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Editorial

CRISPR–Cas System and its Applications

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EDITORIAL

The CRISPR–Cas (Clustered Regularly Interspaced Short Palindromic Repeats–CRISPR-associated proteins) modules are adaptive immunity systems that are present in many archaea and bacteria. These defense systems are encoded by operons that have an extremely varied architecture and a high rate of evolution for both the Cas genes and the unique spacer content. Three major types of CRISPR–Cas system are described, with a further division into numerous subtypes and a few chimeric variants. Given the intricacy of the genomic architectures and the enormously dynamic evolution of the CRISPR–Cas systems, a unified classification of these systems should be based on multiple criteria. The new classification keeps the overall structure of the previous version but is extended to now encompass two classes, five types and 16 subtypes. The relative stability of the classification advises that the most predominant variants of CRISPR–Cas systems. However, the presence of rare, currently unclassifiable variants implies that additional types and subtypes remain to be characterized. The CRISPR-Cas systems belong to two classes, with multi-subunit effector complexes in class 1 and single-protein effector modules in class 2. Concerted genomic and experimental efforts on complete characterization of Class 2 CRISPR-Cas systems led to the identification of two new types and numerous subtypes. The newly categorized type VI systems are the first among the CRISPR-Cas variants to exclusively target RNA. Unexpectedly, in some of the class 2 systems, the effector protein is furthermore responsible for the pre-crRNA processing. Comparative analysis of the effector complexes indicates that class 2 systems developed from mobile genetic elements on multiple, independent occasions.

The prokaryote-derived CRISPR–Cas genome editing systems have transmuted our ability to manipulate, identify, image and annotate particular DNA and RNA sequences in living cells of diverse species. The simplicity of use and robustness of this technology have revolutionized genome editing for research ranging from fundamental science to translational medicine. Initial successes have inspired efforts to determine new systems for targeting and manipulating nucleic acids, comprising those from Cas 9, Cas 12, Cascade and Cas 13 orthologousin viv. Genome editing by CRISPR–Cas can use non-homologous end joining and homology-directed repair for DNA repair, as well as single-base editing enzymes. In addition to targeting DNA, CRISPR–Cas-based RNA-targeting tools are being advanced for research, medicine and diagnostics. Nuclease-inactive and RNA-targeting Cas proteins have been joined to a plethora of effector proteins to regulate gene expression, epigenetic alterations and chromatin interactions. Collectively, the new developments are extensively improving our understanding of biological processes and are propelling CRISPR–Cas-based tools towards clinical use in gene and cell rehabilitations.

Functional explanation of causal genetic variants and elements necessitates precise genome editing approches. The type II prokaryotic CRISPR (clustered regularly interspaced short palindromic repeats)/Cas adaptive immune system has been shown to facilitate RNA-guided site-specific DNA cleavage. Cas 9 can also be changed into a nicking enzyme to facilitate homology-directed repair with minimal mutagenic activity. Lastly, multiple guide sequences can be encoded into a single CRISPR array to permit simultaneous editing of numerous sites within the mammalian genome, demonstrating easy programmability and wide applicability of the RNA-guided nuclease technology.

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