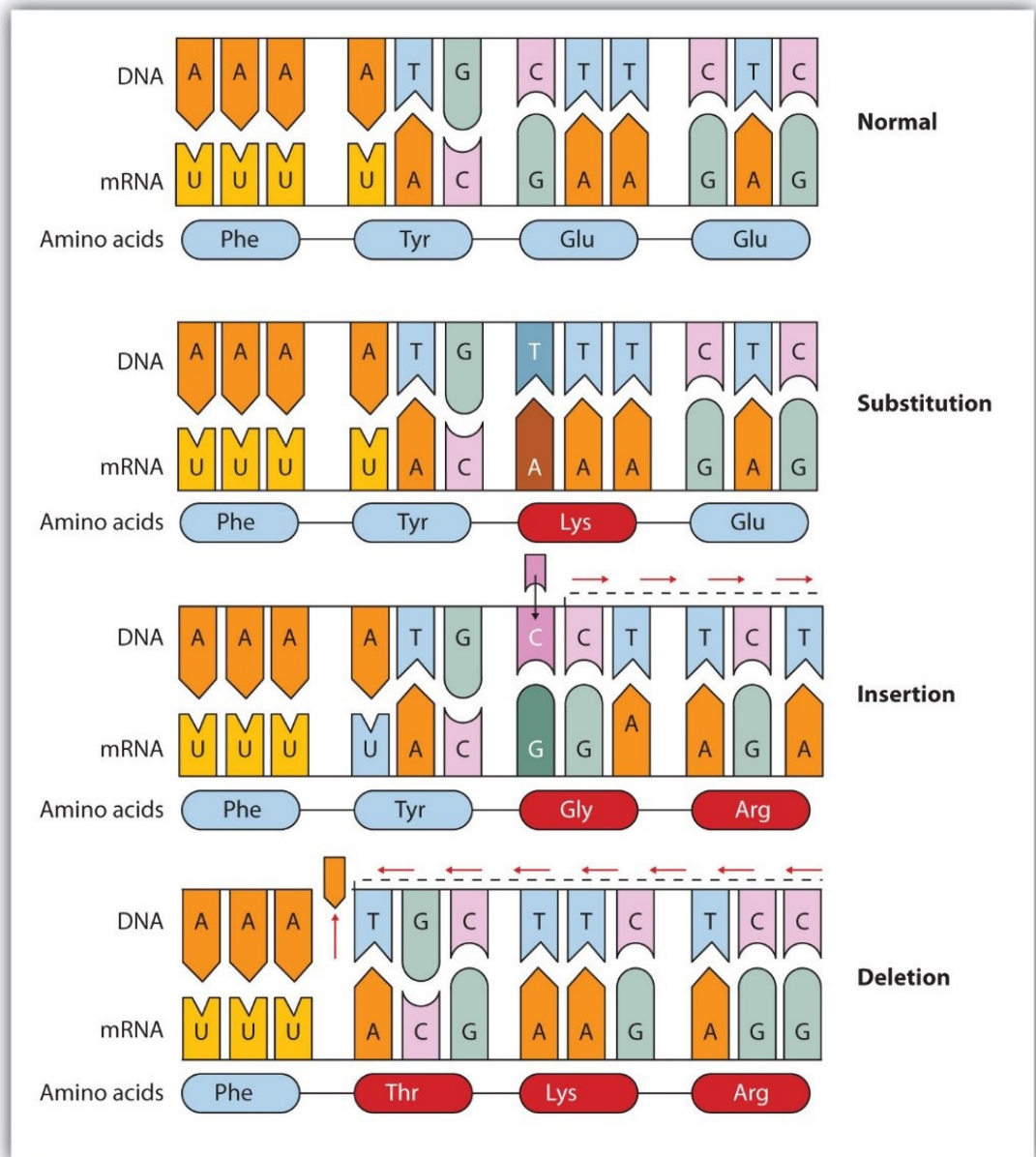# Lesson 13
DNA mutations and their outcome

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)
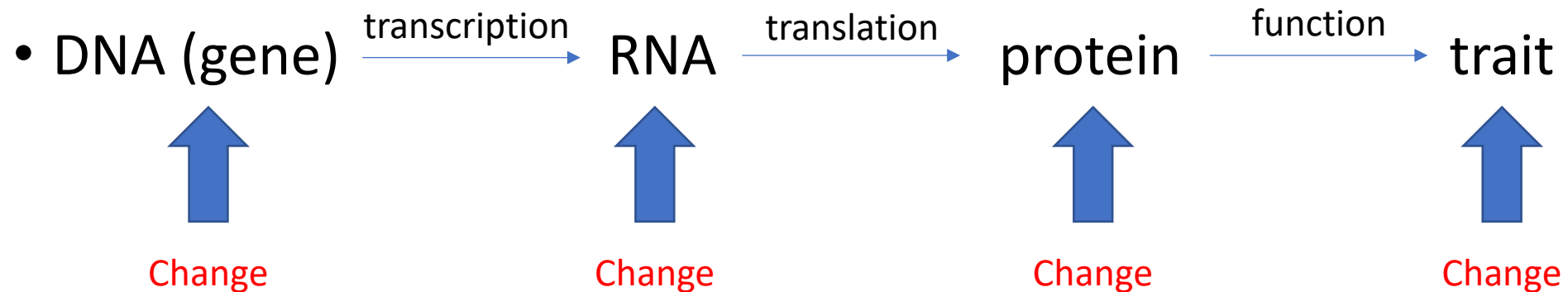or amount of protein made.....

