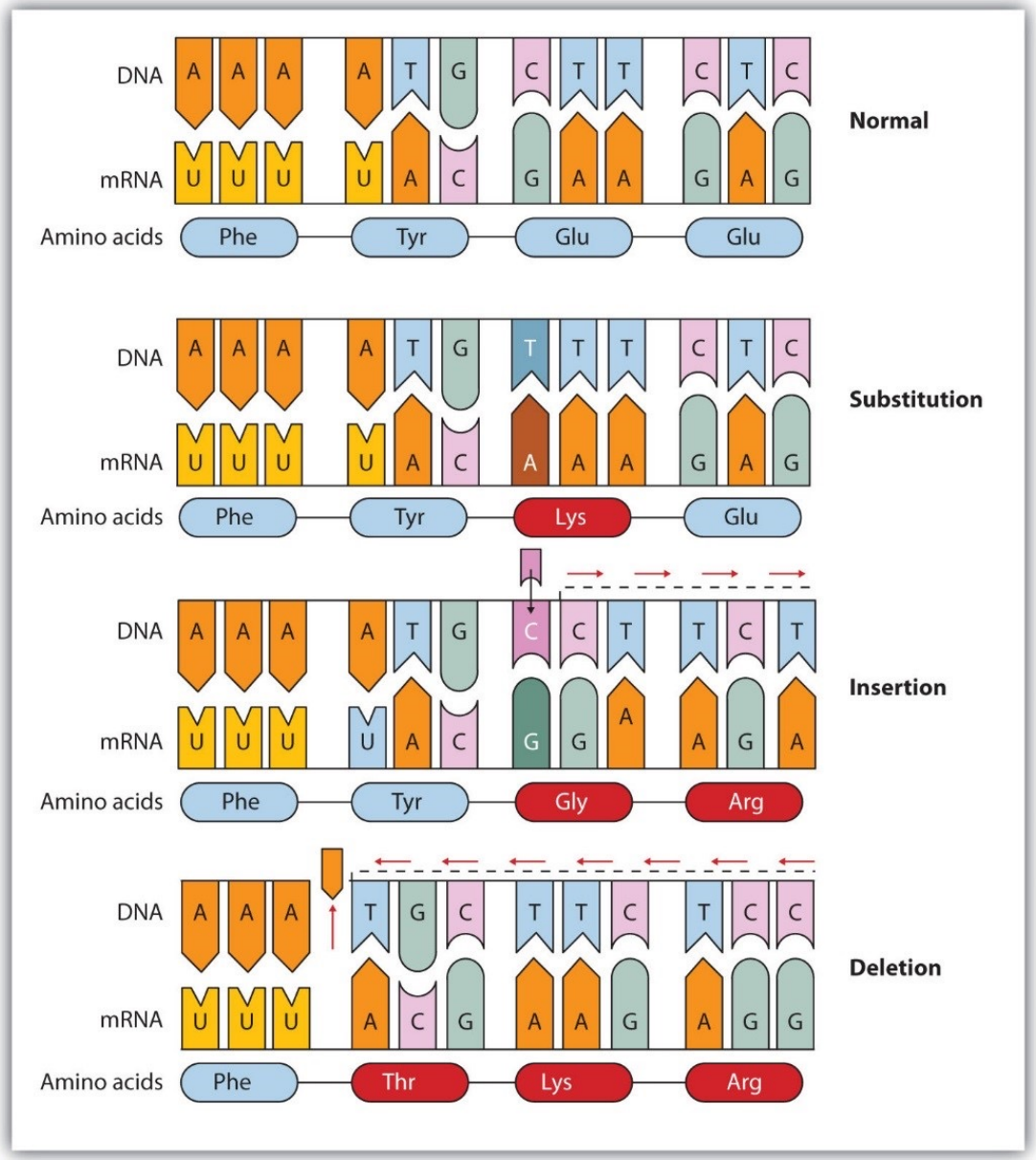
Lesson 13
DNA mutations and their outcome



