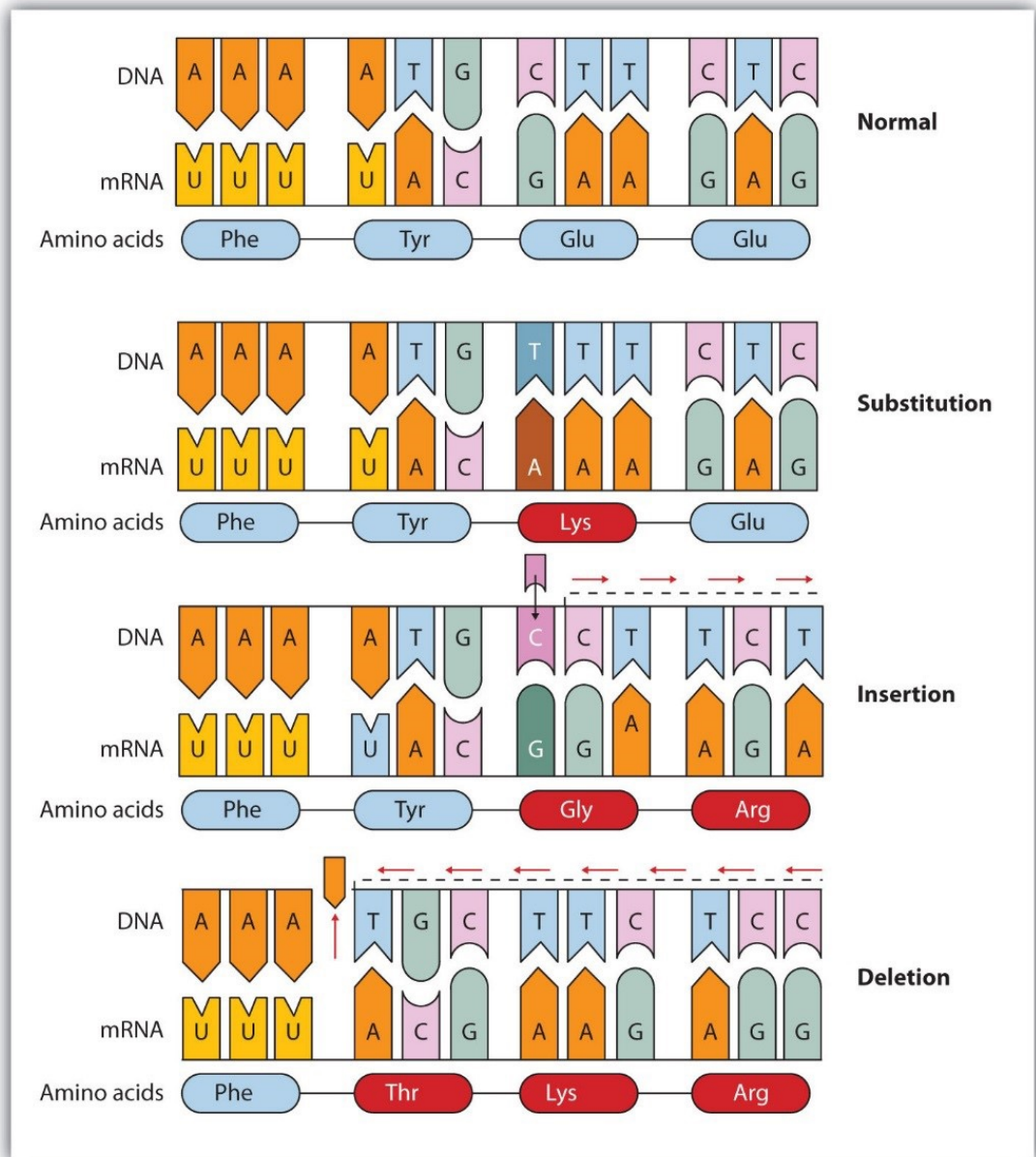


Lesson 13

DNA mutations and their outcome



Phenotype

- Changes in genes (DNA) govern the outcome for the organism
- How does a DNA sequence connect with a trait?
 - Trait = something that you can see, an observable characteristic
 - *E.g.*, your eye color, your hair color, your height,
- The composite observable characteristics or traits of an organism is called a **PHENOTYPE**

Gene \leftrightarrow phenotype



How does DNA sequence connect with a trait? (phenotype)
May alter protein sequence (and therefore function)
or amount of protein made.....

