

Supplemental Table S1. RNA Types: Coding and Non-Coding Overview

RNA Type	Length	Origin / Location	Primary Function	Category	Key Role
Messenger RNA (mRNA)	Variabl e (~500– 10,000 + nt)	Nucleus → cytoplasm	Encodes protein sequence	Coding	Template for protein synthesis at ribosomes
Precursor mRNA (pre-mRNA)	Variabl e	Nucleus	Intermediate for mRNA	Coding (precursor)	Contains introns; undergoes splicing, capping, and polyadenylation
Ribosomal RNA (rRNA)	Variabl e (~120– 5,000 nt)	Nucleolus	Protein synthesis	Housekeepin g ncRNA	Forms ribosomes; catalyzes peptide bond formation
Transfer RNA (tRNA)	~70–90 nt	Nucleus → cytoplasm	Amino acid transport & translation	Housekeepin g ncRNA	Delivers amino acids during translation
Small Nuclear RNA (snRNA)	~150 nt	Nucleus	Splicing and RNA regulation	Both (HK & Reg ncRNA)	Spliceosome component; modulates splicing
Small Nucleolar RNA (snoRNA)	~60– 400 nt	Nucleolus	RNA modification	Both (HK & Reg ncRNA)	Modifies rRNA, tRNA, snRNA; affects expression
RNase P RNA	~350– 400 nt	Nucleus	tRNA maturation	Housekeepin g ncRNA	Processes pre-tRNA to mature form
RNase MRP RNA	~270 nt	Nucleolus, mitochondri a	rRNA processing & mtDNA replication	Housekeepin g ncRNA	Cleaves rRNA precursors, supports mtDNA replication
microRNA (miRNA)	~22 nt	Nucleus → cytoplasm	Post- transcriptional regulation	Regulatory ncRNA	Represses or degrades mRNA
Small Interfering RNA (siRNA)	~21–25 nt	From dsRNA	Gene silencing	Regulatory ncRNA	Targets mRNA for degradation via RISC
Piwi-Interacting RNA (piRNA)	~26–31 nt	Germline cells	Transposon silencing	Regulatory ncRNA	Maintains genome integrity in germline

Circular RNA (circRNA)	Variable	Back-spliced exons	miRNA sponge & protein interaction	Regulatory ncRNA	Sequesters miRNAs; binds transcription machinery
Enhancer RNA (eRNA)	Variable	Enhancer regions	Transcriptional regulation	Regulatory ncRNA	Modulates gene transcription
tRNA-derived Fragments (tRF/tsRNA)	~14–40 nt	tRNA cleavage	Translation repression	Regulatory ncRNA	Controls stress response, signaling
moRNA	~19–22 nt	miRNA flanks	Putative regulation	Regulatory ncRNA	Possible gene regulation role
shRNA-derived miRNA / miRNA	~21–24 nt	Hairpin precursors	Post-transcriptional silencing	Regulatory ncRNA	Functions like miRNAs
PASR	~20–90 nt	Promoter regions	Transcriptional regulation	Regulatory ncRNA	Modulates transcription initiation
TSSa-RNA	~20–90 nt	TSS regions	Transcriptional control	Regulatory ncRNA	Linked to gene activation/inhibition
TASR	~20–90 nt	Gene termini	Transcriptional control	Regulatory ncRNA	May affect transcription elongation/termination
tiRNA	~20–90 nt	TSS regions	Initiation regulation	Regulatory ncRNA	Supports RNA pol recruitment
spliRNA	~20–30 nt	Exon-intron junctions	Splicing regulation	Regulatory ncRNA	Guides splice site selection
snoRNA-derived RNA (sdRNA)	~20–30 nt	snoRNA processing	Translation & stability regulation	Regulatory ncRNA	Post-transcriptional gene regulation
qiRNA	~20–21 nt	DNA damage-induced	Genome integrity	Regulatory ncRNA	Represses expression after DNA damage
Small Vault RNA (svRNA)	~23 nt	Vault RNAs	Drug resistance & regulation	Regulatory ncRNA	Involved in multidrug resistance pathways

