Beyond Cas Nucleases: The Mechanism of an RNA-Guided Protease

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CRISPR RNA-guided nucleases have been the driving force behind the current revolution of genomic medicine. A new wave of discovery defined an atypical Type III CRISPR-Cas system, in which the RNA-guided RNase established cooption with a Caspase-like protease. Together they function as a CRISPR RNA-guided protease – Craspase. In a Science publication last year, my group and Stan Brouns' group applied cryo-EM and molecular genetics approaches to define the conditions leading to the RNA-guided activation and inactivation of Craspase, in vitro and in vivo, and provide a thorough set of high-resolution mechanistic explanations. Since Craspases do not cleave DNA, they may serve as safe alternatives to Cas nucleases in therapeutics.