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 ←→ phenotype

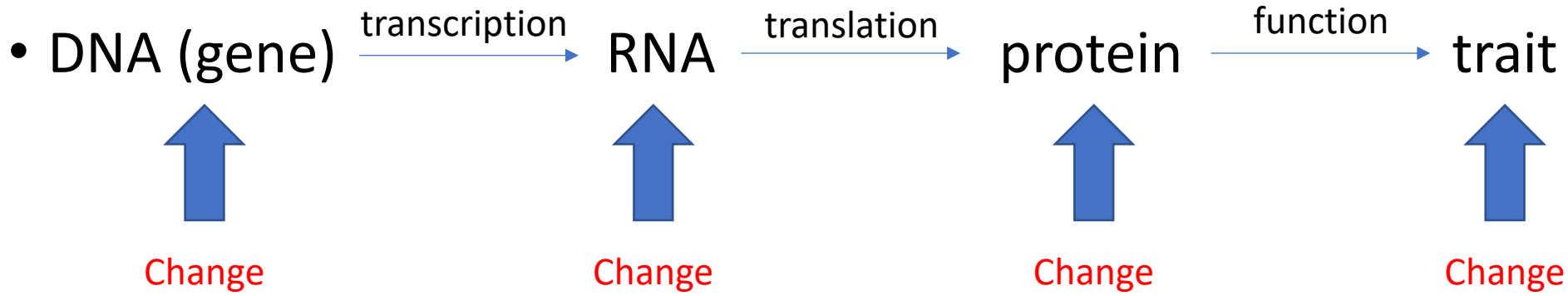
How does DNA sequence connect with a trait? (phenotype)
May alter protein sequence (and therefore function)
or amount of protein made…..

Mutations

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

Mutations

- DNA (gene) —transcription→ RNA —translation→ protein —function→ trait
- Trait = observable characteristic = **phenotype**



Mutations

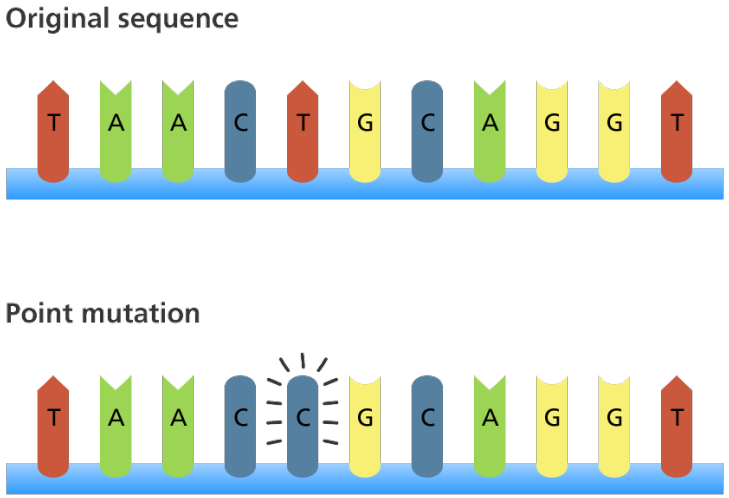
- DNA (gene) transcription RNA translation protein function trait
- Trait = observable characteristic = **phenotype**