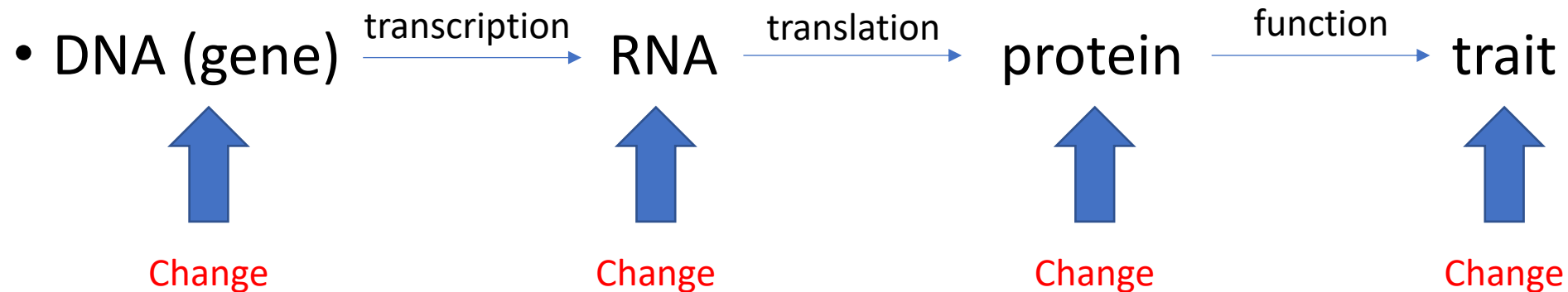


Mutations

- DNA (gene) $\xrightarrow{\text{transcription}}$ RNA $\xrightarrow{\text{translation}}$ protein $\xrightarrow{\text{function}}$ trait
- Trait = observable characteristic = **phenotype**

Mutations

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Mutations

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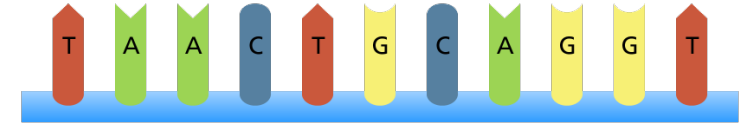


- Changes in DNA nucleotide sequences = **MUTATIONS**
- Mutated DNA generally:
 - Mutated RNA → Mutated protein → mutated trait

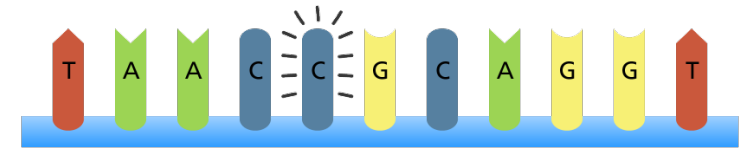
Mutation main types

- Point mutations: change 1 nucleotide of one type with another nucleotide of another type in the original sequence
 - *e.g.*, TAACTT... → TAACCT...

Original sequence



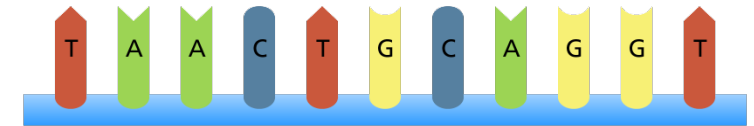
Point mutation



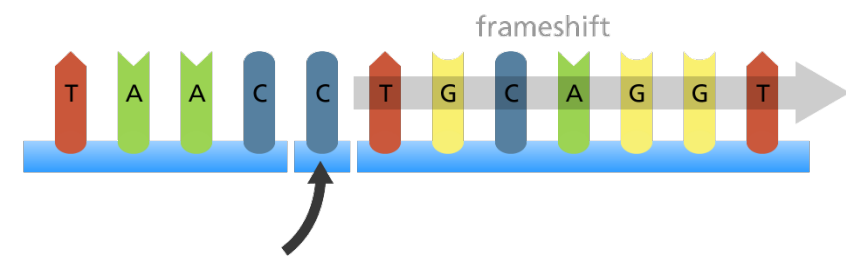
Mutation main types

- Point mutations: change 1 nucleotide of one type with another nucleotide of another type in the original sequence
 - *e.g.*, TAACTT... → TAACCT...
- Insertion: one or more nucleotides are added to the original sequence
 - *e.g.*, TAACT... → TAAC**C**T...

