# Molecular modeling and dynamics simulation of a histidine-tagged TGFβ

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**Abstract:** Transforming growth factor beta (TGFβ), is a small (25 kDa) secreted homodimeric signaling protein. The TGFβ isoforms (TGFβ1, β2 and β3) are involved in many cellular processes, including growth inhibition, immune suppression, invasion, cell migration and extracellular matrix (ECM) remodeling [1]. TGFβs are produced using recombinant eukaryotic cell or bacteria expression systems [2,3,4]. The overexpressed proteins are purified using conventional means (gel filtration, ion-exchange, etc.) or purification tags, such as His-tag. Structurally, the N-terminal of the mature signaling dimer of TGFβ is flexible and accessible, thus provides a suitable site for tagging, while the C-terminal is ordered and buried, thus does not provide an appropriate site for tagging [4,5]. In this survey, the effect of His-tag in N- and C-terminal of dimeric TGFβ has been studied by computational tools. A histidine tag was added in N-terminal and C-terminal of the protein according to pET28a and pET21b multiple cloning site, respectively. After translating these sequences to amino acid, their 3D structures were modeled using MODELLER 9.17. In the next step, molecular dynamics simulations of modelled proteins and TGFβ were studied in water for a period of 50 ns with a 2 fs time step by GROMACS package. The results showed that the root mean square fluctuation (RMSF) in C-TGFβ is greater than N-TGFβ and TGFβ. It is concluded, the C-terminal tagging may cause confusion in the structure and misfolding.

**Keywords:** TGFβ; tagging; purification tag; molecular dynamics simulation; RMSF.

## References

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