From Gene to Protein: Transcription and Translation



- **Roadmap:** DNA → RNA → protein → observable traits (the central dogma)
- **Why it matters:** genetics, medicine (mRNA vaccines, gene therapy), biotechnology
- **Vocabulary preview:** gene, promoter, transcript, codon, anticodon, ribosome, polypeptide
- **Two versions of the dogma:** Crick's 1958 information-flow rule vs. the familiar transcription/translation summary
- **Learning goals** tailored to biology students, adult science learners, and science teachers
- **Misconceptions to surface early:** gene vs. allele, codon vs. anticodon, "one gene = one protein"

Molecular Foundations: DNA, RNA, and the Genetic Code





The Genetic Code

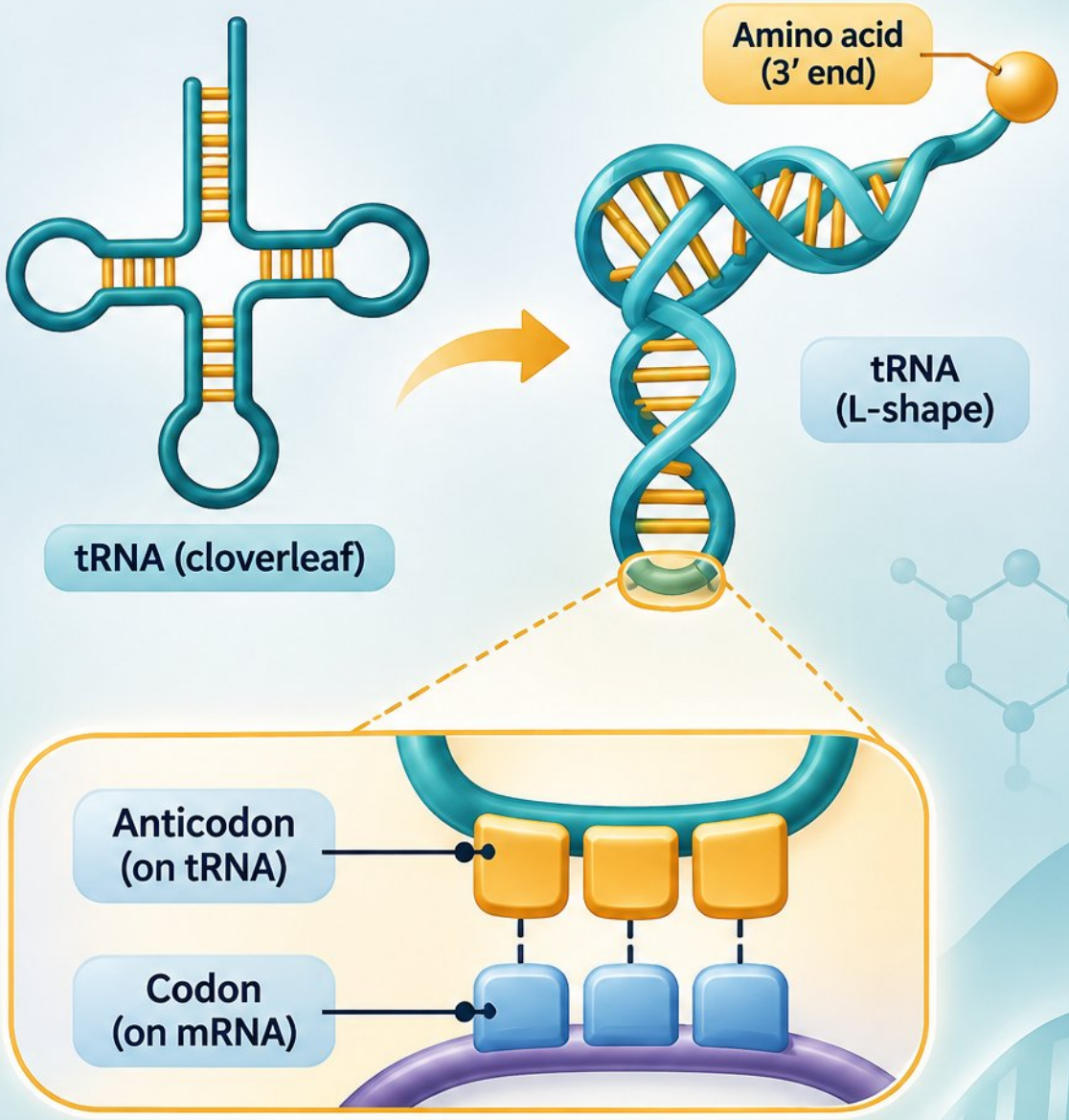
61 Sense Codons	3 Stop Codons (UAA, UAG, UGA)	AUG is Start

5′ → 3′

- DNA vs. RNA: deoxyribose vs. ribose sugar; RNA uses uracil (U) in place of thymine (T)
- RNA is typically single-stranded and less stable than double-stranded DNA
- Three key RNA classes: mRNA (message), tRNA (adaptor), rRNA (ribosome core)
- 64 triplet codons: 61 sense codons, 3 stop codons (UAA, UAG, UGA); AUG is start
- Degeneracy: most amino acids have multiple codons; third base often varies
- Reading frame is set by AUG; frameshifts alter all downstream codons
- **Directionality: nucleic acids read 5′→3′; proteins synthesized N→C**