Supplemental S2. RNA Variation Classification

Variance Classification	RNA Variance
Assorted RNA Variance ○ RNA variance based on gene biotypes producing diverse RNA products. (Antisense is both assorted and processed)	<ul style="list-style-type: none"> ○ <u>Alternative Splicing</u>: Variance in exon inclusion or exclusion leads to multiple RNA isoforms. ○ <u>Exon Skipping</u>: A form of alternative splicing where entire exons are skipped. ○ <u>Intron Retention</u>: A splicing variant where introns are retained within the transcript. ○ <u>Mutually Exclusive Exons</u>: One of two (or more) exons is included in the final transcript. ○ <u>Trans-splicing</u>: Exons from two separate pre-mRNA molecules are joined together. ○ <u>Tandem UTR Variance</u>: Multiple UTR regions are utilized, affecting transcript stability and translation efficiency. ○ <u>Bidirectional Transcription</u>: Transcription initiated from opposite strands of DNA produces overlapping RNA products. ○ <u>Exon Duplication</u>: Additional copies of an exon are included in the mRNA. ○ <u>Exon Deletion</u>: Entire exons are deleted from a transcript during splicing. ○ <u>Pseudogenes</u>: non-functional copies of genes that arise from gene duplication or retrotransposition events.
Processed RNA Variance ○ Productions of different RNA lengths and isoforms from a single gene.	<ul style="list-style-type: none"> ○ <u>Alternative Transcription Start Sites (TSS)</u>: Multiple initiation points lead to diverse RNA isoforms. ○ <u>Alternative Polyadenylation (APA)</u>: Variance in the poly(A) tail addition site, altering the 3' UTRs. ○ <u>Alternative 5' Splice Site</u>: A different splice donor site is used. ○ <u>Alternative 3' Splice Site</u>: A different splice acceptor site is used. ○ <u>Tandem UTR Variance</u>: Multiple UTR regions are utilized, affecting transcript stability and translation efficiency. ○ <u>Bidirectional Transcription</u>: Transcription initiated from opposite strands of DNA produces overlapping RNA products. ○ <u>Cryptic Splicing</u>: The use of non-canonical splice sites, often leading to dysfunctional proteins. ○ <u>mRNA Length Variance</u>: Different transcript lengths arise from alternative TSS, APA, or splicing. ○ <u>Full-Length Transcripts</u>: The complete version of the RNA transcript, as opposed to truncated versions. ○ <u>Truncated Transcripts</u>: Shorter RNA transcripts due to premature termination or incomplete processing.

- Incompletely Spliced Transcripts: RNA molecules that contain retained introns.
- Internal Transcription Start Sites: Initiation of transcription from within the gene, producing shorter RNA variants.
- Multiple Isoforms from a Single Gene: The production of multiple RNA isoforms with distinct lengths and functions.
- Nested Transcripts: One transcript is located within the intronic region of another gene.
- Read-through Transcription: RNA polymerase continues transcription past the normal stop signal, creating extended RNA molecules.
- Fusion Transcripts: Two previously separate genes are transcribed as one RNA molecule, usually due to chromosomal rearrangements.
- Overlapping Transcripts: Two transcripts from different genes overlap on the genome.

Modified RNA Variance
 ○ **Post-transcriptional modifications that affect RNA molecules without altering RNA sequence**

- N6-Methyladenosine (m6A): A common modification that impacts RNA stability and splicing.
- 5-Methylcytosine (m5C): A methylation of cytosine residues in RNA, affecting its function.
- Pseudouridylation: The conversion of uridine to pseudouridine, which can alter RNA secondary structure.
- Adenosine-to-Inosine (A-to-I) Editing: Editing that changes adenosine to inosine, affecting RNA base pairing.
- N1-Methyladenosine (m1A): A modification that affects tRNA and mRNA structure and function.
- 2'-O-Methylation: A modification of the ribose sugar that can impact RNA stability and function.
- Cap-Dependent Modifications (e.g., 7-methylguanosine cap): The 5' cap structure is modified to enhance stability and translation.
- RNA Acetylation (ac4C): Acetylation of cytidine residues, influencing mRNA translation.
- Uridylation: The addition of uridine residues to the 3' end of RNA, often leading to degradation.
- RNA Methylation (m5U): Methylation of uridine residues, altering the stability of tRNA.
- N7-Methylguanosine (m7G): A modification found in tRNAs and mRNAs influencing translation efficiency.
- 2-Thiouridine (s2U): A sulfur-modified uridine affecting tRNA decoding efficiency.
- Queuosine Modification: A tRNA modification that impacts accuracy in translation.
- m6Am Modification: A modification near the 5' cap of mRNA that can influence stability and translation.

- RNA Glycosylation: The addition of sugar molecules to RNA, potentially impacting its function.
- tRNA Modification (e.g., m1G, m3C, t6A): Modifications affecting tRNA stability, folding, and decoding.
- Y-base Modification in tRNA: A hypermodified base found in certain tRNAs that improves translation efficiency.
- RNA Oxidation (8-oxoG): Oxidative modifications that can alter RNA function or lead to degradation.
- RNA Phosphorylation: Phosphorylation of RNA molecules, potentially influencing their activity in stress responses.