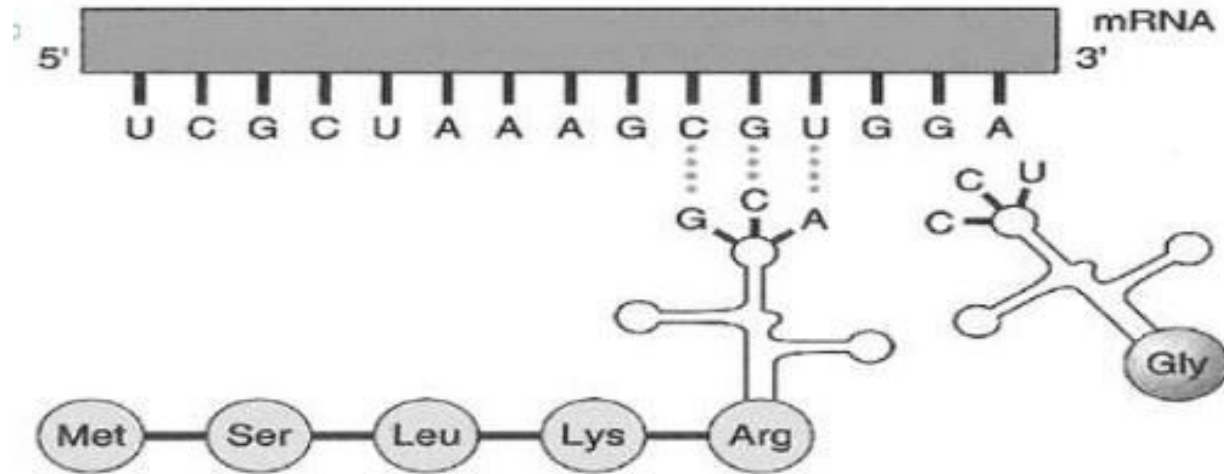


Genetic code

Introduction



Introduction The pathway of protein synthesis is called Translation because the language of nucleotide sequence on mRNA is translated in to the language of an amino acid sequence.

The process of Translation requires a Genetic code, through which the information contained in nucleic acid sequence is expressed to produce a specific sequence of amino acids

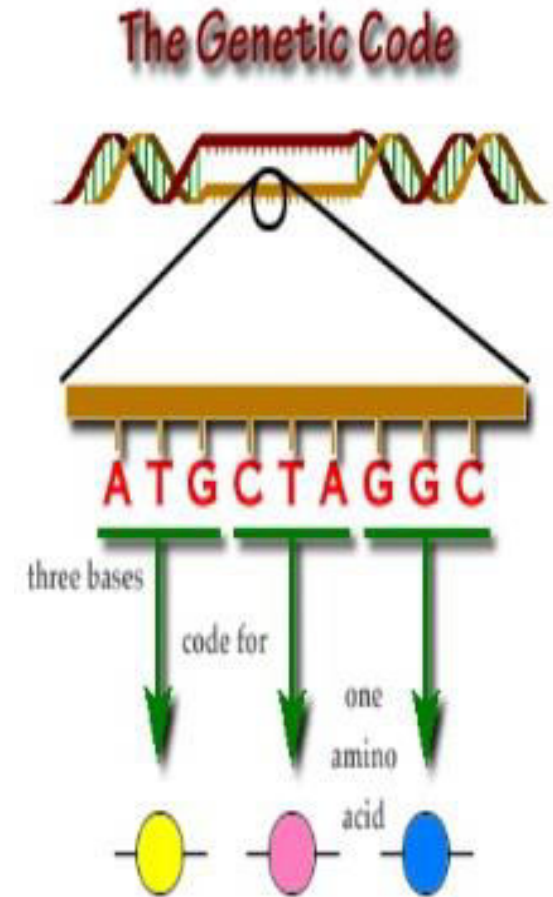
Genetic code

Genetic Code The letters A, G, T and C correspond to the nucleotides found in DNA.

They are organized into codons. The collection of codons is called Genetic code.

For 20 amino acids there should be 20 codons.