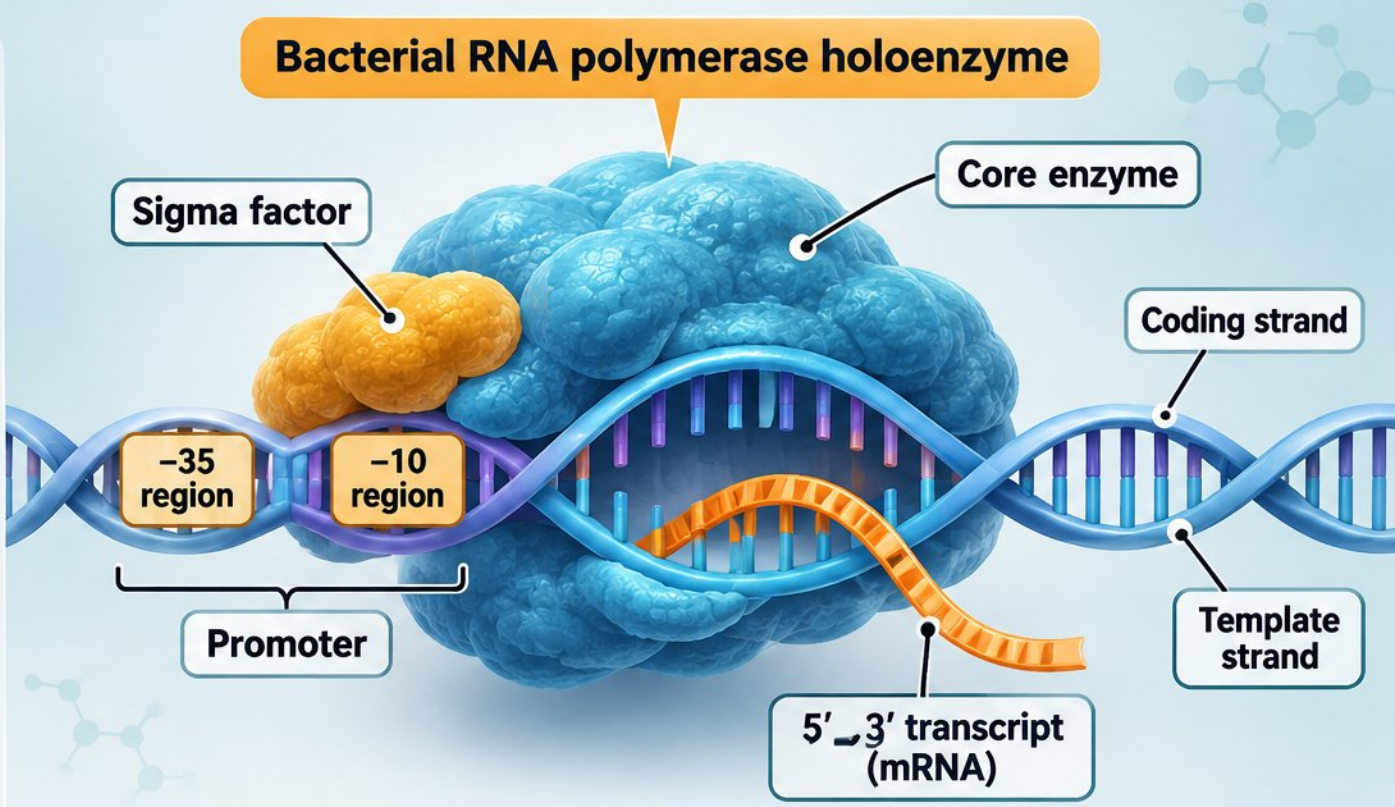
Wobble Pairing and Why the Code Is Degenerate

- Crick's 1966 wobble hypothesis: flexible pairing at the third codon position
- Anticodon G pairs with U or C; U pairs with A or G; inosine with A, U, or C
- tRNA adaptor: anticodon reads the codon, amino acid attaches at the 3′ end
- About 31–32 tRNA types cover all 61 sense codons in bacteria
- Positions 1 and 2 pair strictly, preserving accuracy despite wobble
- Teaching link: wobble explains silent mutations and codon-table patterns



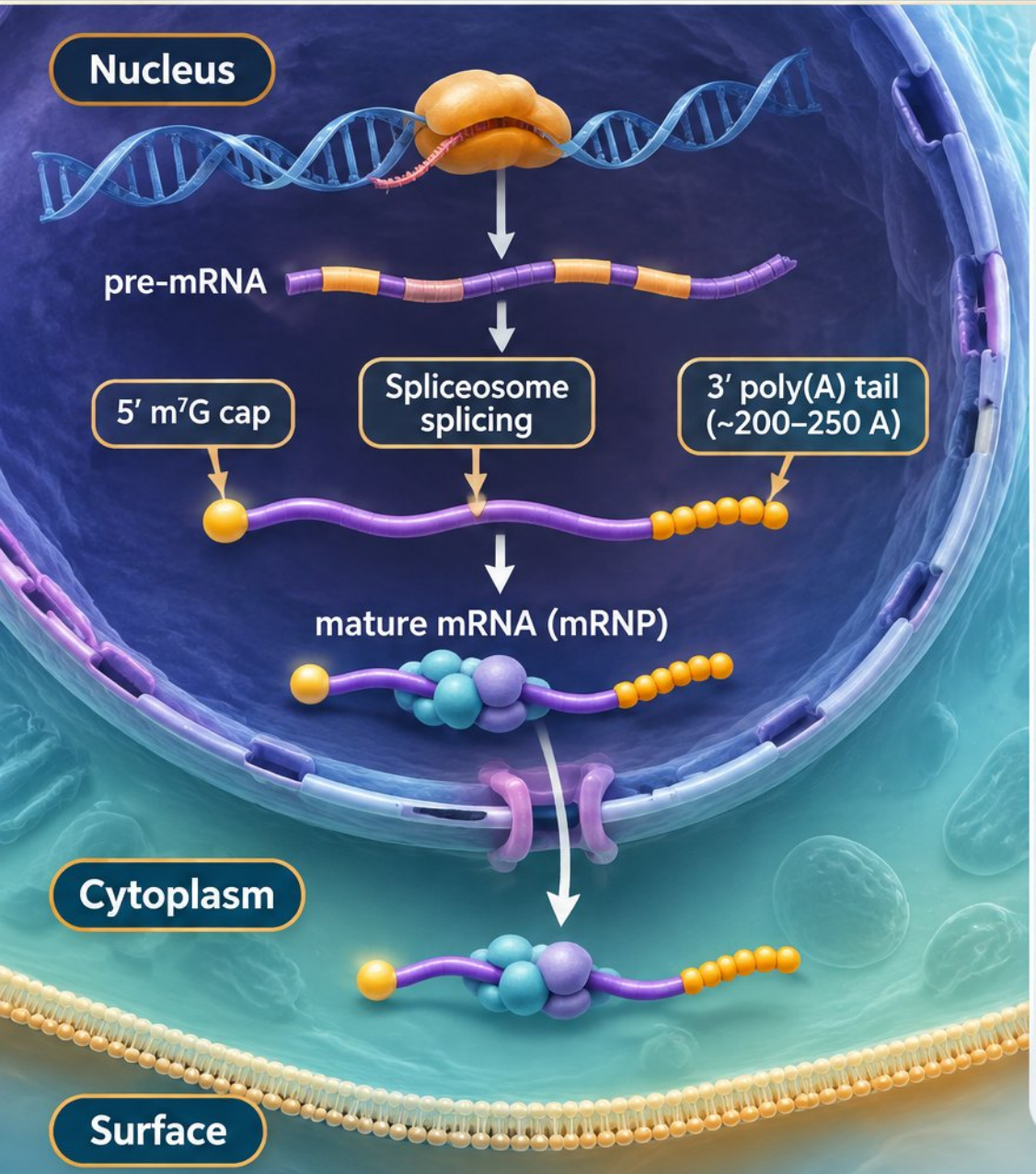
Transcription in Prokaryotes: Mechanism and Machinery

- RNA polymerase holoenzyme = core enzyme + sigma factor for promoter recognition
- Promoter consensus elements: −10 and −35 regions
- Three stages: initiation, elongation, termination
- Template strand read 5′→3′; coding strand matches mRNA
- Termination: Rho-dependent vs. Rho-independent
- Coupled transcription and translation; lac operon as teaching model



