<table>
<thead>
<tr>
<th>First position (5′-end)</th>
<th>Second position</th>
<th>Third position (3′-end)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UUU</td>
<td>UCU</td>
<td>UGU</td>
</tr>
<tr>
<td>phe</td>
<td>ser</td>
<td>cys</td>
</tr>
<tr>
<td>UUC</td>
<td>UCC</td>
<td>UGC</td>
</tr>
<tr>
<td>UUA</td>
<td>UCA</td>
<td>CGU</td>
</tr>
<tr>
<td>leu</td>
<td>pro</td>
<td>arg</td>
</tr>
<tr>
<td>UUG</td>
<td>UCG</td>
<td>CCG</td>
</tr>
<tr>
<td>A</td>
<td>UAG</td>
<td>UGA</td>
</tr>
<tr>
<td>AUG</td>
<td>met</td>
<td>Arg</td>
</tr>
<tr>
<td>G</td>
<td>GUA</td>
<td>AGA</td>
</tr>
<tr>
<td>val</td>
<td>Ala</td>
<td>Arg</td>
</tr>
<tr>
<td>GUU</td>
<td>GCC</td>
<td>GAG</td>
</tr>
<tr>
<td>GUC</td>
<td>GCU</td>
<td>GGU</td>
</tr>
<tr>
<td>GUA</td>
<td>GCA</td>
<td>GGC</td>
</tr>
<tr>
<td>val</td>
<td>Ala</td>
<td>Gly</td>
</tr>
<tr>
<td>GUG</td>
<td>GCG</td>
<td>GGG</td>
</tr>
</tbody>
</table>
Degeneracy

The occurrence of more than one codon for an amino acid (AA). Most differ in only the 3\textsuperscript{rd} (3\textsuperscript{′}) base, with the 1\textsuperscript{st} and 2\textsuperscript{nd} being most important for distinguishing the AA.

Two types of degeneracy:

1) Partial – changing the third base in a codon from a purine to a purine, or from a pyrimidine to a pyrimidine. Ex. Partial degeneracy: (G <-> A), (C <-> U)

2) Complete – Any of the four bases may be replaced for the third base in a codon. Ex. GUU, GUC, GUA, or GUG, all code for valine.
Degeneracy reduces the possibility of mutation as a result of base pairing errors in transcription and translation of DNA information, thereby increasing genotypic and phenotypic stability. Degeneracy also allows for silent mutations. Ex. threonine from ACU, ACC, ACG, and ACA. In contrast to this, AUA for isoleucine, and AUG for methionine.

Because of degeneracy of the genetic code, either several different t-RNAs exist that recognize the different codons specifying a given AA or the anticodon of a given t-RNA must be able to base pair with several different codons. Actually, both of these occur. There are at least two t-RNAs for each AA whose codons exhibit complete degeneracy at the 3rd position.
Wobble

The ability of t-RNA anticodons to recognize different codons specifying a certain AA. Wobble occurs between the 1st (5′) base of an anticodon of t-RNA and the 3rd (3′) base of a codon. Hydrogen bonding between anticodon and codon bases at the 1st and 2nd sites of the codon (2nd and 3rd sites of the anticodon) are “tight”.
<table>
<thead>
<tr>
<th>Subunit Type</th>
<th>Large Subunit</th>
<th>Small Subunit</th>
<th>Large Subunit</th>
<th>Small Subunit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prokaryotes</td>
<td>50S, 1.6 × 10^6 MW</td>
<td>30S, 0.9 × 10^6 MW</td>
<td>60S, 2.8 × 10^6 MW</td>
<td>40S, 1.4 × 10^6 MW</td>
</tr>
<tr>
<td>Eukaryotes</td>
<td>80S, 4.2 × 10^6 MW</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>23S rRNA (2904 nucleotides) + 31 proteins + 5S rRNA (120 nucleotides)</td>
<td>16S rRNA (1541 nucleotides) + 21 proteins</td>
<td>28S rRNA (4718 nucleotides) + 49 proteins + 5S rRNA + 5.8S rRNA (160 + 160 nucleotides)</td>
<td>18S rRNA (1874 nucleotides) + 33 proteins</td>
</tr>
</tbody>
</table>
Translation

1. AA + ATP → amino acyl - AMP + tRNA → amino acyl - tRNA complex

2. 30s ribosomal subunit + amino acyl-tRNA complex + initiation codon on mRNA → initiation complex (binding).

3. Initiation complex + 50s ribosomal subunit. Formation of P and A sites. P site now occupied by amino acyl – tRNA complex, but A-site is unoccupied.

P(site) = peptidyl
A(site) = amino acyl
4. The new amino-acyl - tRNA complex with a 2nd AA enters the A site. Requires \(^3\)EF\(_1\) enzyme.