Each codon should have 3 nucleotides to impart specificity to each of the amino acid for a specific codon



- Genetic code is a dictionary that corresponds with sequence of nucleotides and sequence of Amino Acids.
- Words in dictionary are in the form of codons
- Each codon is a triplet of nucleotides
- 64 codons in total and three out of these are Non Sense codons.
- 61 codons for 20 amino acids

Genetic code table

| | | Second Letter | | | | | | | | | |
|---------------|-----------|---------------|------------|------------|-----------|------------------|---------------|-----------|-----------|------------|------------|
| | | U | | C | | A | | G | | | |
| 1st letter | U | UUU Phe | UCU Ser | UAU Tyr | UGU Cys | U C A G | 3rd letter | UUC Leu | UCC Ser | UAC Stop | UGC Stop |
| | UUA Leu | UCA Ser | UAA Stop | UGA Stop | UGG Trp | | | | | | |
| | UUG Leu | UCG Ser | UAG Stop | UGG Trp | | | | | | | |
| | | | | | | | | | | | |
| 1st letter | C | CUU Leu | CCU Pro | CAU His | CGU Arg | U C A G | 3rd letter | CUC Leu | CCC Pro | CAC Gln | CGC Arg |
| | CUA Leu | CCA Pro | CAA Gln | CGA Arg | | | | | | | |
| | CUG Leu | CCG Pro | CAG Gln | CGG Arg | | | | | | | |
| | | | | | | | | | | | |
| 1st letter | A | AUU Ile | ACU Thr | AAU Asn | AGU Ser | U C A G | 3rd letter | AUC Ile | ACC Thr | AAC Lys | AGC Arg |
| | AUA Ile | ACA Thr | AAA Lys | AGA Arg | | | | | | | |
| | AUG Met | ACG Thr | AAG Lys | AGG Arg | | | | | | | |
| | | | | | | | | | | | |
| 1st letter | G | GUU Val | GCU Ala | GAU Asp | GGU Gly | U C A G | 3rd letter | GUC Val | GCC Ala | GAC Glu | GGC Gly |
| | GUA Val | GCA Ala | GAA Glu | GGA Gly | | | | | | | |
| | GUG Val | GCG Ala | GAG Glu | GGG Gly | | | | | | | |
| | | | | | | | | | | | |

Genetic Code-Characteristics

- **Specificity-** Genetic code is specific (Unambiguous)
- A specific codon always codes for the same amino acid.e.g. UUU codes for Phenyl Alanine,
 - it can not code for any other amino acid
- **Universal-** In all living organism Genetic code is the same.
- The exception to universality is found in mitochondrial codons where AUA codes **for methionine** and UGA for **tryptophan**, instead of isoleucine and termination codon respectively of cytoplasmic protein synthesizing machinery.
- AGA and AGG code for Arginine in cytoplasm but in mitochondria they are termination codons

Genetic Code-Redundant

Redundant- Genetic code is Redundant, also called Degenerate.

Although each codon corresponds to a single amino acid but a single amino acid can have multiple codons.

Except **Tryptophan** and **Methionine** each amino acid has multiple codon

| | U | C | A | G |
|---|--|--------------------------------------|---|---|
| U | UUU } Phe UUC } UUA } Leu UUG } | UCU } Ser UCC } UCA } UCG } | UAU } Tyr UAC } UAA } Stop UAG } | UGU } Cys UGC } UGA } Stop UGG } Trp |
| C | CUU } Leu CUC } CUA } CUG } | CCU } Pro CCC } CCA } CCG } | CAU } His CAC } CAA } Gln CAG } | CGU } Arg CGC } CGA } CGG } |
| A | AUU } Ile AUC } AUA } AUG } Met | ACU } Thr ACC } ACA } ACG } | AAU } Asn AAC } AAA } Lys AAG } | AGU } Ser AGC } AGA } Arg AGG } |
| G | GUU } Val GUC } GUA } GUG } | GCU } Ala GCC } GCA } GCG } | GAU } Asp GAC } GAA } Glu GAG } | GGU } Gly GGC } GGA } GGG } |

Genetic Code- Non Overlapping

- Non Punctuated- All codons are independent sets of 3 bases.
- There is no overlapping ,
- Codon is read from a fixed starting point as a continuous sequence of bases, taken three at a time.
- The starting point is extremely important and this is called **Reading frame**.