Three stages of transcription: Initiation → Elongation → Termination

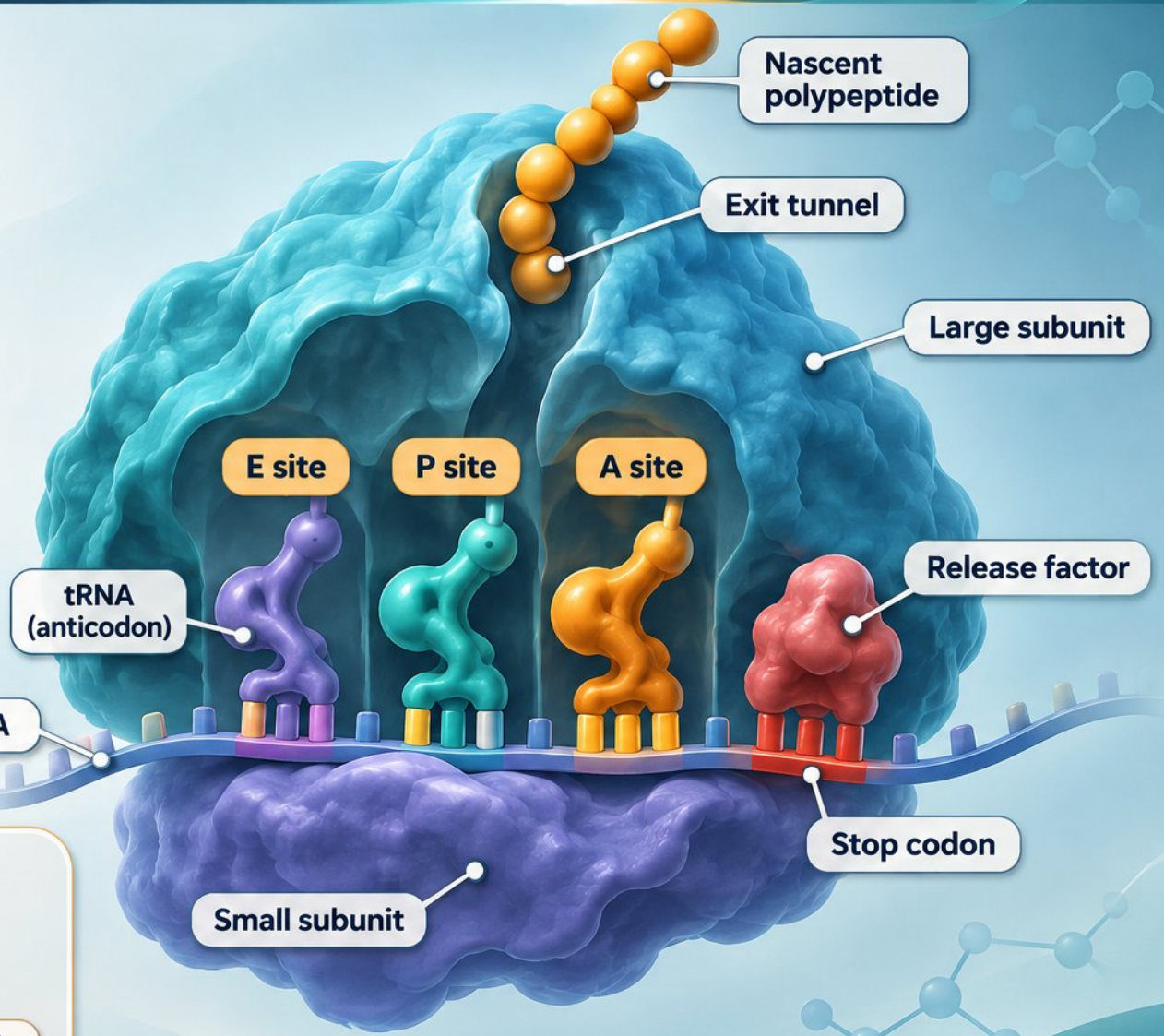
Transcription in Eukaryotes: Compartmentalization and Processing



- Nuclear transcription is physically separated from cytoplasmic translation
- Three RNA polymerases: Pol I makes rRNA, Pol II makes mRNA, Pol III makes tRNA and small RNAs
- Regulated initiation at TATA-box promoters and enhancers
- Co-transcriptional processing: 5′ m^7G cap, spliceosome splicing, 3′ poly(A) tail (~200–250 A)
- Alternative splicing affects over 90% of human genes, greatly expanding proteome diversity
- Distinguish pre-mRNA from mature mRNA; export of the mature mRNP

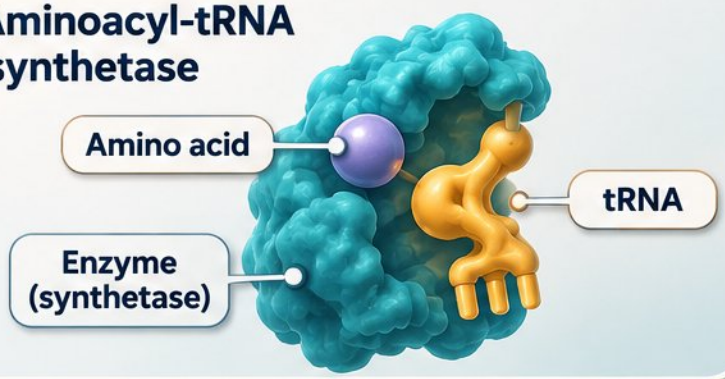
Translation: The Ribosome at Work

- **Ribosome:** large and small subunits; A, P, and E tRNA sites
- **Aminoacyl-tRNA synthetases** charge tRNAs — the "second genetic code"
- **Initiation:** Shine–Dalgarno (bacteria) vs. cap-dependent scanning (eukaryotes)
- **Elongation** cycle: codon recognition, peptidyl transfer (rRNA), three-nucleotide translocation
- Stop codons recruit release factors; hydrolysis adds water, not an amino acid



