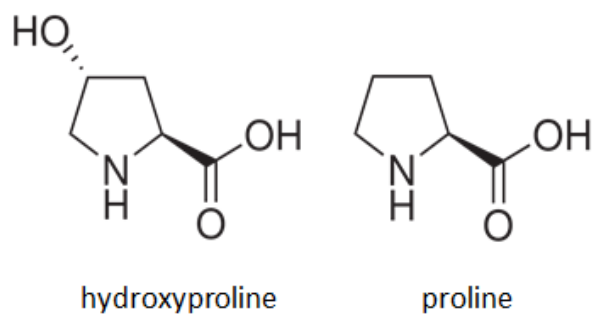


Project 1

Gunica Sharma

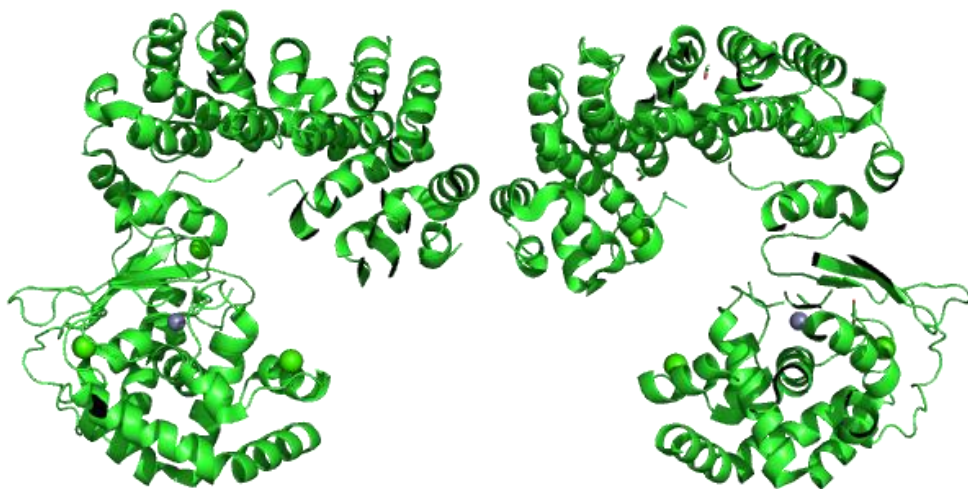
Part 1: HYP Amino Acid

HYP stands for hydroxyproline which is a unique amino acid found in certain proteins. Hydroxyproline plays a significant role in structural proteins particularly collagen. Collagen is considered one of the primary building blocks of the human body. It is estimated that it makes up to 30% of the human body and is found in skin, muscles, bones, tendons etc. Hydroxyproline is one of the main amino acid that makes up the collagen. There lies a key difference between proline and hydroxyproline.



As seen by the image hydroxyproline contains an additional hydroxyl group on the gamma carbon. This modification happens when post translation, proline is modified by the enzyme 4-proyl hydroxylase. It also differs from proline in how it is catabolized by the body.

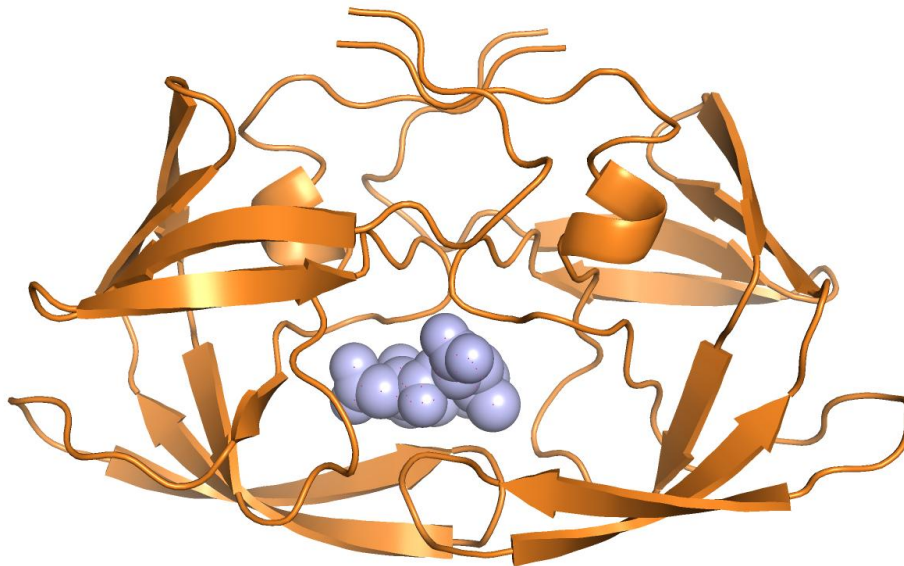
One of the proteins that HYP is found in is collagenase. This particular one is from the gram-negative bacterium *Grimontia hollisae* which is an enzyme used to degrade collagen. One of the ways this enzyme does this is due to higher substrate specificity.