Non Sense Codons

There are 3 codons out of 64 in genetic code which do not encode for any Amino Acid.

These are called termination codons or stop codons or nonsense codons.

The stop codons are UAA, UAG, and UGA.

They encode no amino acid.

The ribosome pauses and falls off the mRNA.

| | | Second letter | | | | |
|---|-----------|---------------|------------|------------|------------------|--|
| | | U | C | A | G | |
| U | UUU } Phe | UCU } Ser | UAU } Tyr | UGU } Cys | U C A G | |
| | UUC } Phe | UCC } Ser | UAC } Tyr | UGC } Cys | | |
| | UUA } Leu | UCA } Ser | UAA } Stop | UGA } Stop | | |
| | UUG } Leu | UCG } Ser | UAG } Stop | UGG } Trp | | |
| C | CUU } Leu | CCU } Pro | CAU } His | CGU } Arg | U C A G | |
| | CUC } Leu | CCC } Pro | CAC } His | CGC } Arg | | |
| | CUA } Leu | CCA } Pro | CAA } Gln | CGA } Arg | | |
| | CUG } Leu | CCG } Pro | CAG } Gln | CGG } Arg | | |
| A | AUU } Ile | ACU } Thr | AAU } Asn | AGU } Ser | U C A G | |
| | AUC } Ile | ACC } Thr | AAC } Asn | AGC } Ser | | |
| | AUA } Ile | ACA } Thr | AAA } Lys | AGA } Arg | | |
| | AUG } Met | ACG } Thr | AAG } Lys | AGG } Arg | | |
| G | GUU } Val | GCU } Ala | GAU } Asp | GGU } Gly | U C A G | |
| | GUC } Val | GCC } Ala | GAC } Asp | GGC } Gly | | |
| | GUA } Val | GCA } Ala | GAA } Glu | GGA } Gly | | |
| | GUG } Val | GCG } Ala | GAG } Glu | GGG } Gly | | |