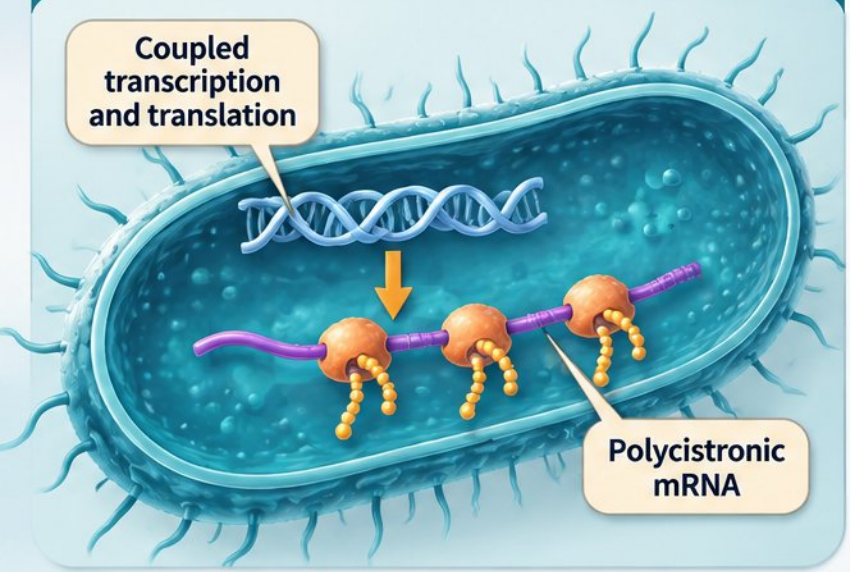
Molecular machine

Aminoacyl-tRNA synthetase

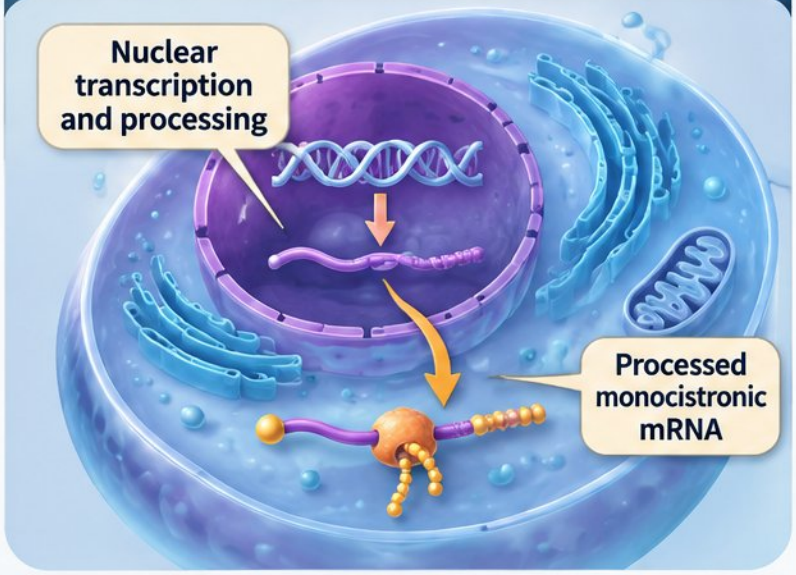


Prokaryotic vs. Eukaryotic Expression: A Side-by-Side Comparison

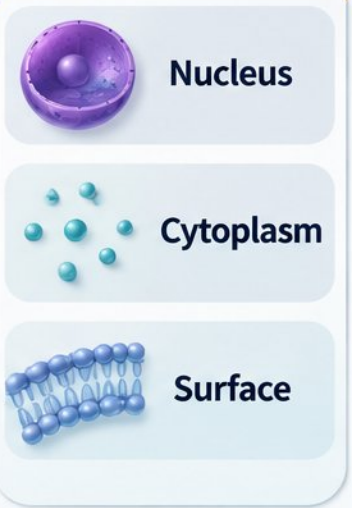
Bacteria (Prokaryote)