- DNA (gene) transcription RNA translation protein function trait

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

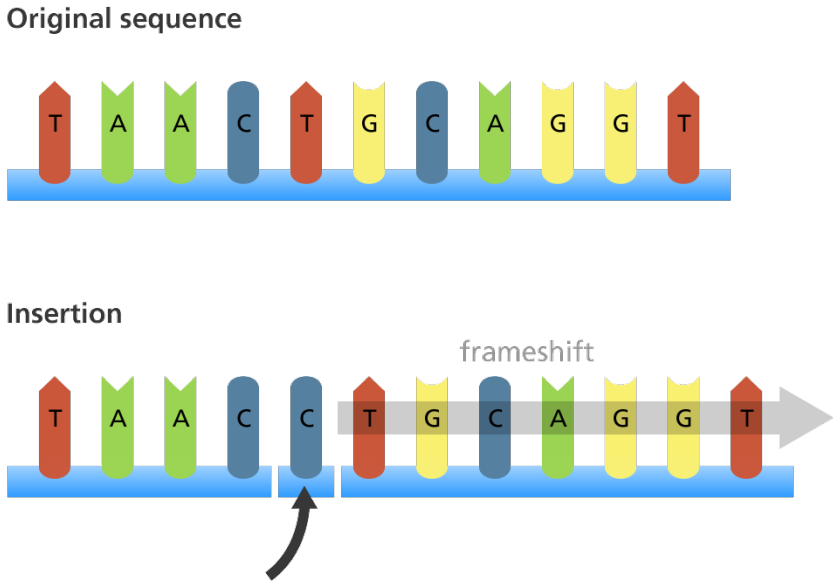
Mutation main types

- Point mutations: change 1 nucleotide of one type with another nucleotide of another type in the original sequence
  - *e.g.*, TAAC**T**T… → TAAC**C**T…



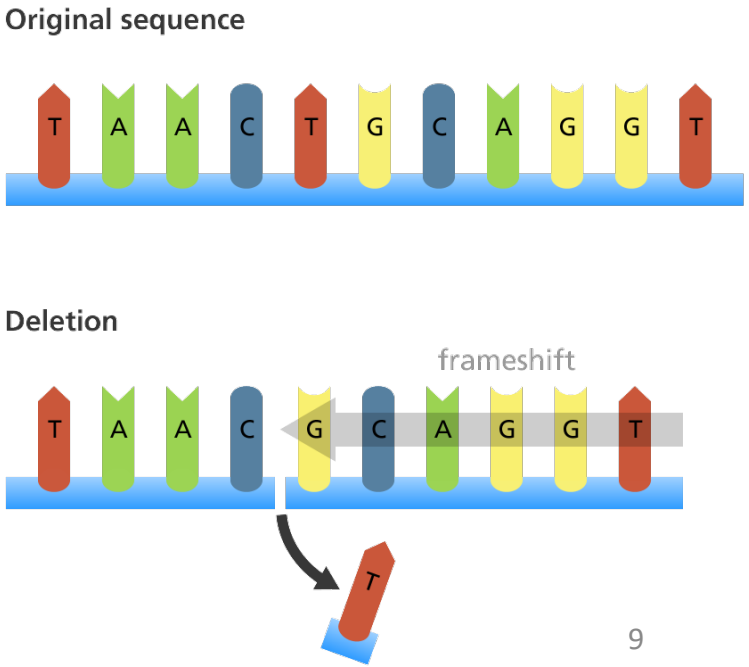
Mutation main types

- 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…



Mutation main types

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



Point mutations

Coding strand → 5’ ATGTGGCTCCTGGATTAA 3’

Template strand → 3’TACACCGAGGACCTAATT5’

DNA

mRNA → 5’ AUGUGGCUCCUGGAUUAA 3’

protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutations

Coding strand → 5’ ATGTGGCTCCTGGATTAA 3’

Template strand → 3’TACACCGAGGACCTAATT5’

DNA

mRNA → 5’ AUGUGGCUCCUGGAUUAA 3’

protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutation (**MISSENSE**)

Coding strand → 5’ ATGTGGCTCCTGGTTTAA 3’

Template strand → 3’ TACACCGAGGACC**A**AATT5’

mRNA → 5’ AUGUGGCUCCUGG**U**UUAA 3’

protein → N-Met-Trp-Leu-Leu**-Val-C** (stop)

Point mutations

Coding strand → 5’ ATGTGGCTCCTGGATTAA 3’

Template strand → 3’ TACACCGAGGACCTAATT5’

DNA

mRNA → 5’ AUGUGGCUCCUGGAUUAA 3’

protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutation (**NONSENSE**)

Coding strand → 5’ ATGTAGCTCCTGGATTAA 3’

Template strand → 3’ TACATCGAGGACCTAATT5’

mRNA → 5’ AUGUAGCUCCUGGAUUAA 3’

protein → N-Met-**Stop**

Point mutations

Coding strand → 5’ ATGTGGCTCCTGGATTAA 3’

Template strand → 3’ TACACCGAGGACCTAATT5’

DNA

mRNA → 5’ AUGUGGCUCCUGGAUUAA 3’

protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Point mutation (**SILENT**)

