Proteins are the machines and the building blocks of the body. Humans have over 20,000 different proteins that each perform vital tasks to keeps us alive and well. The most abundant protein in vertebrate animals, including humans, is collagen. Collagen is what gives our tissues structure, elasticity and strength. It does so through a process, called fibrillogenesis, where numerous of individual collagen molecules assemble into specific fibrous structures. The structures are different from tissue to tissue depending on the tissues requirements e.g. skin needs to be elastic while in bone it acts as a scaffold for the minerals to deposit on and gives bones fracture resistance. Although there has been researched in collagen for more than a century many of the processes regarding how collagen assembles, and how assembly of it differs from tissue to tissue, is still not fully understood. This is problematic since collagen is so important for the body that when mistakes in fibrillogenesis occurs many different disorders develops. These disorders are quite diverse; from brittle bone disease, in which bones break easily due to mutations in collagen, to cancer where the cancer cells are able to exploit collagen to grow and spread to other tissues of the body. Hence, learning about how collagen is assembled could assist in finding treatments to the diseases where collagen is involved. One thing about collagen fibrillogenesis is known; that a lot of collagen-binding proteins assist in correctly assembling collagen. However, how they do so is less understood. In this PhD project, it was discovered how one of these collagen-binding proteins, called dermatopontin, binds to collagen and where on collagen it binds. This will be valuable knowledge in precisely figuring out its function and in finding treatments for the diseases that collagen and dermatopontin is involved in.

Just as you can get a whole story in the English language by reading different combinations of 26 letters that creates various words, sentences and chapters of a book, so does life use combinations of 20 different molecules called amino acids to create proteins. This is done by putting the 20 different amino acids together one by one into long chains or sequences. The combination of amino acids that are used and the length of the chain is what gives proteins their unique functions required for life to exist. However, life can tweak the functions of proteins by modifying their amino acids, just like diacritical marks can be added to letters to change their sounds. One of these modifications are called tyrosine sulfation. The number of tyrosine sulfations in dermatopontin was identified in this project together with their location. Additionally, by comparing the amino acid sequences of dermatopontin and another group of collagen-binding proteins, called small leucine-rich proteins (SLRPs), from many different vertebrate species, it was discovered that not all animals’ dermatopontin and SLRPs carry these modifications. This means that the extra function that has been given to proteins with tyrosine sulfation modifications in some animals is missing in the same proteins from other animals. This is part of why animals are different from each other.

Hence, in addition to adding pieces to the grand puzzle of how life works, the results from this project can potentially be used for developing treatments against disorders that collagen and dermatopontin are involved in. Additionally, with collagen being the most abundant protein in the human body, these results could also be used in regenerative medicine to replace tissues and organs lost to disease or trauma by creating the collagen structure that is needed for the replacement tissue.