Eukaryote



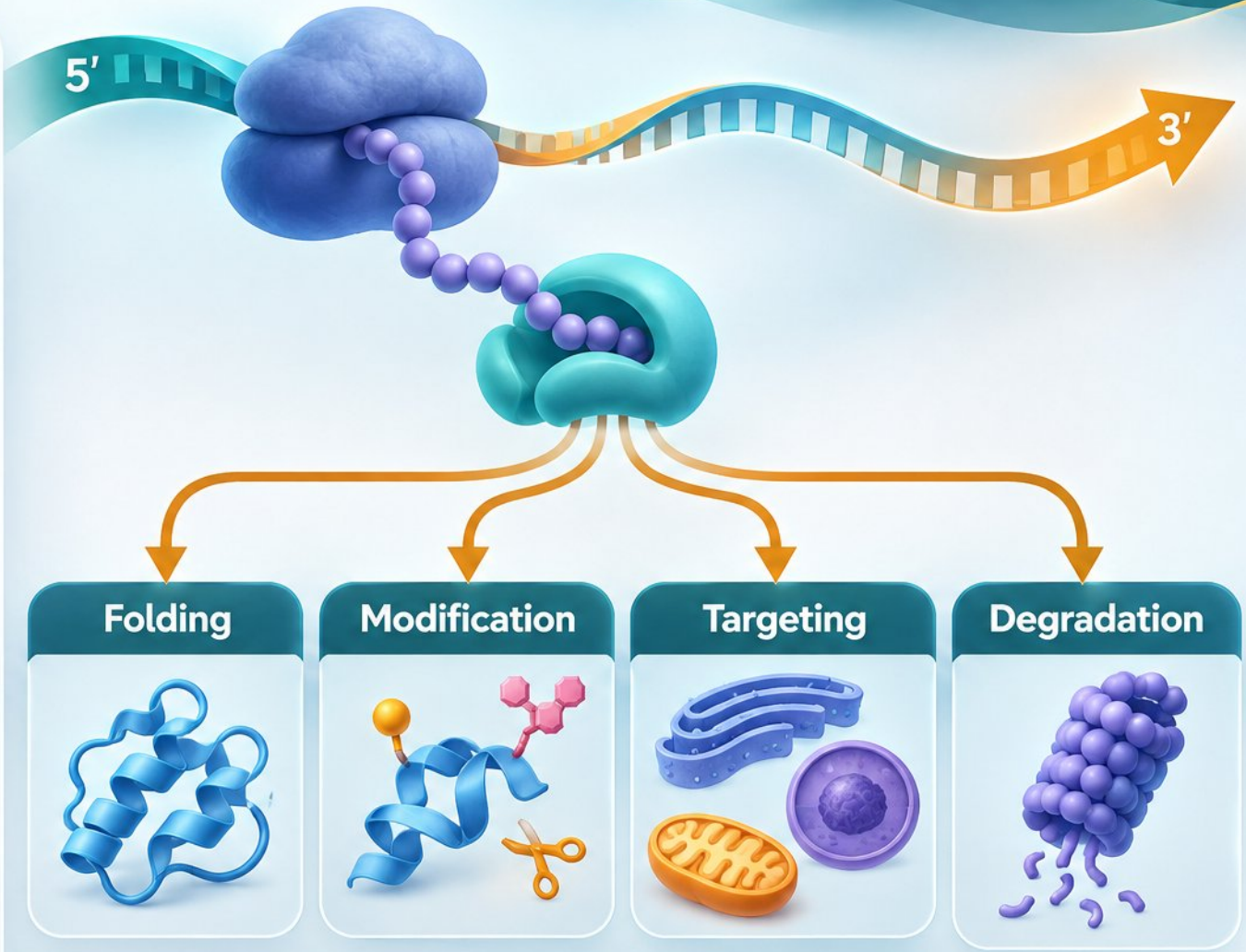
Three-Zone Cell Map



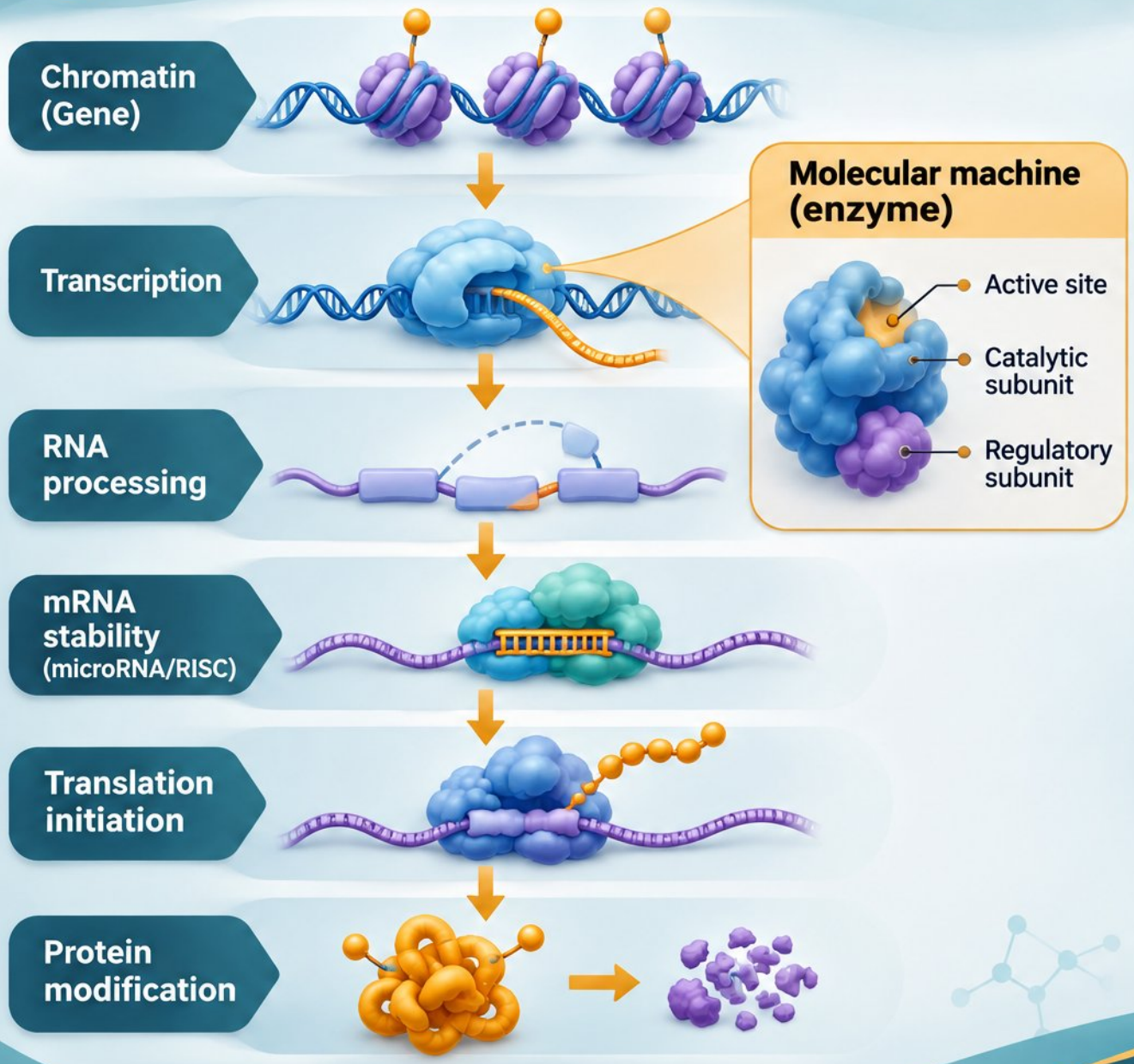
- Bacteria: transcription and translation coupled in the cytoplasm; control mainly transcriptional
- Eukaryotes: nuclear transcription and processing separated from cytoplasmic translation
- Bacteria: sigma factor recognizes promoters; Shine–Dalgarno sequence positions the ribosome
- Eukaryotes: general transcription factors, 5′ cap recognition, and ribosomal scanning
- Bacterial mRNAs are largely unprocessed and often polycistronic; eukaryotic mRNAs get cap, splicing, and poly(A)
- Prokaryotes rely chiefly on transcriptional control; eukaryotes regulate at many levels
- Selective antibiotic targets: bacterial ribosome, RNA polymerase

From Polypeptide to Functional Protein: Folding, Modification, and Targeting

- Co-translational folding with chaperone assistance shapes the final structure
- Post-translational modifications: phosphorylation, glycosylation, proteolytic cleavage
- Signal peptides direct proteins to ER, mitochondria, or nucleus
- Ubiquitin–proteasome system controls protein degradation and turnover
- Misfolding diseases (cystic fibrosis, Alzheimer's) show indirect genotype–phenotype mapping
- Why genotype–phenotype mapping is indirect: many steps after translation