Mutations

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

Mutations

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

- DNA (gene) $\xrightarrow{\text{transcription}}$ RNA $\xrightarrow{\text{translation}}$ protein $\xrightarrow{\text{function}}$ trait

Change   Change   Change   Change

Mutations

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

- DNA (gene) —transcription→ RNA —translation→ protein —function→ trait

Change   Change   Change   Change
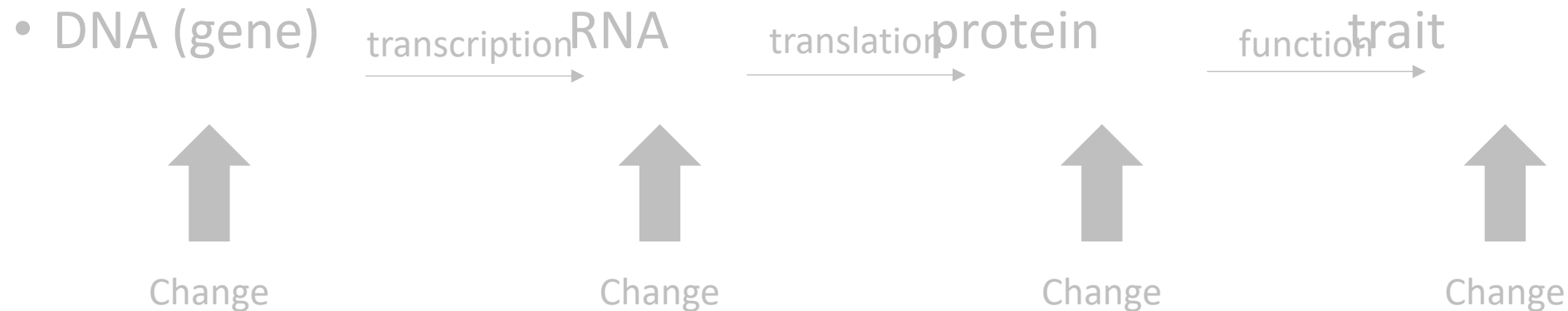
- Changes in DNA nucleotide sequences = **MUTATIONS**

- Mutated DNA generally:
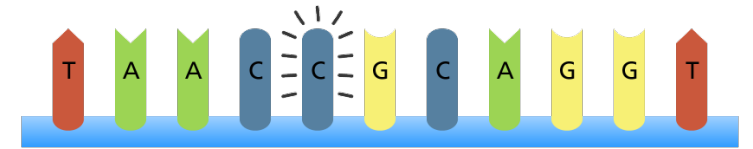 - Mutated RNA –> Mutated protein → mutated trait

Mutation main types

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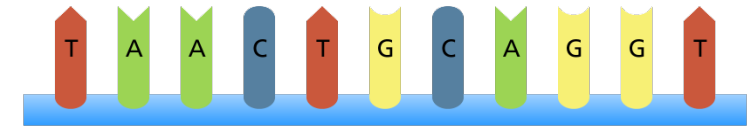 - *e.g.,* TAAC**T**T... → TAAC**C**T...