5. Transfer of AA in P-site to 2nd AA in A site. Requires \(^4\)peptidyl transferase.

6. tRNA in the P-site drops out. Translocation or a shift in the 5' \(\rightarrow\) 3' direction on mRNA by 3 nucleotides or 1 codon. Now a full P-site, but empty A-site. (Requires \(^5\)EF\(_2\) enzyme.)

7. Repeat processes 4-6.

8. Reach termination (one of 3 possible) codon. Occupation of A-site by releasing factor. (STOP)

9. Removal of N-terminal met in eukaryotes and f - met in prokaryotes.
(Above and right page): Schematic drawing of the steps involved in translation.
Elongation factors $E_{f-T_s}$, $E_{f-T_u}$

GDP + $\mathbb{P}$ → GTP

50S ribosomal subunit

GDP + $\mathbb{P}$ → GDP

Peptidyl transferase (50S ribosomal subunit-bound enzyme)

(Above and right page): Schematic drawing of the steps involved in translation.
1. mRNA binds to small subunit along with initiation factors (IF1, 2, 3)

2. Initiator tRNA\textsuperscript{fmet} binds to mRNA codon in P site; IF3 released

3. Large subunit binds to complex; IF1 and IF2 released; EF-Tu binds to tRNA, facilitating entry into A site
1. mRNA binds to small subunit along with initiation factors (IF1, 2, 3)

2. Initiator tRNA^{fmet} binds to mRNA codon in P site; IF3 released
Initiation complex

2. Initiator tRNA$_{f_{met}}$ binds to mRNA codon in P site; IF3 released

3. Large subunit binds to complex; IF1 and IF2 released; EF-Tu binds to tRNA, facilitating entry into A site
1. Second charged tRNA has entered A site, facilitated by EF-Tu; first elongation step commences.
2. Dipeptide bond forms; uncharged tRNA moves to E-site and then out of ribosome.
3. mRNA has shifted by 3 bases; EF-G facilitates the translocation step; first elongation step completed
4. Third charged tRNA has entered A site, facilitated by EF-Tu; second elongation step begins.
5. Tripeptide formed; second elongation step completed; uncharged tRNA moves to E site

6. Polypeptide chain synthesized and exiting ribosome
Termination

1. tRNA and polypeptide chain released

2. GTP-dependent termination factors activated; components separate; polypeptide folds into protein
2. GTP-dependent termination factors activated; components separate; polypeptide folds into protein
DNA Antisense Strand
(Triplet codes)

Transcription

mRNA
(codons)

Translation

Polypeptide

Peptide bonds

A T G C T A T G C

A U C

C G U

5' 3'

3' 5'

3' Asp

3' Thr

3' Tyr

G U A

5' 3'

5' 3'
DNA Antisense Strand
(Triplet codes)

A T G C T A G C
Transcription

5' 3'
U A C G A U A C G
mRNA (codons)

Translation

Tyr Asp Thr
Polypeptide

Peptide bonds

5' 3'
G U A
3' 5'
A U C
3' Thr
3' Tyr
3' Asp
1. Nonpolar: Hydrophobic

- Alanine (ala-A)
- Valine (val-V)
- Leucine (leu-L)
- Isoleucine (ile-I)
- Proline (pro-P)
- Methionine (met-M)
- Phenylalanine (phe-F)
- Tryptophan (trp-W)
2. Polar: Hydrophilic

- Glycine (gly–G)
- Serine (ser–S)
- Threonine (thr–T)
- Cysteine (cys–C)
- Tyrosine (tyr–Y)
- Asparagine (asn–N)
- Glutamine (gln–Q)
3. Polar: positively charged (basic)

Lysine (lys-K)

Arginine (arg-R)

Histidine (his-H)
4. Polar: negatively charged (acidic)

Aspartic acid (asp-D)
Glutamic acid (glu-E)

Amino acid structure
Amino group
Carboxyl group
The diagram illustrates the formation of a peptide bond. The process involves the reaction of an amino group with a carboxyl group, releasing water ($H_2O$). The resulting peptide bond connects the amino end to the carboxyl end, creating a new chemical structure.
DNA

1. Regulation of transcription

Pre-mRNA (primary transcript)

2. Regulation of splicing and processing

mRNA

Cap AAA

3. Regulation of transport

Nucleus

Nuclear membrane

Nuclear pore

Ribosome

Cytoplasm

4. Translational regulation

Translation

Protein product

5. Activity of protein
# Translation

## Prokaryotes
- on free ribosomes
- transcription and translation coupled
- polygenic mRNAs
- First AA is N-formyl methionine (f-met)
- 50S, 30S ribosomal subunits

## Eukaryotes
- on free and ER-bound ribosomes
- transcription and translation separate
- monogenic mRNAs
- First AA is methionine (met)
- 60S, 40S ribosomal subunits

## Properties and functions of 6 important proteins

- rho (only in prokaryote transcription)
- RF-1 (only in translation—in both prokaryotes and eukaryotes)
- Sigma-70 subunit (only in prokaryote transcription)
- SSBP (only in replication—in both prokaryotes and eukaryotes)
- transcription factors (only in eukaryotes)
- repressor protein (only in prokaryote transcription)
### Possible points of control for gene expression.