Coding strand → 5’ ATGTGGCTCCTGGACTAA 3’

Template strand → 3’ TACACCGAGGACCT**G**ATT5’

mRNA → 5’ AUGUGGCUCCUGGA**C**UAA 3’

protein → N-Met-Trp-Leu-Leu**-Asp-C** (stop)

Insertions

Coding strand → 5’ ATGTGGCTCCTGGATTAA 3’

Template strand → 3’ TACACCGAGGACCTAATT5’

DNA

mRNA → 5’ AUGUGGCUCCUGGAUUAA 3’

protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Insertion (reading frame shift)

Coding strand → 5’ ATGTGG**A**CTCCTGGATTAA 3’

Template strand → 3’ TACACC**T**GAGGACCTAATT5’

Reading frame shift

mRNA → 5’ AUGUGG**A**CUCCUGGAUUAA 3’

protein → N-Met-Trp-**Thr-Pro-Gly-Leu-C**

Deletions

Coding strand → 5’ ATGTGGCTCCTGGATTAA 3’

Template strand → 3’ TACACCGAGGACCTAATT5’

DNA

mRNA → 3’ AUGUGGCUCCUGGAUUAA 5’

protein → N-Met-Trp-Leu-Leu-Asp-C (stop)

Deletion (reading frame shift)

Coding strand → 5’ ATGTGCTCCTGGATTAA 3’

Template strand → 3’ TACACGAGGACCTAATT5’

Reading frame shift

mRNA → 5’ AUGUGCUGGUGGAUUAA 3’

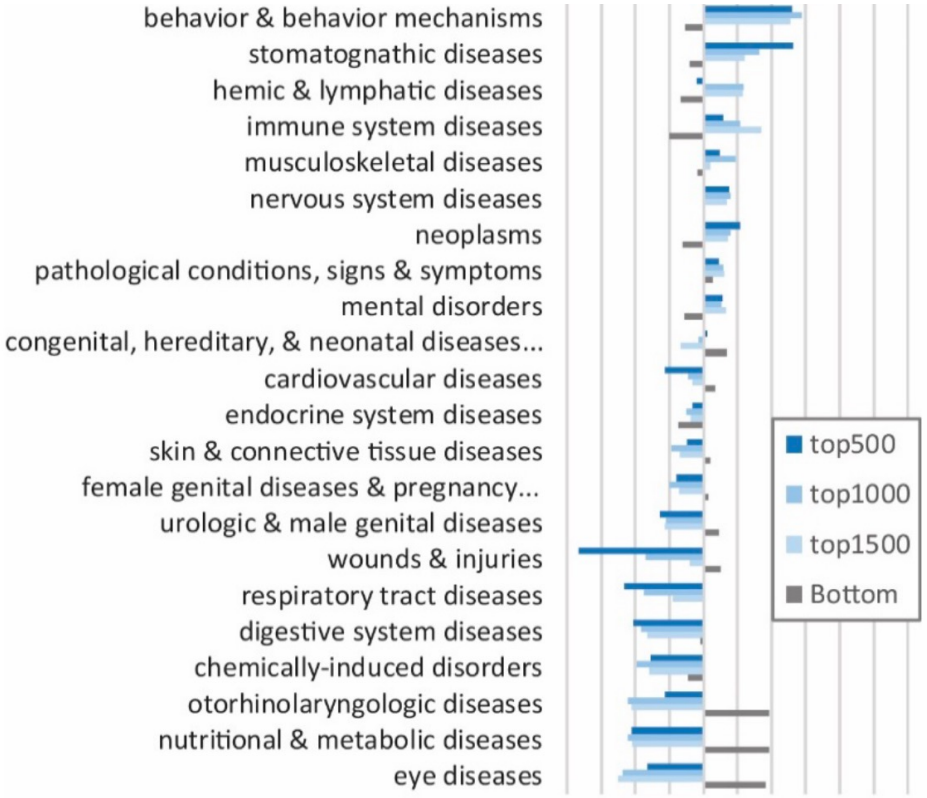
protein → N-Met-**Cys-Trp-Trp-Ile-C**

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