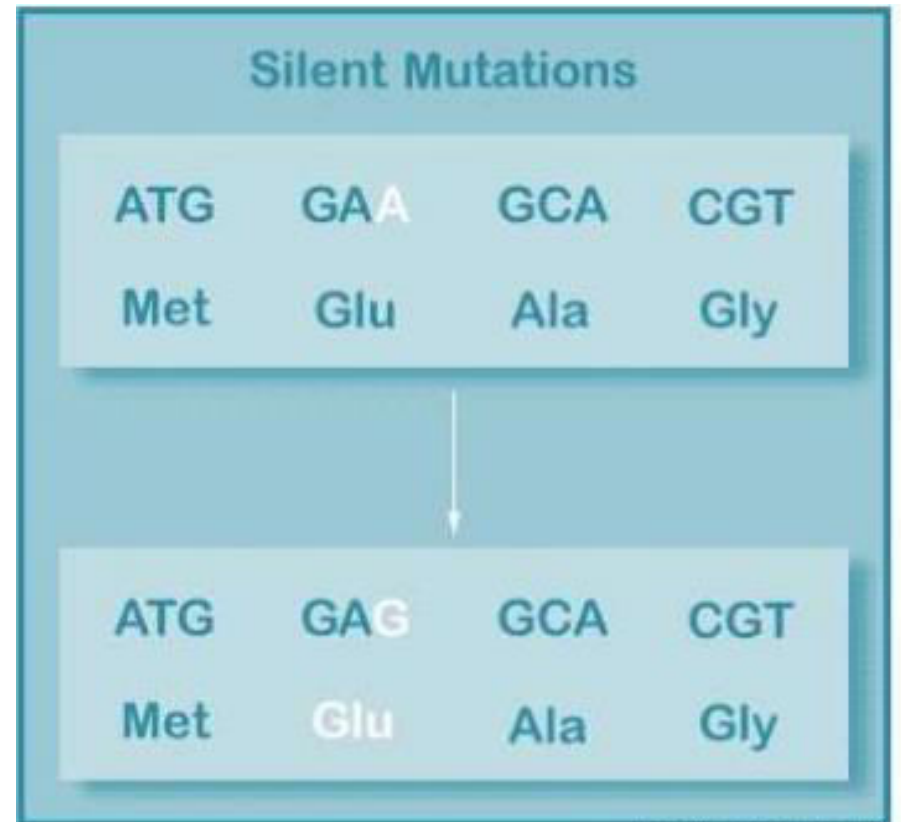
Initiator codon

- AUG is the initiator codon in majority of proteins-
- In a few cases GUG may be the initiator codon
- Methionine is the only amino acid specified by just one codon, AUG
- **Clinical Significance**
 - Mutations can be well explained using the genetic code.
 - A) Point Mutations
 - 1) Silent
 - 2) Misense
 - 3)Nonsense
 - B) Frame shift mutations

Silent Mutations

Single nucleotide change-A to G, same amino acid is incorporated.

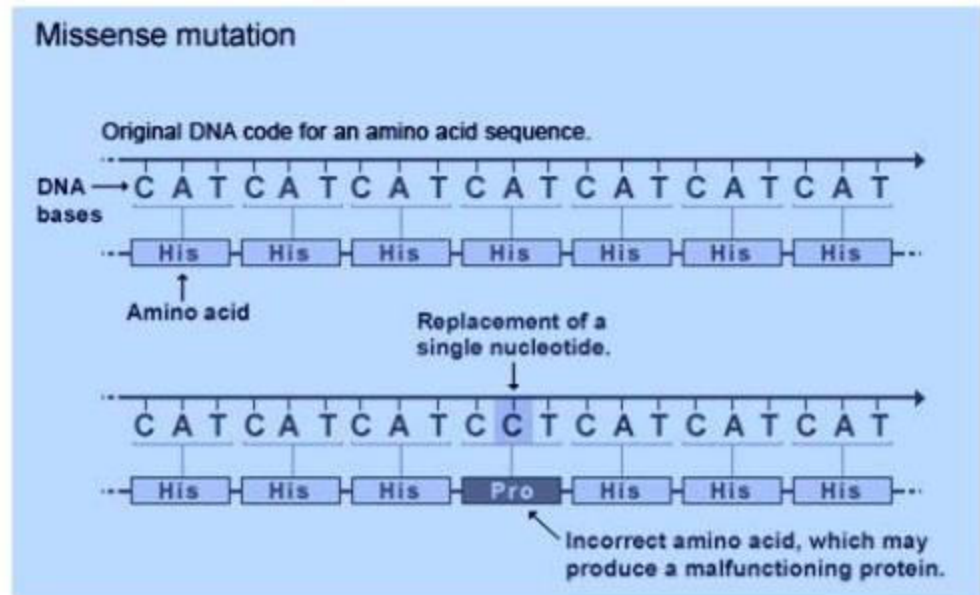
Mutation goes unnoticed



Missense mutations

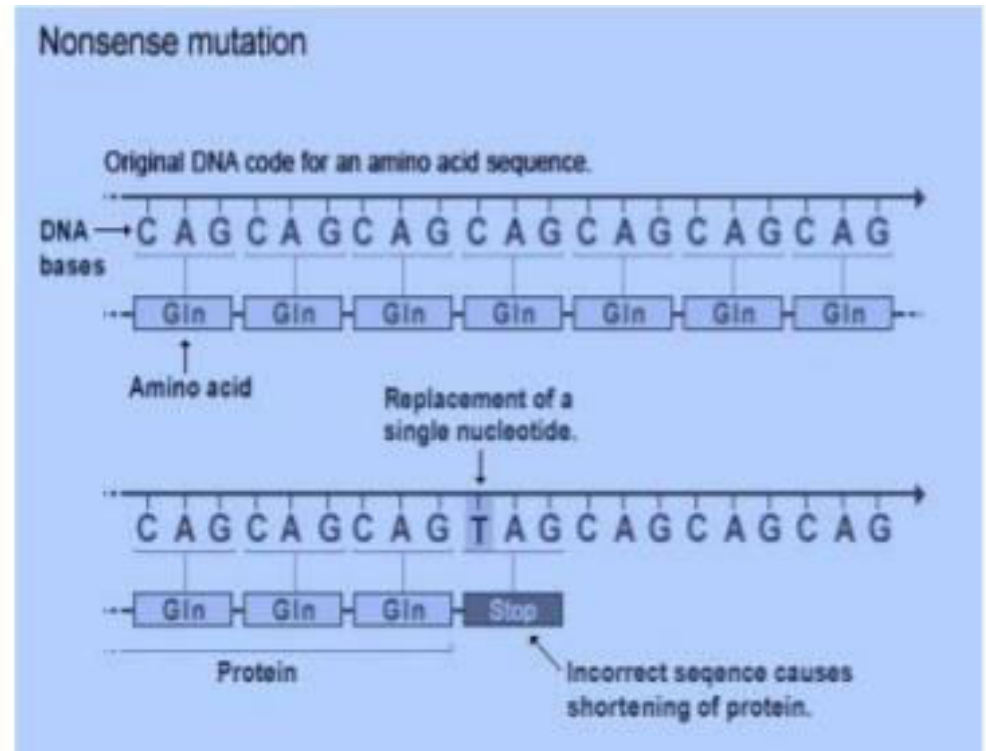
Single nucleotide change
A to C – different amino
acid incorporated.

