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Abstract:	Most of the prokaryotic and eukaryotic proteins are constituted of multi-domains. Although domains are considered independent folded unit, the inter-domain linker (IDLs) plays an important role in maintaining structural stability and conformational flexibility of entire protein. One such multidomain protein is Cadherin-23, which constitutes the tip-link in inner ear and acts as gating spring in relaying sound induced mechanical signal to ion channel. The IDLs of Cadherin-23 binds to calcium ions, which provide rigidity and structural stability to the protein. Depending on the extent of Ca ²⁺ binding, the linkers are divided into two types: Canonical linker (CL) and Non-canonical linker (NCL). In this study, we have designed a NCL and compared it to the CL. Ca ²⁺ binding affinity; thermodynamic stability and force mediated unfolding pattern for both the proteins have been investigated. Differential effect of NCL and CL on the force propagation through tip-link is the focus of this study. Information from this investigation will influence the subject area of studying the mechanism of inner ear mechanotransduction along with the mystery behind hearing diseases and deafness.
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