<table>
<thead>
<tr>
<th>Level of control</th>
<th>Possible controllable event</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome</td>
<td>√ Specific chromosomes of chromosomal regions are inactivated by condensation to heterochromatin during development. Specific chromosomal regions may be activated by translocation.</td>
<td>The inactive X chromosome in female mammalian cells is heterochromatic. Genes for the variables and constant regions of antibody molecules may be joined by translocation before they are activated. The somatic cells of <em>Ascaris</em> lack certain chromosomes.</td>
</tr>
</tbody>
</table>
Possible points of control for gene expression. (continued)

<table>
<thead>
<tr>
<th>Level of control</th>
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<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene (transcriptional controls) - Primary point of</td>
<td>√ The presence of many identical or nearly identical genes in the haploid complement (gene</td>
<td><em>Xenopus</em> has about 900 ribosomal genes in each somatic cell.</td>
</tr>
<tr>
<td>hormonal influence</td>
<td>reiteration) permits the corresponding transcripts to be made at a high rate.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>The extrachromosomal replication of ribosomal genes (gene amplification) permits more</td>
<td>The <em>Xenopus</em> ribosomal gene complement is amplified 1000-fold in the</td>
</tr>
<tr>
<td></td>
<td>rapid production of rRNA.</td>
<td>oocyte.</td>
</tr>
<tr>
<td></td>
<td>√ Specific genes can be activated for transcription.</td>
<td>Different tissues contain different populations of mRNAs.</td>
</tr>
<tr>
<td></td>
<td>Gene activation is accompanied by changes in the macromolecular structure of the chromosome.</td>
<td>Activation of genes on polytene chromosomes is accompanied by “puffing.”</td>
</tr>
</tbody>
</table>
### Possible points of control for gene expression. (continued)

<table>
<thead>
<tr>
<th>Level of control</th>
<th>Possible controllable event</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA (post-transcriptional controls)</td>
<td>√ Primary transcripts may require processing to produce active cytoplasmic RNA species.</td>
<td>Ribosomal RNA gene transcripts are cleaved to yield rRNA molecules for ribosome assembly.</td>
</tr>
<tr>
<td></td>
<td>√ mRNA must be transported from the nucleus to the cytoplasm.</td>
<td>The drug cordycepin blocks appearance of new mRNA in the cytoplasm, probably by blocking synthesis of poly-A terminal required for transport.</td>
</tr>
<tr>
<td></td>
<td>√ RNA degradation takes place both in the nucleus and in the cytoplasm.</td>
<td>Hemoglobin mRNA has a half-life of ~100 days; whereas, the average HeLa cell mRNA has a half-life of 2–3 hours.</td>
</tr>
<tr>
<td></td>
<td>mRNA in the cytoplasm may be “masked” in an inactive form.</td>
<td>Maternal mRNA in eggs remain inactive until after fertilization.</td>
</tr>
<tr>
<td></td>
<td>√ mRNA must attach to ribosomes for initiation of polypeptide synthesis.</td>
<td>A variety of initiation factors are involved in attachments of mRNA and initiation of polypeptide synthesis.</td>
</tr>
<tr>
<td></td>
<td>√ Translation on polyribosomes may occur at varying rates.</td>
<td>The α and β chains of hemoglobin appear to be translated at different rates.</td>
</tr>
</tbody>
</table>
Possible points of control for gene expression. (continued)

<table>
<thead>
<tr>
<th>Level of control</th>
<th>Possible controllable event</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (post-translational</td>
<td>√ Proteins may be stored in vesicles and secreted when required.</td>
<td>Potentially destructive hydrolytic enzymes are often stored in lysosomes until needed. Proinsulin must be cleaved to form active insulin; proline residues in procollagen must be hydroxylated and partially glycosylated to allow secretion and proper assembly of collagen fibers.</td>
</tr>
<tr>
<td>controls)</td>
<td>Proteins may require modification of their covalent structure for activation.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>√ Proteins are degraded at different rates.</td>
<td>Antibodies of one class (IgG) have a half-life in the serum of 25 days; whereas, antibodies of another class (IgE) have a half-life of 2 days.</td>
</tr>
</tbody>
</table>