Loss of functional capacity
of protein



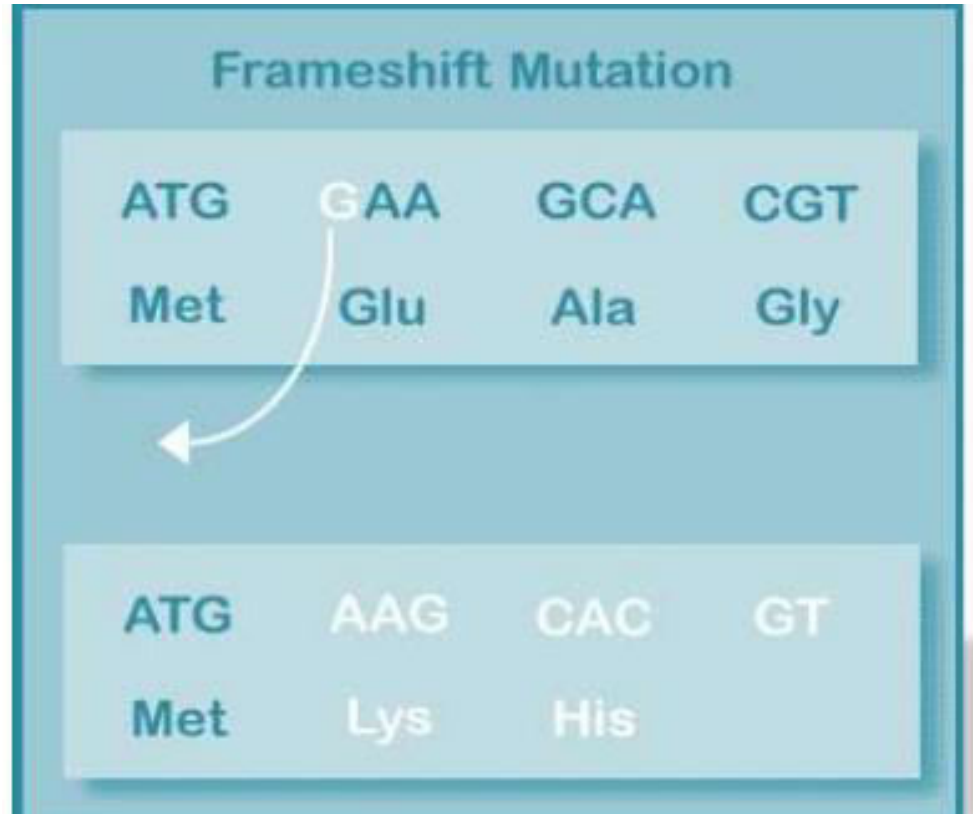
Non sense Mutation

Single nucleotide change from C to T, stop codon is generated (In m RNA represented by UAG), premature termination of chain, may be incompatible with life



