**SPLICING MATTERS**

*Titin*, which codes for a protein in muscle, is one example of a gene whose pre-mRNA transcript can be spliced in multiple ways to yield different protein isoforms. During development of the fetal heart, more exons are left in during splicing, which produces a relatively long, springy protein. In adult hearts, an RNA-binding protein called RBM20 associates with long stretches of the mRNA transcript during splicing, forcing the spliceosome to cut out those bits of DNA. The result is a relatively short, stiff protein. If RBM20 is missing or defective in adult hearts, these hearts will produce more fetal, springy *titin* protein relative to the stiff adult version. This is thought to reduce the capacity of the heart to contract, contributing to a condition known as dilated cardiomyopathy.

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**FETAL SPLICING SCENARIO**

1. **Transcription**
   - *RBM20*
2. **Splicing**
   - Alternative exons
3. **Translation**
   - Long, springy *titin* protein
4. **High ratio of fetal to adult *titin***
5. **Healthy fetal heart**

**ADULT SPLICING SCENARIO**

1. **Transcription**
2. **Splicing**
   - High levels of RBM20 force the splicing machinery to leave out a number of exons from the final *titin* mRNA transcript.
3. **Translation**
   - Short, stiff *titin* protein
4. **Low ratio of fetal to adult *titin***
5. **Healthy adult heart**

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A higher-than-normal proportion of fetal *titin* in an adult heart can contribute to a heart that’s too elastic, a condition called dilated cardiomyopathy.