

SARS2 Nsp15 is Mad for U

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SARS-CoV-2 is the virus responsible for the current Covid-19 global pandemic which has infected millions worldwide. Nsp15 is a viral endoribonuclease found in all coronaviruses that processes viral RNA to prevent detection by the host immune system. Nsp15 is a promising anti-viral target, however how it cuts RNA is poorly understood. Through the combination of cryo-EM, mass-spectrometry, biochemistry, and molecular dynamics we are defining how Nsp15 recognizes and processes viral RNA. Atomic resolution structures of Nsp15 bound to RNA in pre and post cleavage states revealed the significance of active site residues in uridine specificity and catalysis. The structures along with a series of biochemical assays have revealed molecular details of how Nsp15 recognizes viral RNA and will hopefully aid in the design of urgently needed anti-viral therapeutics.