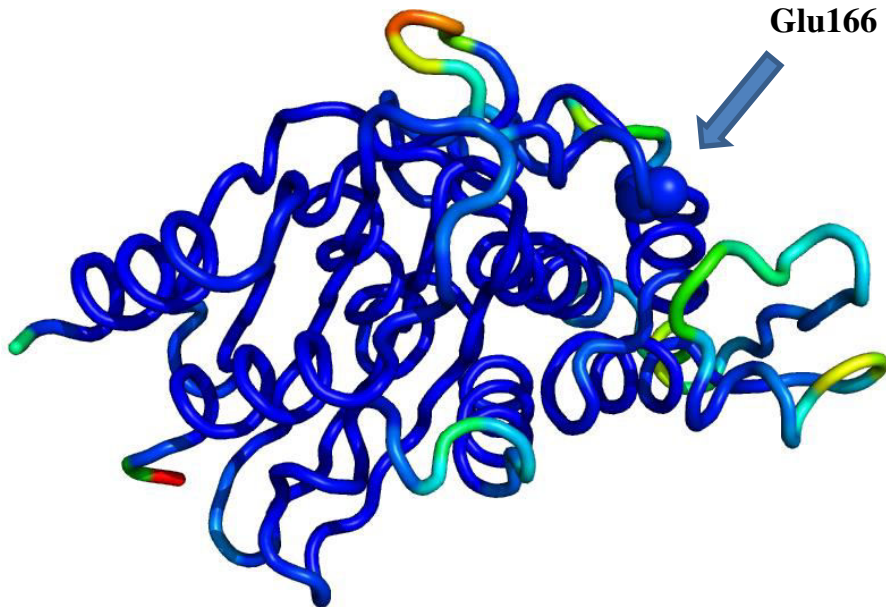
Frame shift Mutations

Insertion or removal of a base/bases can alter the reading frame with the resultant incorporation of different amino acids