Regulation of Gene Expression: Adding Control Layers

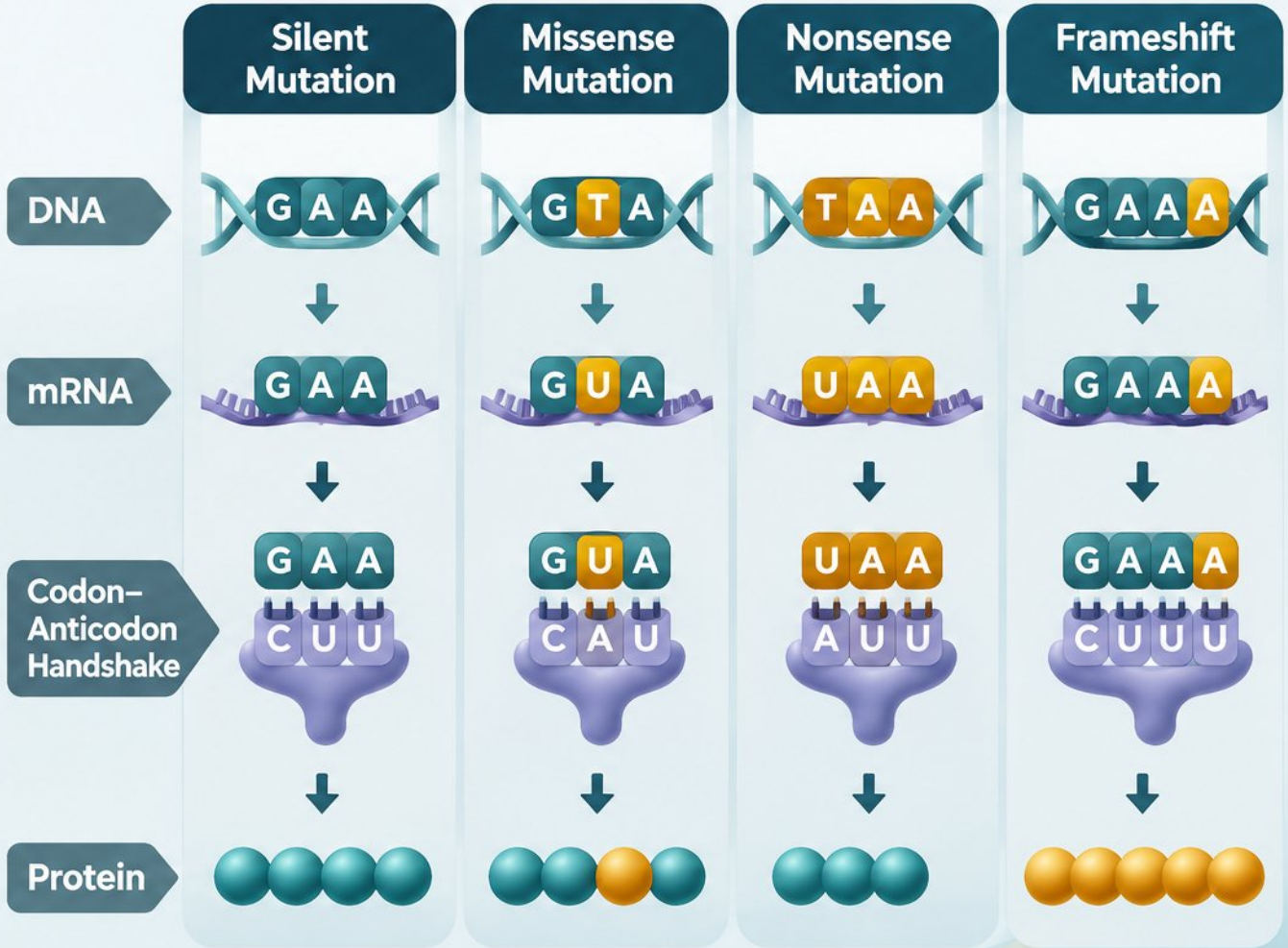


- **Transcriptional control:** activators, repressors, enhancers, chromatin remodeling
- **Epigenetic control:** chromatin accessibility and DNA methylation
- **Post-transcriptional:** alternative splicing, mRNA stability, microRNAs (21–24 nt) and RISC
- **Translational control:** eIF-2 phosphorylation, mRNA localization
- **Post-translational:** modifications and proteasome degradation

- **Why it matters:** differentiation, energy economy, and disease

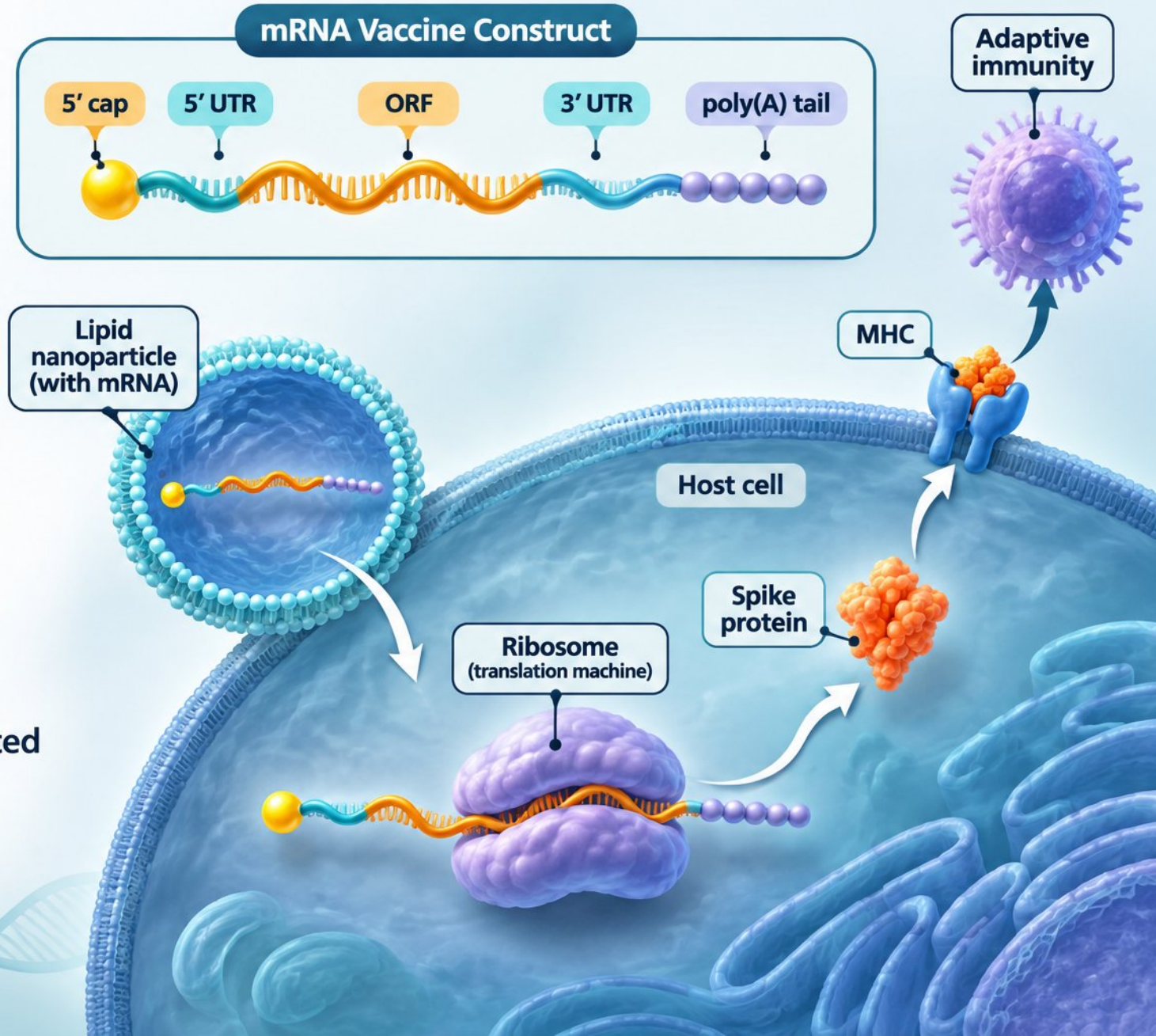
Mutations and Their Consequences for the Protein Product