Above is the image of the collagenase derived from the bacterium. There are ligand complexes present that each bind at the active site with the HYP which provides higher substrate affinity as most types of collagens contain high amounts of HYP. So, this protein has better receptors for the collagen allowing it to have better binding affinity.

Part 2

The next protein is the HIV protease. Protease are enzymes that cut up different proteins and peptides into smaller pieces. In the case of the HIV protease, this enzyme is used by retroviruses such as HIV (human immunodeficiency virus) to cut down peptide bonds formed between different proteins in its host. This protease cuts newly created proteins such as the Gag and Gag-Pol to create the different components of the HIV virus. This means the HIV protease is a key component in the life cycle for the HIV virus.



Above is the protease shown with its two chains along with the ligand. The ligand is a tripeptide inhibitor Glu – Asp – Leu. There are hydrogen bond interactions between the ligand with the protease monomer chains.

The significance of this is the ligand tripeptide acts as an inhibitor for the protease. These are the hydrophilic peptides that act in a way that prevents the protease from performing its

functions. In the scope of the virus this can help halt its cycle of replication. Speaking more broadly this can potentially further a way towards the cure of HIV in humans and animals.

Part 3

The next protein is the complex between two different proteins. The first protein being the cyclosporin A and the second being cyclophilin A/ peptidyl – prolyl cis-trans isomerase A. They are covalently linked to form this macromolecule.



In this image the chain A is represented by the green in cartoon form and the attached ligand (chain c) is represented in a stick model.

There are two components to the protein. Chain A is the peptidyl – prolyl cis-trans isomerase A and the chain C is the ligand cyclosporin A. Their respective sizes can be determined by the protein sequence. Chain A has a total of 161 amino acid sequences and chain C has a total of 11 sequences. For the secondary structure of chain A from the model it can be observed that there are 3 alpha helixes and approximately 8 beta pleated sheets.

There are some interesting properties about this molecule including some non-standard amino acids. These include ABA which is modified alanine which means there is an extra carbon

present on the chiral carbon. BMT which is modified threonine, in this case there are additional methyl and butenyl groups present. MEL is a modified leucine where the amino group is methylated and there are additional carbons present. MVA is a methylated version of valine. Lastly SAR has a methyl group attached to the amino. These are the modified versions of the amino acids present in the protein in its chain C.

There is importance associated with this molecule. Cyclophilins are responsible for their assistance in stabilizing the cis-trans transition states to speed up isomerization. This means they help speed up the process of molecules going between different isomeric states. In this case it is bound to cyclosporin A, which is an immunosuppressor. Since both are bound together, they inhibit T-Cell activation. This means this complex can actively suppress the immune system by preventing the activation of T-cells.

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Images + Data Base Links

<https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.quora.com%2FWhy-is-hydroxyproline-important-component-of-collagen&psig=AOvVaw1DdejFOGPthV4Otw9Uvt5m&ust=170630162227000&source=images&cd=vfe&opi=89978449&ved=0CBMQjRxqFwoTCKDi6lOz-YMDFQAAAAAdAAAAABAD>

[https://www.jbc.org/article/S0021-9258\(22\)00550-6/fulltext](https://www.jbc.org/article/S0021-9258(22)00550-6/fulltext)

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