Original sequence
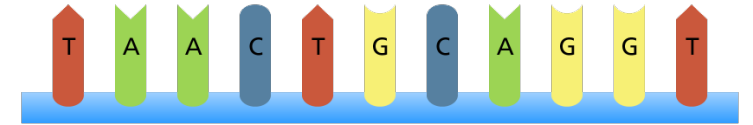
Point mutation

Mutation main types

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

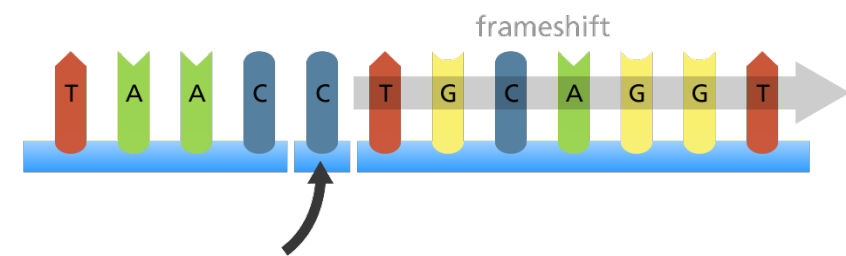**Original sequence**


Insertion

frameshift

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**

Original sequence
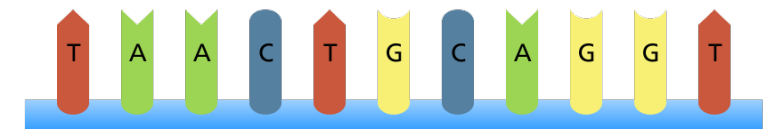
Deletion
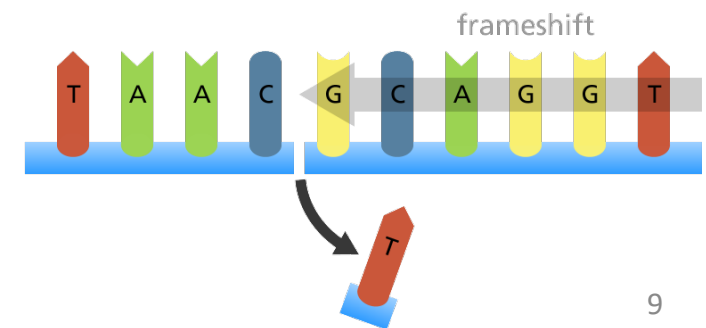
frameshift

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' ATGTGGCTCCTG GAT TAA 3'

Template strand → 3' TACACCGAGGAC CTA ATT 5'   DNA

mRNA → 5' AUGUGGCUCCUG GAU UAA 3'

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

Point mutation (**MISSENSE**)

Coding strand → 5' ATGTGGCTCCTG G**T** TAA 3'

Template strand → 3' TACACCGAGGAC C**A** ATT 5'

mRNA → 5' AUGUGGCUCCUG G**U** 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' AUGUGGCUCCUGGAUUAA 3'

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

Point mutation (**NONSENSE**)

Coding strand   →   5' ATG**TA**GCTCCTGGATTAA 3'

Template strand   →   3' TACA**T**CGAGGACCTAATT5'

mRNA →   5' AUGU**A**GCUCCUGGAUUAA 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' TACACCGAGGACCTGATT5'

mRNA → 5' AUGUGGCUCCUGGACUAA 3'

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

Insertions

Coding strand → 5' ATGTGGCTCCTGGATTAA 3'   DNA

Template strand → 3' TACACCGAGGACCTAATT 5'

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**GAGGACCTAATT 5'

Reading frame shift

mRNA → 5' AUGUGG**A**CUCCUGGAUUAA 3'

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

Deletions

Coding strand   →   5' ATGTGGCTCCTGGATTAA 3'   DNA

Template strand   →   3' TACACCGAGGACCTAATT5'

mRNA →   3' AUGUGGCUCCUGGAUUAA 5'

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

Deletion (reading frame shift)

Coding strand   →   5' ATG TGC TCCTGGATTAA 3'

Template strand   →   3' TAC ACG AGGACCTAATT5'

Reading frame shift

mRNA →   5' AUG UGC UGGUGGAUUAA 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**
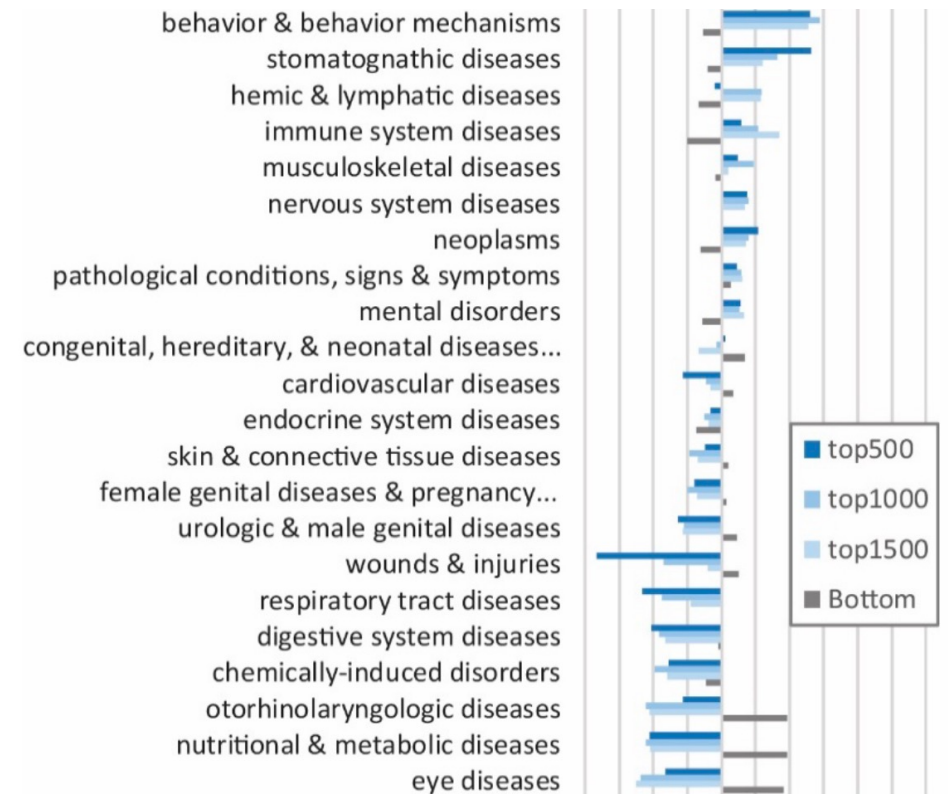
Other mutations

- 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