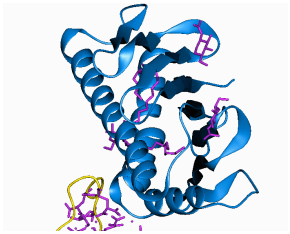
An example of how a change in a gene leads to a disorder

Disease: Hemophilia
Gene: Clotting factor gene
Protein: Clotting factor
Mutation: many different kinds & severities
Result for affected: -- can't clot wounds
-- bleed excessively



Genes can be affected by different kinds of mutations:

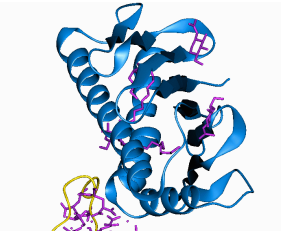
A deletion

Does not have disease	Has disease
5'–…ATGCCG**ATCGTTATCGGA**TCT…–3' 3'–…TACGGC**TAGCAATAGCCT**AGA…–5'	5'–…ATGCCGTCT…–3' 3'–…TACGGCAGA…–5'

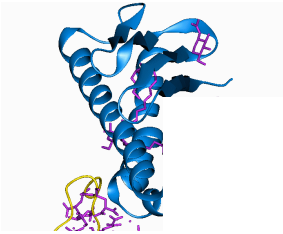
DNA → mRNA → protein

How do changes in genes lead to diseases?

An example of how a deletion mutation can cause loss of protein function



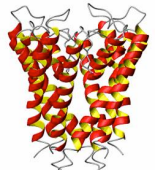
Clotting factor protein
(not mutated)
in people without hemophilia



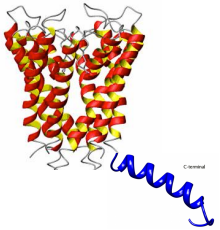
Clotting factor protein
(mutated with deletion)
in people with hemophilia

- Would providing the non-mutated gene or protein help the patient?
- What could a drug do, in this case, in order to help the patient?

An example of how an insertion mutation can cause a gain of a new protein function



Non-mutated protein
in people without the disease



Mutated protein
in people with the disease

- Would providing the non-mutated gene or protein help the patient?
- What could a drug do, in this case, in order to help the patient?

Genes can be affected by different kinds of mutations:

An insertion

Does not have disease

5'–…ATGCCGATCGTTATCGGA**TC**T…–3'
3'–…TACGGCTAGCAATAGCCT**AG**A….–5'

Has disease

5'–ATGCCGATCGTTATCGGA**T**ATACCGGTC**C**T…–3'
3'–TACGGCTAGCAATAGCCT**A**TATGGCCAG**G**A….–5'

Genes can be affected by different kinds of mutations:

A substitution

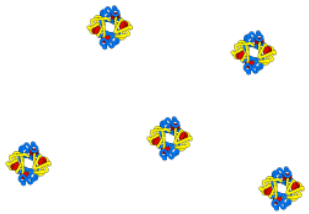
Does not have disease

5'–…ATGCCGATCGTTATCGGATCT…–3'
3'–…TACGGCTAGCAATAGCCTAGA….–5'

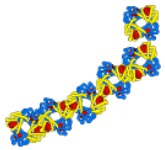
Has disease

5'–…ATGCCAATCGTTATCGGATCT…–3'
3'–…TACGGTTAGCAATAGCCTAGA….–5'

An example of how a substitution can cause gain of a new protein function



Non-mutated hemoglobin
in people without sickle cell anemia



Mutated hemoglobin
in people with sickle cell anemia

- Would providing the non-mutated gene or protein help the patient?
- What could a drug do, in this case, in order to help the patient?

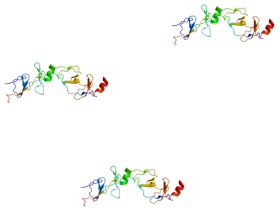
Genes can be affected by different kinds of mutations:

A regulatory mutation

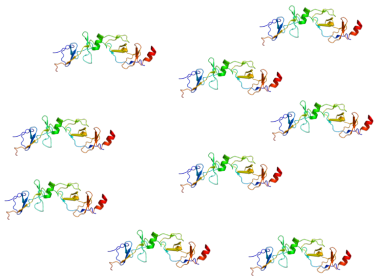
Does not have disease	Has disease
5'–…ATGCCGATCGTTATCGGATCT…–3' 3'–…TACGGCTAGCAATAGCCTAGA…–5'	5'–…ATGCCGATCGTTATCGGATCT…–3' 3'–…TACGGCTAGCAATAGCCTAGA…–5'

Mutated DNA sequence would occur here,
in the DNA sequences that regulate when this gene is "on" or "off"

An example of how a regulatory mutation can cause increased protein function



Non-mutated protein
in people without the disease



Non-mutated protein
in people with the disease

- Would providing the non-mutated gene or protein help the patient?
- What could a drug do, in this case, in order to help the patient?

An anti-cancer drug binding and inhibiting a protein mutated in some cancer cells