

P046 Molecular dynamics simulations and free energy calculations of base flipping in dsRNA

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The family of ADARs (adenosine deaminases acting on RNA) targets mainly double stranded RNA. Some substrates are promiscuously deaminated whereas others, such as the mammalian glutamate receptor B (gluR-B) pre-mRNA, are more selectively deaminated. Many DNA/RNA-base modification enzymes use a base flipping mechanism to be able to reach their target base and it is believed that ADARs function in a similar way. In this study we used molecular dynamics (MD) simulations to describe two sites on the gluR-B pre-mRNA, the selectively targeted R/G site and the non-targeted 46 site, in an attempt to explain the substrate specificity. We used regular MD and also a forced base flipping method with umbrella sampling to calculate the free energy of base opening. Spontaneous opening of the adenosine could be observed for the R/G site but not for the 46 site.