Pipelines for studying in potential motifs in a collagen-integrin system

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Extracellular matrices (ECMs), such as collagen, laminin, and fibronectin, play a significant role in human body. They operate not only integrate the whole human tissues and cells, but also orchestrate crucial cell activities via cell-cell and cell-matrix communications. The investigation of the mechanism of ECM-extracellular receptors interactions remains predominant, as the arrangement of basic cellular events, like cell migration, cell proliferation, heavily relies on this type of interaction. Their interaction involves specific binding motifs on the ECMs and conformational changes of receptors. For example, the notable binding motif on collagen is GFOGER (O is hydroxyproline) sequence, and known motifs in collagen are less than 30, which is very few, compared to the possible sequence space of possibilities. We expect that other binding motifs are likely to exist which can increase specificity and binding affinity in targeting specific integrins. Here, we will leverage existing methods and build a pipeline to discover natural/non-natural binding motifs on the extracellular matrixes and to uncover the conformational changes in the ECM receptors. We will use FoldX and Rosetta FlexddG as fast-screening tools to give us a prior picture about the $\Delta\Delta G$ referring to each point mutation in the fast-screening step, and then we will employ Modelling Employing Limited Data (MELD) approach and thermodynamic integration to narrow down the motifs with higher affinity. Discovery of new binding motifs and studies in the binding process will deepen our understanding for the ECMs-receptors systems, even for other similar biological process, and develop new therapeutics.