RNA Types and Functions

Messenger RNA (mRNA)

- Encodes protein information
- Short-lived in cells
- 5' cap and poly(A) tail
- Template for translation

Transfer RNA (tRNA)

- Adapter molecule
- Brings amino acids to ribosome
- ~75-90 nucleotides
- Post-transcriptional modifications

Small Regulatory RNAs

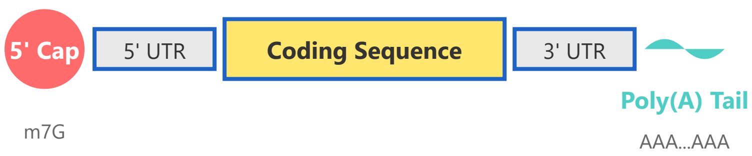
- miRNA: post-transcriptional silencing
- siRNA: gene knockdown
- ~20-25 nucleotides
- Therapeutic potential

Long Non-coding RNAs

- >200 nucleotides
- Chromatin remodeling
- Transcription regulation
- Emerging therapeutic targets

Detailed Overview of RNA Types

1. Messenger RNA (mRNA)



Function and Characteristics:

mRNA serves as the intermediary between genetic information stored in DNA and protein synthesis. It carries the genetic code from the nucleus to the cytoplasm where ribosomes translate it into proteins.

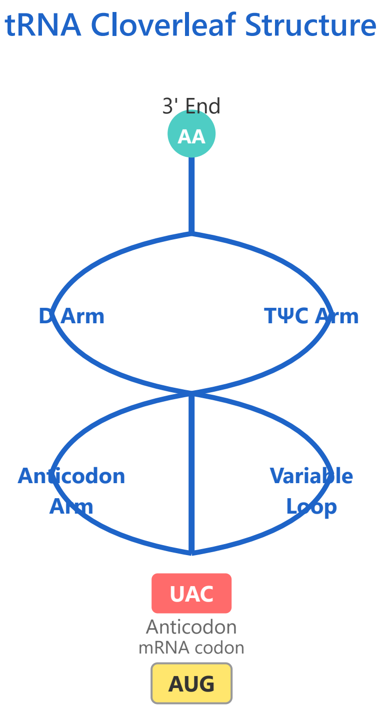
Key Features:

- **5' Cap (m7G):** Methylguanosine cap protects mRNA from degradation and aids in ribosome binding
- **5' UTR:** Untranslated region containing regulatory elements
- **Coding Sequence:** Contains codons that specify amino acid sequence
- **3' UTR:** Contains stability and localization signals
- **Poly(A) Tail:** ~200 adenine nucleotides that enhance stability and translation efficiency

Clinical Relevance:

mRNA technology has revolutionized vaccine development (COVID-19 vaccines) and shows promise in cancer immunotherapy and genetic disease treatment.

2. Transfer RNA (tRNA)



Function and Characteristics:

tRNA molecules serve as adapters that decode mRNA sequences into amino acids during translation. Each tRNA carries a specific amino acid and recognizes corresponding codons on mRNA through base pairing.

Structural Features:

- **Acceptor Stem:** 3' CCA end where amino acids attach
- **D Arm:** Contains dihydrouridine modifications
- **Anticodon Arm:** Contains the three-nucleotide anticodon that pairs with mRNA codons
- **TΨC Arm:** Contains thymine and pseudouridine; interacts with ribosome
- **Variable Loop:** Size varies among different tRNAs

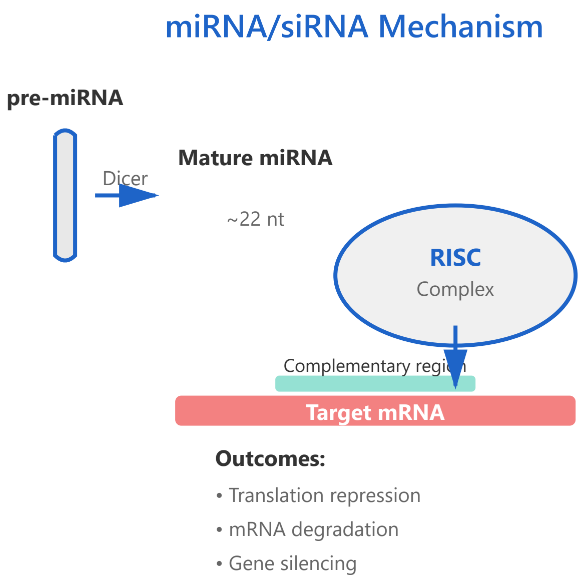
Modifications:

tRNAs undergo extensive post-transcriptional modifications (>100 types known), including pseudouridine (Ψ), dihydrouridine (D), and inosine (I), which are crucial for proper function and stability.