Original sequence



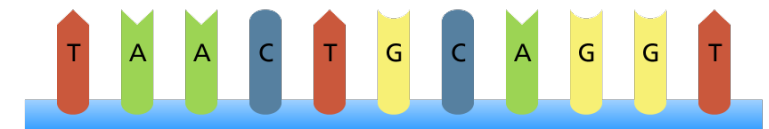
Insertion



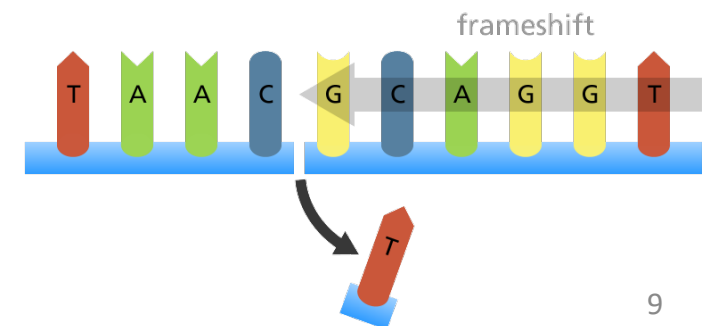
Mutation main types

- Point mutations: change 1 nucleotide of one type with another nucleotide of another type in the original sequence
 - *e.g.*, TAACTT... → TAACCT...
- Insertion: one or more nucleotides are added to the original sequence
 - *e.g.*, TAACT... → TAACCT...
- **Deletion: one or more nucleotides are removed from the original sequence**
 - *e.g.*, TAACT**T**GC... → TAACGC

Original sequence



Deletion



Point mutations

Coding strand → 5' ATGTGGCTCCTGGATTAA 3' DNA
Template strand → 3' TACACCGAGGACCTAATT5' DNA

mRNA → 5' AUGUGGCUCCUGGAUCAA 3'
protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutations

Coding strand → 5' ATGTGGCTCCTG **GAT** TAA 3' DNA
Template strand → 3' TACACCGAGGAC **CTA** ATT 5'
mRNA → 5' AUGUGGCUCCUG **GAU** UAA 3'
protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutation (**MISSENSE**)

Coding strand → 5' ATGTGGCTCCTG **GTT** TAA 3'
Template strand → 3' TACACCGAGGAC **CAA** ATT 5'
mRNA → 5' AUGUGGCUCCUG **GUU** UAA 3'
protein → N-Met-Trp-Leu-Leu-**Val**-C (stop)

Point mutations

Coding strand → 5' ATGTGGCTCCTGGATTAA 3' DNA
Template strand → 3' TACACCGAGGACCTAATT5'
mRNA → 5' AUGUGGCUC CUGGAUUAA 3'
protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutation (**NONSENSE**)

Coding strand → 5' ATGT**AG**CTCCTGGATTAA 3'
Template strand → 3' TAC**ATC**GAGGACCTAATT5'
mRNA → 5' AUG**UAG**CUC CUGGAUUAA 3'
protein → N-Met-**Stop**

Point mutations

Coding strand → 5' ATGTGGCTCCTGGATTAA 3' DNA
Template strand → 3' TACACCGAGGACCTAATT5'
mRNA → 5' AUGUGGCUCCUGGAUUA 3'
protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutation (SILENT)

Coding strand → 5' ATGTGGCTCCTGG**A**CTAA 3'
Template strand → 3' TACACCGAGGAC**CTG**ATT5'
mRNA → 5' AUGUGGCUCCUG**GAC**UAA 3'
protein → N-Met-Trp-Leu-Leu-**Asp**-C (stop)

Insertions

Coding strand → 5' ATGTGGCTCCTGGATTAA 3' DNA
Template strand → 3' TACACCGAGGACCTAATT5'
mRNA → 5' AUGUGGCUC CUGGAUUAA 3'
protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Insertion (reading frame shift)

Coding strand → 5' ATGTGG **ACT** CCTGGATTAA 3'
Template strand → 3' TACACCT **TGA** GGACCTAATT5'
mRNA → 5' AUGUGG **ACU** CCUGGAUUAA 3'
protein → N-Met-Trp-**Thr-Pro-Gly-Leu-C**