- Point mutations: silent, missense, nonsense — each with a predicted protein effect
- Insertions and deletions shift the reading frame, altering all downstream codons
- Splice-site mutations change mRNA processing and exon content
- Loss-of-function vs. gain-of-function: distinct phenotypic outcomes
- Sickle cell: single substitution in hemoglobin beta; cystic fibrosis: CFTR defect
- Map mutation class → protein structure/function → observable phenotype



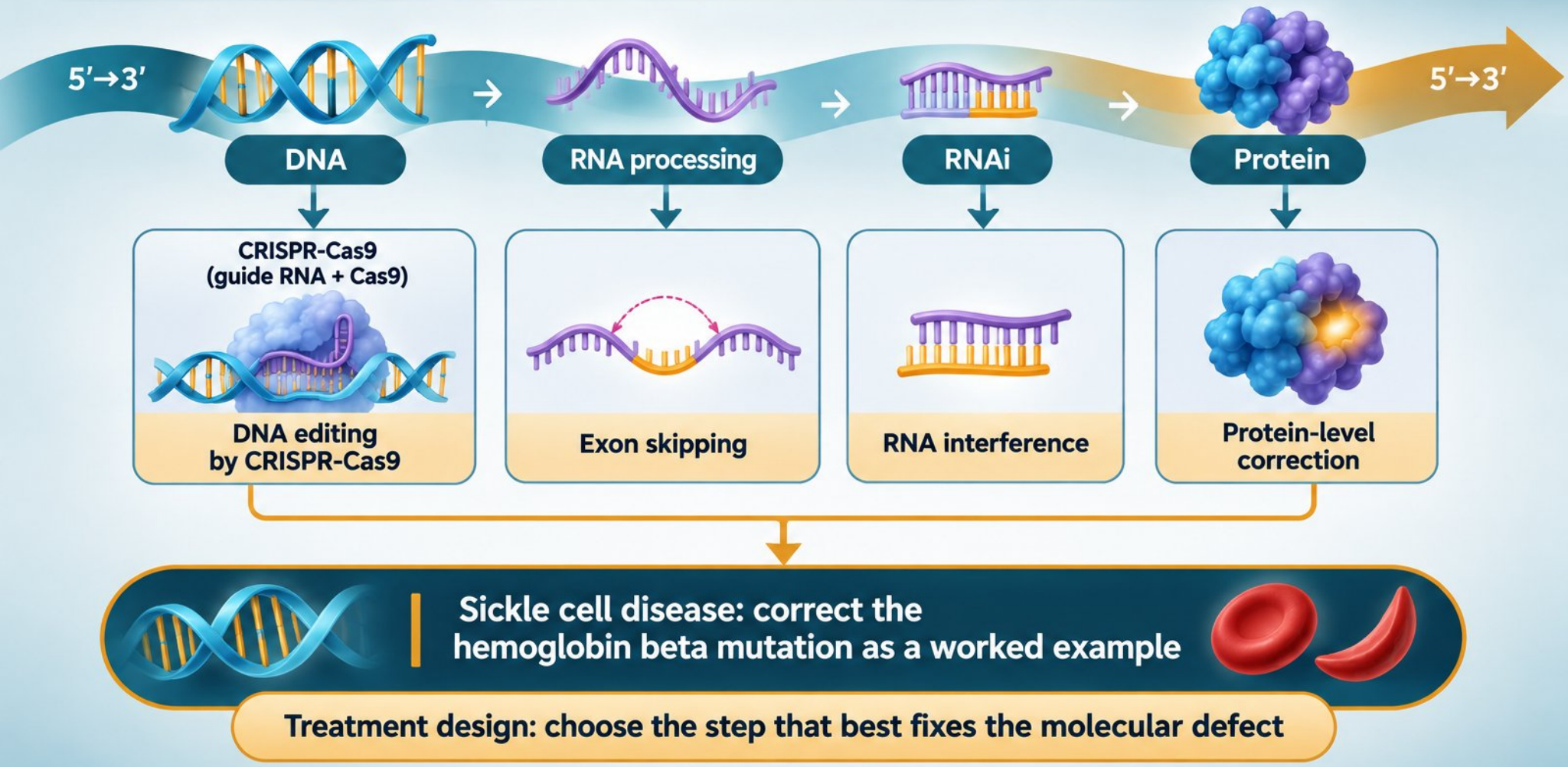
Case Study: mRNA Vaccines as Translation in Action

- Construct: 5′ cap, 5′ UTR, ORF, 3′ UTR, poly(A) tail
- Codon optimization and pseudouridine boost translation, reduce innate sensing
- Lipid nanoparticles deliver mRNA; host ribosomes translate the antigen
- Spike protein processed and presented via MHC to activate adaptive immunity
- Vaccine must be translated in situ — translation machinery in action