Wobble Base Pairing:

The third position of the codon allows non-Watson-Crick base pairing, enabling one tRNA to recognize multiple codons for the same amino acid.

3. Small Regulatory RNAs



Types and Functions:

MicroRNAs (miRNAs):

- Endogenous regulatory molecules (21-23 nucleotides)
- Processed from hairpin precursors by Drosha and Dicer
- Bind to 3' UTR of target mRNAs with partial complementarity
- Regulate ~60% of human protein-coding genes
- Critical for development, differentiation, and homeostasis

Small Interfering RNAs (siRNAs):

- Typically exogenous or derived from long dsRNA
- Perfect or near-perfect complementarity to targets
- Induce mRNA cleavage and degradation
- Used extensively in research for gene knockdown
- Therapeutic applications in viral infections and genetic disorders

Mechanism of Action:

Both miRNAs and siRNAs are loaded into the RNA-Induced Silencing Complex (RISC). The guide strand directs RISC to complementary mRNA sequences, resulting in translational repression or mRNA degradation.

Therapeutic Applications:

FDA-approved siRNA drugs include Patisiran (for hereditary transthyretin amyloidosis) and Givosiran (for acute hepatic porphyria). Many others are in clinical trials for cancer, cardiovascular, and neurological diseases.

4. Long Non-coding RNAs (lncRNAs)

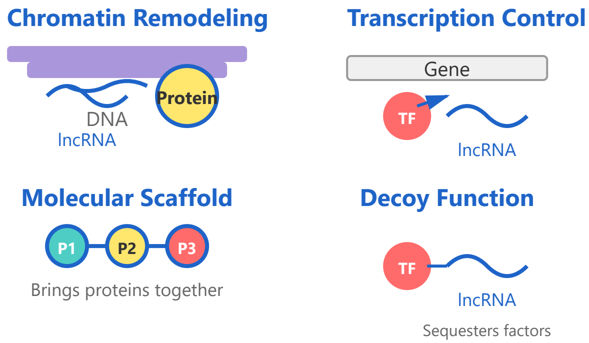
lncRNA Functions

Definition and Characteristics:

Long non-coding RNAs are transcripts longer than 200 nucleotides that do not encode proteins. They represent a large and diverse class of regulatory RNAs with critical roles in gene expression and cellular processes.

Functional Mechanisms:

- **Chromatin Remodeling:** Guide chromatin-modifying complexes to specific genomic loci (e.g., XIST recruits PRC2 for X-inactivation)
- **Transcriptional Regulation:** Act as enhancers, recruit transcription factors, or interfere with promoter activity



Notable Examples

XIST: X-chromosome inactivation
HOTAIR: HOX gene regulation, cancer metastasis
MALAT1: RNA splicing, cancer progression
H19: Imprinting, cell proliferation

- **Scaffold:** Bring multiple proteins together to form functional complexes
- **Decoy:** Sequester transcription factors, miRNAs, or proteins away from their targets
- **Guide:** Direct proteins to specific genomic locations

Biological Importance:

lncRNAs are essential for development, cell differentiation, immune responses, and maintaining cellular homeostasis. Dysregulation is implicated in cancer, neurological disorders, and cardiovascular diseases.

Therapeutic Potential:

Emerging as drug targets and biomarkers. Antisense oligonucleotides (ASOs) can modulate lncRNA function. Several lncRNAs show promise as diagnostic markers for cancer and other diseases.

Research Challenges:

Many lncRNAs remain poorly characterized. Understanding their mechanisms, tissue specificity, and evolutionary conservation remains an active area of research.