Substitution: replace, do not shift

A substitution replaces a nucleotide in DNA. In a protein-coding region it changes one triplet without moving the boundaries of the triplets that follow.

1. KEEP THE SAME READING FRAME

Original coding DNA

ATG	GCT	TTT	GAA	CCG	TAA

Replace C with T in the second triplet

ATG	GTT	TTT	GAA	CCG	TAA

Coding strand shown 5' to 3'. Triplet boundaries stay aligned. These are illustrative sequences, not a named gene.

2. SAME AMINO ACID - SYNONYMOUS

Coding DNA GCT becomes GCC. The mRNA codon changes from GCU to GCC, but both specify alanine. The amino-acid sequence stays the same.

3. DIFFERENT AMINO ACID - MISSENSE

In the diagram, GCT becomes GTT: mRNA GCU becomes GUU, so alanine becomes valine. This may alter folding or function, but loss of function is not inevitable.

4. EARLY STOP - NONSENSE

An internal coding triplet TAT can become TAA. In mRNA, UAU (tyrosine) becomes UAA (stop). Translation ends early, producing a shorter polypeptide.

Replacement of a nucleotide: NHGRI, Substitution.
Codon meanings and degeneracy: OpenStax Biology 2e, section 15.1.

Scope: Cambridge Biology 9700 syllabus, section 6.2, outcome 7, p. 25.

One base changes the grouping

Deletion removes a nucleotide; insertion adds one. Within a coding region, a one-base change shifts how the remaining sequence is divided into triplets.

1. ORIGINAL: READ FROM THE SAME START

ATG | GCT | TTT | GAA | CCG | TAA

mRNA: AUG GCU UUU GAA CCG UAA

Met - Ala - Phe - Glu - Pro - STOP

Coding DNA above; all DNA and RNA sequences run 5' to 3'.

2. DELETE THE G IMMEDIATELY AFTER ATG

ATG | CTT | TTG | AAC | CGT | AA

mRNA: AUG CUU UUG AAC CGU AA...

Met - Leu - Leu - Asn - Arg - ...

AA is an incomplete triplet; further DNA is not shown.

3. INSERT AN A IMMEDIATELY AFTER ATG

ATG | AGC | TTT | TGA | ACC | GTA | A

mRNA: AUG AGC UUU UGA ACC GUA A...

Met - Ser - Phe - STOP (UGA)

Triplets after the new stop are not translated.

A frameshift changes downstream grouping, not the bases upstream. Some amino acids may coincide by chance; an early stop is possible, not guaranteed.

Loss and addition of DNA nucleotides: NHGRI, Deletion and Insertion.
Reading-frame shifts and premature stops: NHGRI, Frameshift Mutation.

Scope: Cambridge Biology 9700 syllabus, section 6.2, outcome 7, p. 25.

Count the bases that change

For an insertion or deletion within a coding region, ask whether the number of nucleotides added or removed is a multiple of three. This predicts a downstream frameshift, not the severity of the effect.

1. ONE OR TWO BASES: THE FRAME SHIFTS

Adding or removing 1, 2, 4 or 5 bases changes downstream triplet grouping. The original start still defines the reading frame; do not restart grouping at the mutation.

2. THREE BASES: THE DOWNSTREAM FRAME IS RETAINED

Delete the complete GCT triplet from the page 2 original:

ATG	TTT	GAA	CCG	TAA

Met - Phe - Glu - Pro - STOP: alanine is removed.

Insert GGT between ATG and GCT in the original:

ATG	GGT	GCT	TTT	GAA	CCG	TAA

Met - Gly - Ala - Phe - Glu - Pro - STOP: glycine is added.

Coding DNA, 5' to 3'; here the edits fall at triplet boundaries.

3. NO FRAMESHIFT DOES NOT MEAN NO EFFECT

A multiple-of-three change preserves the downstream frame, but amino acids are added or lost. If the edit crosses triplet boundaries, amino acids at the junction can also change. Protein function can still be affected.

Always connect the levels: DNA change, mRNA codons, amino-acid sequence, then possible protein effects. These examples concern coding sequences; do not apply the codon rule directly to an intron or regulatory region.

Insertions and their variable effects: NHGRI, Insertion.
Triplet code and in-frame changes: OpenStax Biology 2e, section 15.1.

Scope: Cambridge Biology 9700 syllabus, section 6.2, outcome 7, p. 25.