Rapid dissociation of a high affinity colicin:immunity protein complex by a force-activated trigger

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Colicin:immunity protein complexes are amongst the strongest protein complexes known (K_d ~ 10^{-14} M, k_{off} ~ 10^{-6} s^{-1}). Despite this, immunity protein release is a prerequisite of colicin intoxication which occurs on a timescale of minutes. Here we use dynamic force spectroscopy (DFS) to show that the application of low forces (< 20 pN) increases complex dissociation 10^6-fold, to a timescale commensurate with intoxication.

Normally the colicin:immunity protein interaction is high affinity with a half life of around a week however, during the attack of competing cells and the subsequent translocation process across the cell membrane, the immunity protein is released allowing the colicin to kill its target on the timescale of minutes. DFS performed in this work has highlighted a possible force induced switching mechanism from a long lived complex (k_{off} ~ 1*10^{-5} s^{-1}) in a zero/low force regime to a much shorter lived state (k_{off} ~ 5 s^{-1}) under the application of small biologically relevant forces. The decrease in complex lifetime under force is several orders of magnitude greater than that predicted by current models to explain the effects of force on non-covalent interactions and can be abrogated by introduction of disulfide cross-links. This suggests that protein dynamics lie at the heart of the bipartite function of the complex switching from a highly stable complex protective to the host, to one where rapid dissociation facilitates competitor death.