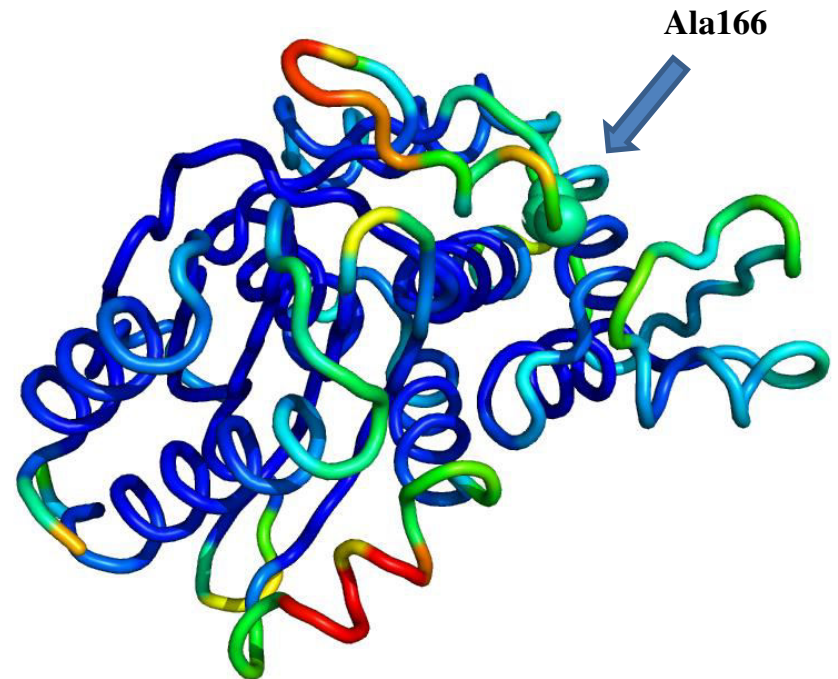


B-Factor

Wild type

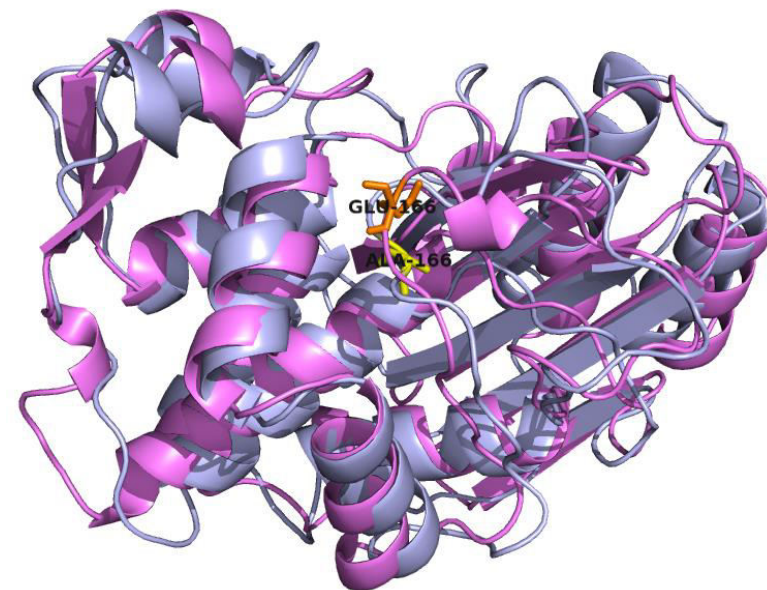
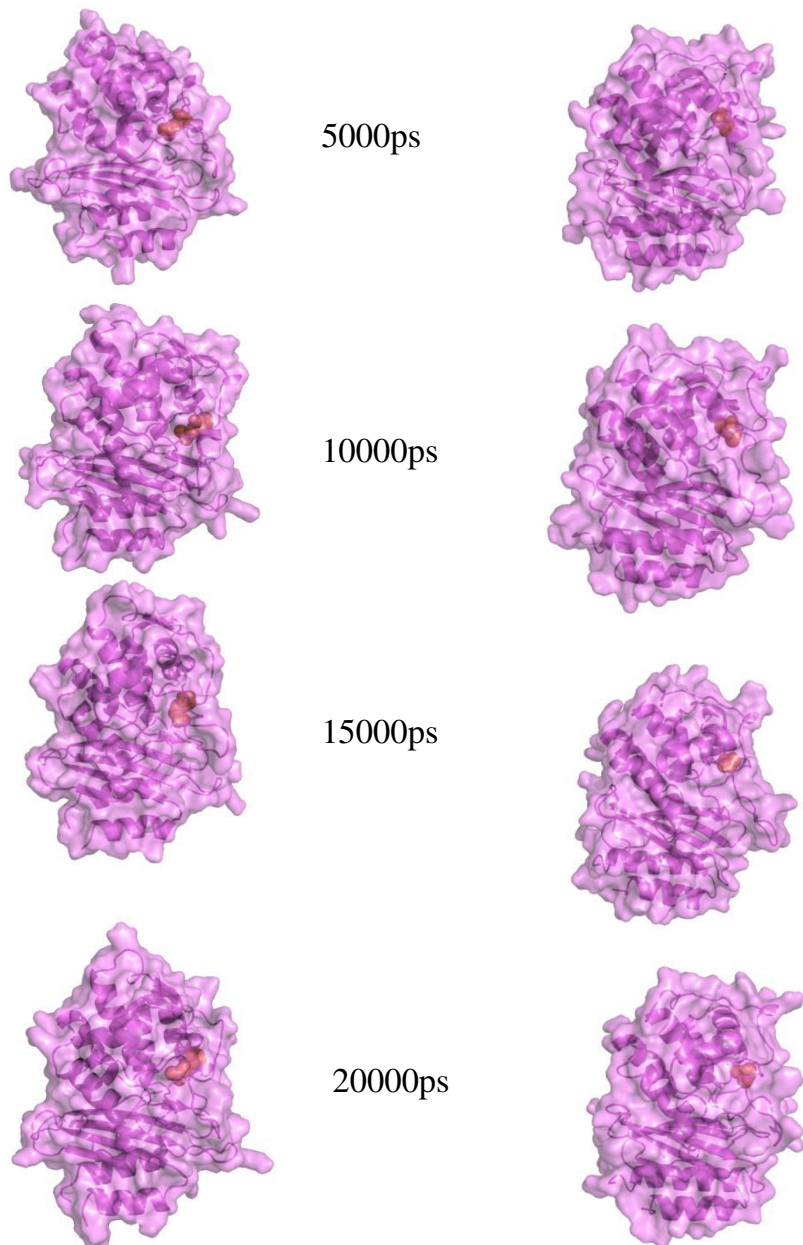


