INTRODUCTION:
Nonsense-mediated mRNA decay (NMD) is an RNA surveillance system that degrades aberrant isoforms containing a premature termination codon. This pathway is conserved throughout eukaryotes and protects against the production of harmful truncated proteins. Additionally, NMD coupled with alternative splicing is a mechanism of post-transcriptional gene regulation that affects the mRNA levels of hundreds of genes in human [1].

GOALS:
How are conserved are the targets of alternative splicing coupled with NMD? What features define a premature termination codon in different species?

APPRAOCH:
1. Control RNA on UPF1
2. NMD inhibition through knockdown of UPF1.
3. Directional and paired-end RNA-seq library preparation.
4. High throughput Illumina sequencing.
5. Transcript assembly and quantification with Cufflinks [5] or JunCbase [6].
6. Premature termination codon prediction.

REFERENCES:
1. Lewis BP, Green RE, Brenner SE. Evidence for the widespread coupling of alternative splicing and nonsense-mediated decay in humans. PNAS. 2003;100:189-192

The 50nt rule is a strong predictor of NMD in all three species while a longer 3’ UTR has a limited effect

SRSF5/B2 is an NMD target conserved between human and fly

CONCLUSIONS:
Thousands of alternatively spliced genes (>20%) produce transcripts that fall into our strict set of NMD targets in human.

Hundred of alternatively spliced genes (10-30%) produce transcripts possibly degraded by NMD in fly and zebrafish.

Splicing genes are significantly enriched in NMD targeted genes in human and in fly.

The 50nt rule is a strong predictor of NMD in human and also appears to have a role in fly and zebrafish.

3’ UTR length has little correlation with NMD in human, fly, and zebrafish.

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