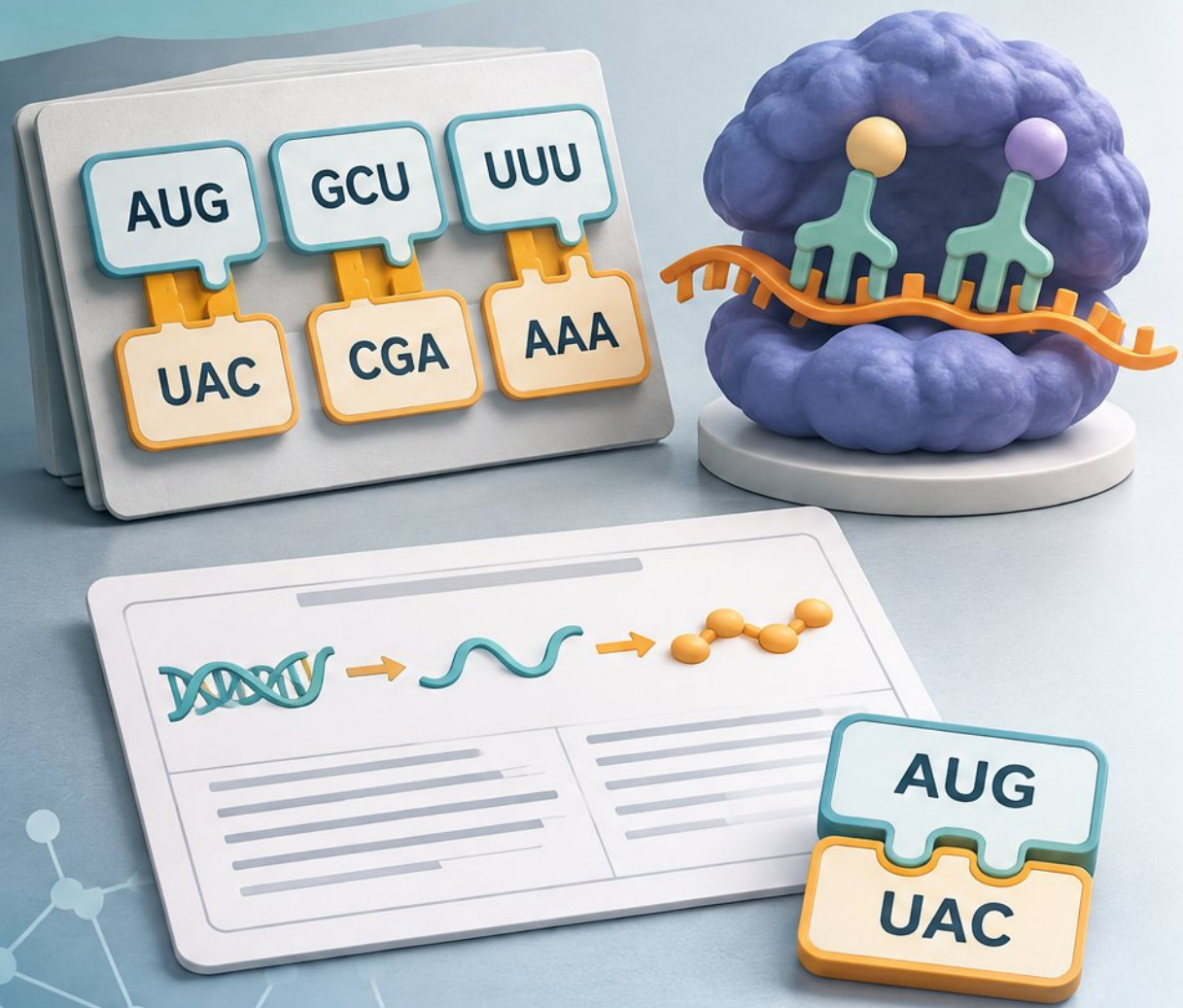


Case Study: Gene Therapy and CRISPR at the Level of Expression Steps

- Target any expression step: DNA, RNA processing, RNAi, or protein function
- CRISPR-Cas9: guide RNA finds target; Cas9 cuts DNA; cell repair edits sequence
- Sickle cell disease: correct the hemoglobin beta mutation as a worked example
- Treatment design: choose the step that best fixes the molecular defect
- Ethics: germline vs. somatic editing, access, and "designer babies" debates



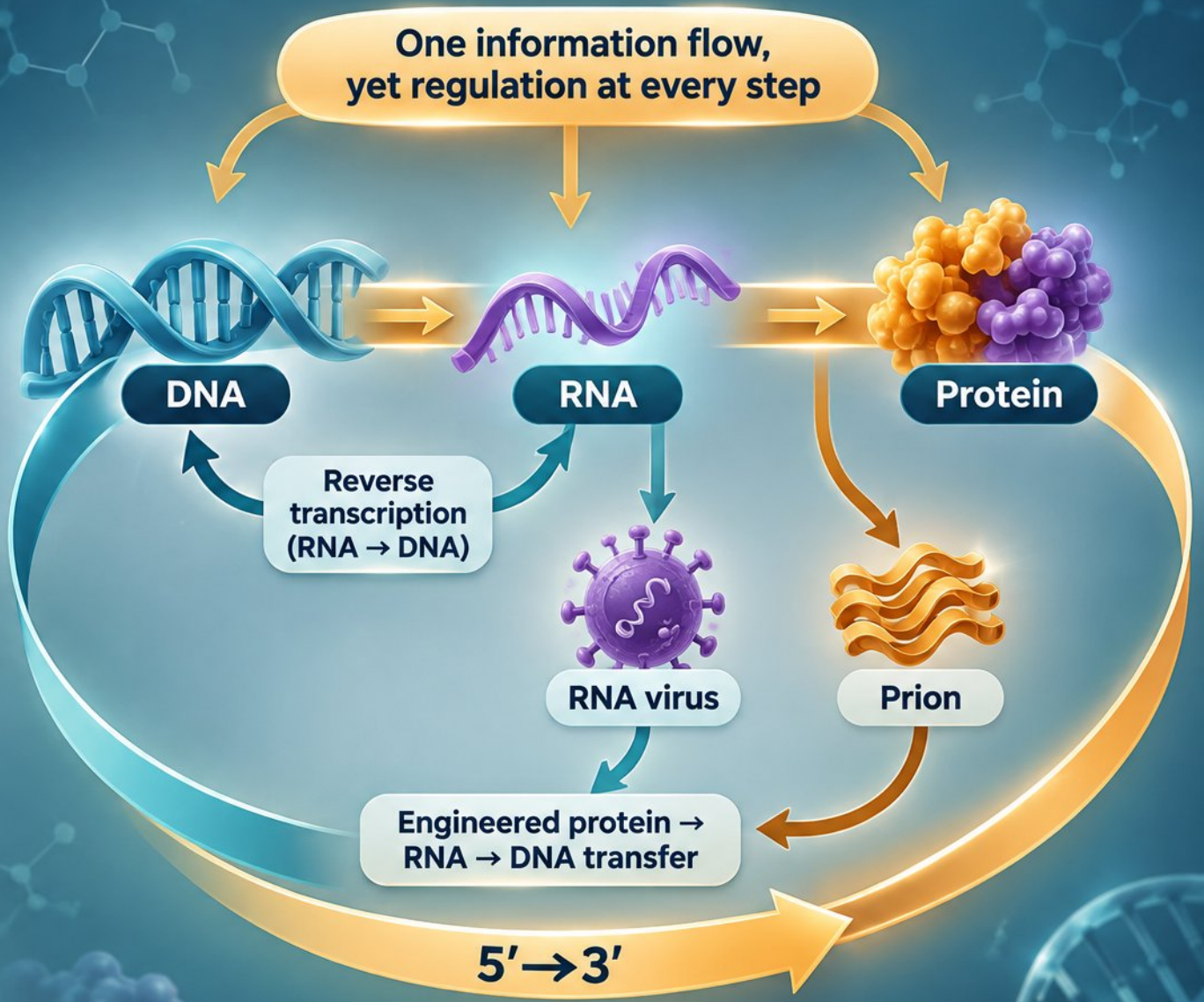
Teaching Toolkit: Models, Activities, and Assessment Design



- Analogies and physical models make transcription and translation visible
- Card-sorting tasks: sequence the central dogma, then revisit and revise
- Predict protein effects from DNA → mRNA → amino acid changes
- Anchor cases: *lac* operon, hemoglobin and sickle cell, cystic fibrosis
- Virtual labs, narrated animations, and interactive modules for varied audiences
- Formative checks that surface codon, reading-frame, and gene-definition misconceptions

Wrap-Up: The Central Dogma Revisited and Modern Refinements

- One information flow, yet regulation at every step
- RNA does far more than carry messages: tRNA, rRNA, microRNAs
- Reverse transcription (RNA → DNA) stays within Crick's information rule
- Prions: infectious protein conformations, no nucleic acid template
- Engineered protein → RNA → DNA transfer tests the dogma's boundaries
- Next topics: replication, gene regulation, protein structure



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