

Abstract for general public

Our body is composed of billions of cells and each of our cell produces thousands of different proteins, using 20 different amino acids as building blocks. Hence, a protein is essentially a chain of different amino acids arranged in a given order. Once the proteins carry out their designated function/s in the cell, they are turned over by enzymes called Proteases, that breaks the bond between the amino acids chain. The proteases are expressed in all living organisms and were initially thought to be required solely for the degradation of the proteins. However, the research over the past decades has demonstrated that proteases are also required for several cellular processes such as cell division, wound healing, immune response etc., and for processing or trimming of the premature proteins to eventually produce a mature and functional protein. Certain proteins are produced as “nascent polyproteins” and each of the individual protein is “liberated” from the polyprotein by the action of proteases. For example, the 3C-like protease or M^{pro} of SARS corona virus processes the coronavirus replicase polyprotein and is required for viral replication, hence inhibitors of M^{pro} are being explored as a treatment option for COVID19.

The proteases are divided into different families and one such family is DiPeptidyl Peptidase IV (DPPIV). It comprises seven members: DPP2, DPP4, DPP8, DPP9, PRCP (Prolyl Carboxypeptidase), PPCE (Post-Proline Cleaving Enzyme) and FAP (Fibroblast Activation Protein). The DPPIV family proteases are evolutionarily conserved (these proteins are expressed across several organisms from simple organisms such as fungus to humans) and are of clinical significance, exemplified by the usage of inhibitors of DPP4 to treat type II diabetes. The biological pathways in which, all but DPP4 of the DPPIV family members function are poorly understood.

However, it is difficult, time consuming and expensive to study about these proteases in widely used model organisms such as mice and is impossible to study in humans. Hence, I plan to use a simple, soil dwelling non-pathogenic nematode, *Caenorhabditis elegans* as a model organism to understand the function/s of these proteases. *C. elegans* is a transparent animal that can be grown in large numbers in a short span of time (3-5 days) using bacteria as a food source and most importantly about 60% of the genes expressed in humans are also expressed in this organism including the DPPIV family proteases. The *C. elegans* expresses 7 different DPF proteins named DPF-1 through 7. My previous research has revealed the role of DPF-3, the *C. elegans* homolog of human DPP8/9 in silencing the Transposable Elements (TEs), that are pieces of DNA moving across the genome “jumping” from one location to another (transposition), taking advantage of the host’s cellular machinery. Approximately 50% and 12% of the human and *C. elegans* genomes, respectively, codes for TEs. Though the TEs were discovered more than 70 years ago, we do not yet comprehensively understand their silencing mechanisms. Transposition of the TEs could be devastating and can result in more than 75 human diseases including cancer. With the aid of the NCN grant SONATA BIS, I wish to explore the function/s of DPPIV family proteases in TE silencing and genome maintenance.