were removed.

Pre-mRNA: 5' Intron 1 Exon 1 Intron 2 Exon 2 Intron 3 Exon 3 Intron 4 Exon 4 Intron 5 Exon 5 3'

Mature mRNA: 5' Guanine Cap Exon 1 Exon 4 Exon 5 AAA (Poly A tail) 3'

Alternative splicing allows for multiple different proteins to be produced from the same gene. Removing exons from an mRNA transcript produces a different sequence of bases. Because each three nucleotides in the mRNA codes for an amino acid to be recruited to the growing polypeptide, removing some exons from an mRNA transcript that is used in translation results in a different amino acid sequence. This change in amino acid sequence may result in a large change in protein folding and function in the body.

Learning Objectives:

- Understand and be able to explain what splicing and alternative splicing are.
- Know differences between splicing and alternative splicing.
- Identify if an mRNA transcript is immature or mature.
- Be able to make a mature mRNA transcript from an immature mRNA transcript.
- Be able to provide examples of mRNA transcripts that result from alternative splicing given pre-mRNA transcripts.
- Remember that splicing only occurs in eukaryotic organisms.

Order of Activities:

1. Review what splicing and alternative splicing are using your notes and then watch this video <https://youtu.be/xZwSmUNRBQQ>
2. Test yourself by completing the [corresponding worksheet for this material](#). Attempt to first complete this on your own, then pair up with a partner or group to discuss when possible. There is [an answer key provided](#) so you can check your work and read through all explanations for the questions. Any questions you get wrong or confused about you should attempt to explain why the answer is correct and then complete again after you finish the activities in this guide.
3. Watch the following video to review alternative splicing: <https://youtu.be/JhP3kHVmicw>
4. After reviewing any topic, it is a good idea to have a metacognition check. Ask yourself the following questions:
 - What are my emotional responses to learning this material? Which material am I frustrated with and need aid in understanding?
 - What difficulties have I had with the learning tasks? What specific tasks will I do to master this content?
 - Do I understand all of the learning goals? Can I explain each of them out loud to someone clearly and concisely?
 - How is what I learned related to other things I have learned in this class? How is it related to other classes, my career, and my life?
5. If you would like to have more aid in learning this material, please reach out. There are numerous individuals who want to help you feel confident in your understanding. If your course has learning assistants or teaching assistant(s), you should reach out to them to review concepts you want to learn more about. Your professor is also a great resource to go to when you do not understand a topic. You can study with your peers or receive academic support through the LRC as well. If you would like help identifying how to receive the support you need, do not hesitate to contact the CU Denver Learning Resources Center at LRC@ucdenver.edu or stop by our front desk in the learning commons building.
6. Further learning opportunities:
 - Think about how splicing and alternative splicing are incorporated into the central dogma of biology. If needed, review what the central dogma is before continuing with the activity guide.
 - To learn more about splicing and its mechanism, you can view this video: <https://youtu.be/IJQv1H-2lol>
 - For more information about how splicing occurs, please read this article: <https://www.nature.com/scitable/topicpage/rna-splicing-introns-exons-and-spliceosome-12375/>