# Allele variants and ADH enzyme activity

***Adh-S*** and ***Adh-F*** are two alternative forms of the same gene, *Adh*. These are known as **alleles**, and code for the enzyme alcohol dehydrogenase (ADH) in natural populations of *Drosophila melanogaster*.
*Adh* is said to be **polymorphic**.

Answer the questions below to identify where *Adh-S* and *Adh-F* differ at the genetic level and determine what effect this may have at the protein level.

1. **The coding DNA strand below represents a section of the nucleotide sequence that codes for the *Adh-S* allele of the *Adh* gene.**

| | |
|---|---|
| **DNA (coding strand)** | C A C / A A G / T T C / A A C / T C C / T G G |
| **DNA (template strand)** | G T C / T T C / A A G / T T G / A G G / A C C |
| **mRNA strand** | C A C / A A G / U U C / A A C / U C C / U G G |
| **Amino acid sequence** | His / Lys / Phe / Asn / Ser / Trp |

a. Determine the mRNA sequence from the coding DNA strand. Divide the sequence into triplet bases to help you.
b. Using the genetic code table, write out the sequence of amino acids for which the mRNA codes.
c. State the name of the process occurring in the cytoplasm that gives rise to a polypeptide chain.
Translation

2. **The coding DNA strand below represents the same section as above, but this time coding for the *Adh-F* allele of the *Adh* gene.**

| | |
|---|---|
| **DNA (coding strand)** | C A C / A **C** G / T T C / A A C / T C **T** / T G G |
| **DNA (template strand)** | G T C / T **G** C / A A G / T T G / A G **A** / A C C |
| **mRNA strand** | C A C / A **C** G / U U C / A A C / U C **U** / U G G |
| **Amino acid sequence** | His / **Thr** / Phe / Asn / Ser / Trp |

a. How do the nucleotide sequences coding for ADH-S and ADH-F differ? Underline the differences on the DNA coding strand.
b. Do these base changes affect the reading frame? What type of mutation is this?

Both mutations are base substitutions (no effect on the reading frame; note that a deletion or an insertion would have shifted the reading frame).

- First mutation (5th nuncleotide base): adenine to cytosine transversion (A→ C);
- Second mutation (15th nucleotide): cytosine to thymine transition (C → T).

*NB: If a purine is replaced by another purine (A↔G), or a pyrimidine is replaced by another pyrimidine (C↔T), this is called a **transition**. Transition mutations therefore involve bases of similar shape (one-ring OR two-ring).*
*If a purine is replaced by a pyrimidine or a pyrimidine by a purine, this is called a **transversion** (A↔ C, A↔T, G↔ C or G↔T). Transversions therefore involve the exchange of one-ring and two-ring structures.*

c. Write out the sequence of amino acids for which the mRNA codes. What effect does the first mutation have on the polypeptide chain? How about the second mutation?

The A → C transversion is responsible for the amino acid substitution Lysine → Threonine.

The C → T transition is silent as both codons (UCC and UCU) code for the amino acid Serine.
Note that the genetic code is **degenerate**.

**3. Suggest what effect the allele variants (*Adh-S* and *Adh-F*) may have on the final protein product.**

Students are prompted to think about how an amino acid substitution may impact upon protein function. The substituted amino acid may have properties that are different from the original amino acid, thus resulting in a non-functional protein, a less functional protein, or even a better functioning protein.
An amino acid substitution changes the primary structure of the protein and can therefore affect:

- Overall conformation (protein folding; secondary/tertiary/quaternary structure);
- Changes in the enzyme binding site (substrate or coenzyme/cofactor)
- Changes in the catalytic site.

**The Genetic Code**

| | U | C | A | G | |
|---|---|---|---|---|---|
| U | UUU Phenyl alanine<br>UUC<br>UUG Leucine<br>UUA | UCU Serine<br>UCC<br>UCA<br>UCG | UAU Tyrosine<br>UAC<br>UAA Stop<br>UAG | UGU Cysteine<br>UGC<br>UGA Stop<br>UGG Tryptophan | U<br>C<br>A<br>G |
| C | CUU Leucine<br>CUC<br>CUA<br>CUG | CCU Proline<br>CCC<br>CCA<br>CCG | CAU Histidine<br>CAC<br>CAA Glutamine<br>CAG | CGU Arginine<br>CGC<br>CGA<br>CGG | U<br>C<br>A<br>G |
| A | AUU Isoleucine<br>AUC<br>AUA<br>AUG Methionine | ACU Threonine<br>ACC<br>ACA<br>ACG | AAU Asparagine<br>AAC<br>AAA Lysine<br>AAG | AGU Serine<br>AGC<br>AGA Arginine<br>AGG | U<br>C<br>A<br>G |
| G | GUU Valine<br>GUC<br>GUA<br>GUG | GCU Alanine<br>GCC<br>GCA<br>GCG | GAU Aspartic acid<br>GAC<br>GAA Glutamic acid<br>GAG | GGU Glycine<br>GGC<br>GGA<br>GGG | U<br>C<br>A<br>G |