Interdomain communication and interaction in the motor subunit of restriction modification system EcoR1241 from *E. coli*

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Type1 restriction modification system are intriguing multifunctional multisubunit molecular motors that can catalyze both restriction and modification activity. These enzymes binds to its target sequence and its activity as an endonuclease or methyltransferase is determined by the methylation state of the target sequence. If the target sequence is unmodified, the enzyme while bound to its target site is believed to translocate or pull the DNA towards itself simultaneously in both directions in an ATP dependent manner.
The crystal structure of the motor subunit R has been determined by our group but the molecular mechanism by which these enzymes translocate and cleave the DNA is not fully understood.

The type I motor subunit has a square planar arrangement of globular domains with a prominent cleft that can accommodate DNA extending between two canonical helicase domains to the endonuclease active site. ATP binding is proposed to play a major role in coupling the both the activities as the crystal structure shows an unexpected contact of endonulease LYS220 to the translocase bound ATP. We believe this contact play a major role in signal transfer.
To explain the underpinning molecular mechanisms of coupling ATP-dependent DNA translocation and DNA cleavage and the communication pathway through the motor subunit, we carried out molecular dynamics simulations with selected mutations on the endonuclease 220 and 180 loop, that could be potentially engaged in conformational changes that occur once translocation is stalled and a signal is transmitted to the endonuclease.
Additional in silico mutants and their simulations demonstrate the importance of inter domain interactions between helical-helicase2 domain and at the helical-endonulease interface close to the proposed DNA path for DNA translocation and consequent restriction activity.

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