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Structure-based mechanistic insights into PAM-dependent spacer acquisition for incorporation into the CRISPR array

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Bacteria obtain a memory of viral invaders by incorporating their DNA sequence elements into the host CRISPR locus, generating a new 33-nt spacer within the CRISPR array. We report on the crystal structure of a Cas1-Cas2-dual-forked DNA complex in efforts towards understanding how the protospacer is selected for insertion into the CRISPR locus. Our structure of the complex reveals a protospacer DNA containing a 23-bp duplex bracketed by tyrosine residues, together with anchored flanking 3'-overhang segments. The complementary PAM sequence in the 3'-overhangs are recognized by Cas1a catalytic subunits in a base-specific manner for protospacer selection and subsequent cleavage at positions 5-nts from the duplex boundary, thereby generating a 33-nt DNA intermediate for incorporation into the CRISPR array. Upon protospacer binding, the Cas1-Cas2 complex undergoes a significant conformational change, generating a flat surface conducive to proper protospacer recognition. Overall, our studies reveal unanticipated structure-based mechanistic insights into PAM-dependent spacer acquisition.

Biography

Yanli Wang has completed her PhD from University of Science and Technology of China and Post-doctoral studies from Memorial Sloan-Kettering Cancer Center. She is a Principle Investigator of Institute of Biophysics, Chinese Academy of Sciences. She has published more than 25 papers in reputed journals and has been serving as an Editorial Board Member of *Non-Coding RNA*.

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