Reading frame shift →

Deletions

Coding strand → 5' ATGTG**G**CTCCTGGATTAA 3' DNA
Template strand → 3' TACAC**C**GAGGACCTAATT5'
mRNA → 3' AUGUG**G**CUCCUGGAUUAA 5'
protein → N-Met-**Trp**-Leu-**Leu**-Asp-C (stop)

Deletion (reading frame shift)

Coding strand → 5' ATGT**G**CTCCTGGATTAA 3'
Template strand → 3' TAC**A**CGAGGACCTAATT5'
mRNA → 5' AUG**U**GCUGGUGGAUUAA 3'
protein → N-Met-**Cys-Trp-Trp-Ile-C**

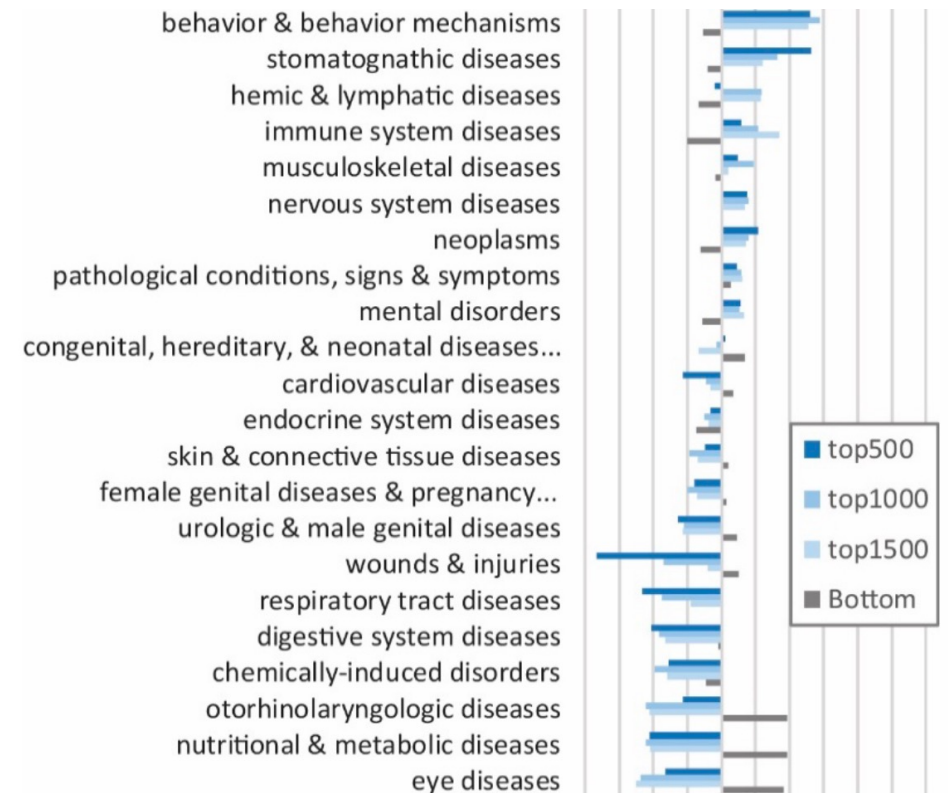
Reading frame shift

Mutations - recap

- **Missense mutation** → Changes one protein into another
- **Nonsense mutation** → Prematurely stops mRNA translation resulting in a truncated protein
- **Silent mutation** → The results of the translation is again the wild-type protein
 - This is because of the “redundancy” of the genetic code (more codons codify for the same amino acid – see The codon chart)
- **Insertion/deletion** → Change the reading frame and the protein that is encoded in the mutated gene

Mutations - recap

- Proteins resulting from any of these gene mutations (except from silent mutations) may:
 - Be non-functional (**loss of function**)
 - Be over-functional (**gain of function**)
 - Have a **new function**
- All these aspects may result in **important human pathologies**



Other mutations

- There are a plethora of other mutations that take place in other DNA regions
 - *e.g.*, the so-called “DNA control region”
 - That DNA region (sequence) that controls RNA synthesis and transcription
 - This can change *e.g.*, the amount of mRNA and, hence, of protein produced