Point mutant E166A



Flexibility 

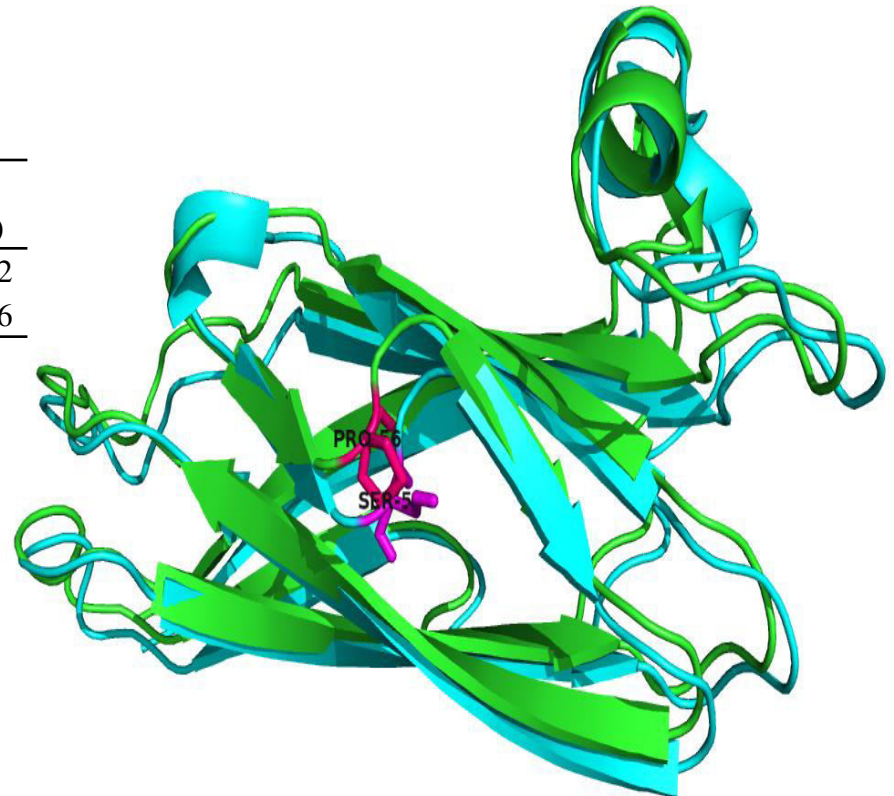
Wild-point mutant E166A form of class A β -lactamase



Superimposed structure of wild and point mutant

RMSD : 2.93 Å

| Duration | Helix (%) | Sheet (%) | Other (%) |
|--------------------------------|-----------|-----------|-----------|
| Before MD simulation (at 0 ns) | 0 | 44.8 | 55.2 |
| After MD simulation (at 45 ns) | 3.2 | 43.2 | 53.6 |



Kumar et al, 2015, Protein aggregation due to nsSNP resulting in P56S VABP protein is associated with amyotrophic lateral sclerosis , Journal of theoretical biology, 72-80

Lysosomal Enzymes and Phosphorylation of Mannose

- Lysosomal enzymes are glycosylated and modified in a characteristic way. Most importantly, when they arrive in the Golgi apparatus, specific mannose residues in their oligosaccharide chains are phosphorylated.
- This phosphorylation is the critical event that removes them from the secretion pathway and directs them to lysosomes.
- Genetic defects affecting this phosphorylation produce I-cell disease in which lysosomal enzymes are released into the extracellular space, and inclusion bodies accumulate in the cell, compromising its function.

Major Symptoms of I-Cell Disease

- Coarse facial features, gingival hyperplasia, macroglossia
- Craniofacial abnormalities, joint immobility, club-foot, claw-hand, scoliosis
- Psychomotor retardation, growth retardation
- Cardiorespiratory failure, death in first decade



Genetic code- Summary

- Genetic code is unambiguous, universal, degenerate, commaless and non overlapping.
- UAG, UGA and UAA are termination codons .
- AUG is the start codon
- Mutations can be well described using genetic code