NMR Dynamics Study Reveals the Zα Domain of Human RNA Editing Enzyme ADAR1 More Slowly Binds to Z-RNA than Z-DNA

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Human RNA editing enzyme ADAR1 deaminates adenine in pre-mRNA to yield inosine. The Zα domains of human ADAR1 ($hZα_{ADAR1}$) binds specifically to left-handed Z-RNA as well as Z-DNA and stabilizes the Z-conformation. To answer the question of how $hZα_{ADAR1}$ can induce both B–Z transition of DNA and A–Z transition of RNA, we investigated the structure and dynamics of $hZα_{ADAR1}$ in complexes with 6-bp Z-DNA or Z-RNA. We performed chemical shift perturbation and relaxation dispersion experiments of $hZα_{ADAR1}$ upon binding to Z-DNA as well as Z-RNA. Our study demonstrates the unique dynamic feature of $hZα_{ADAR1}$ during A–Z transition of RNA, in which the $hZα_{ADAR1}$ protein forms thermodynamically stable complex with Z-RNA like Z-DNA but kinetically more slowly converts to Z-RNA than Z-DNA. We also found the distinct structural features of the $hZα_{ADAR1}$ in the Z-RNA binding conformation. Our results suggest that the A–Z transition of RNA by $hZα_{ADAR1}$ displays the unique structural and dynamic feature that may be involved in targeting ADAR1 for a role in recognition of RNA substrates.