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Title:	Interdomain linkers tailor the stability of immunoglobulin repeats in polyproteins
Authors:	Joshi, Tanuja (/jspui/browse?type=author&value=Joshi%2C+Tanuja) Garg, Surbhi (/jspui/browse?type=author&value=Garg%2C+Surbhi) Das, Sayan (/jspui/browse?type=author&value=Das%2C+Sayan) Kamath, Anjana R. (/jspui/browse?type=author&value=Kamath%2C+Anjana+R.) Sagar, Amin (/jspui/browse?type=author&value=Sagar%2C+Amin) Rakshit, Sabyasachi (/jspui/browse?type=author&value=Rakshit%2C+Sabyasachi)
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Abstract:	Linkers in polyproteins are considered as mere spacers between two adjacent domains. However, a series of studies using single-molecule force spectroscopy have recently reported distinct thermodynamic stability of I27 in polyproteins with varying linkers and indicated the vital role of linkers in domain stability. A flexible glycine rich linker $-(GGG)_n$, $n \geq 3$ featured unfolding at lower forces than the regularly used arg-ser (RS) based linker. Interdomain interactions among I27 domains in Gly-rich linkers were suggested to lead to reduced domain stability. However, the negative impact of inter domain interactions on domain stability is thermodynamically counter-intuitive and demanded thorough investigations. Here, using an array of ensemble equilibrium experiments and in-silico measurements with I27 singlet and doublets with two aforementioned linkers, we delineate that the inter-domain interactions in fact raise the stability of the polyprotein with RS linker. More surprisingly, a highly flexible Gly-rich linker has no interference on the stability of polyprotein. Overall, we conclude that flexible linkers are preferred in a polyprotein for maintaining domain's independence.
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