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CRISPR-Cas: a brief overview

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Abstract. *CRISPR-Cas is an adaptive immunity in prokaryotes against infections by viruses and plasmids. CRISPR array recognizes foreign sequences of the invaders and Cas destroys them. Using this system seems possible to find the unwanted sequences in the genome and to destroy or to change them with the suitable ones. This system might not only protect ourselves from the future infections but also correct congenital abnormalities which may predispose to carcinogenesis or some congenital diseases.*
Keywords: *CRISPR-Cas; adaptive immunity; future infections; genome editing; carcinogenesis*

CRISPR-Cas systems are RNA-guided defence mechanisms against invasions by viruses and plasmids. CRISPR (clustered regularly interspaced short palindromic repeats)-Cas (CRISPR-associated system) is an adaptive immune system of the prokaryotes. CRISPRs are specialized streches of DNA, and Cas is an enzyme that serve to cut the targetted part of the DNA. As mentionned, this system is a natural defense mechanism of bacteria and archea. Prokaryotes memorize previous infections by integrating short sequences of invading genomes (spacers) into the CRISPR locus; these spacers interspaced with repeats are expressed as small guide CRISPR RNAs (crRNAs) that are employed by Cas proteins to target invaders sequence-specifically upon a reoccuring infection. Targetting DNA sequences using programmable RNAs has been used for genome editing offering high potential in therapeutical applications.

The system was first discovered by researcher Yoshizumi and his coleagues from Osaka University in 1987; but they did not know the function of the interrupted clustered repeats [1].

Researchers from Netherlands in 1993 recognized the diversity of the sequences [2].

Francisco Mojica found that the clustered repeats had a role in correctly segregating replicated DNA into daughter cells during cell division because plasmids and chromosomes with identical repeat arrays could not coexist. Thanscription of the interrupted repeats was also noted for the first time, this was the first full characterization of CRISPR [3, 4].

Jansen's observation clarified that the prokaryote repeat cluster was accompanied by a set of homologous genes that make up CRISPR-associated systems or Cas genes. However the function of CRISPR still was not very well understood [5, 6].

Independent researchers have shown in 2005 that some CRISPR spacers are derived from phage DNA and extrachromosomal DNA such as plasmids [7–9].

In 2007, the first experimental evidence that CRISPR was an adaptive immune system was published by Barrangou et al. [10].

During the last two decades, the prokaryote adaptive immune system CRISPR-Cas has caught increasing attention in the scientific field not only as an adaptive immunity but also as a therapeutic potential. As already mentionned in this system, small guide RNAs (cr RNAs) are used for sequence-specific interference with invading nucleic acids. CRISPR-Cas comprises a genomic locus called CRISPR (short repetitive elements-repeats) separated by spacers which can originate from mobile genetic elements such as bacteriophages, viruses or plasmids. CRISPR array is preceded by an AT-rich leader sequence and is usually flanked by a set of cas genes encoding the Cas proteins. CRISPR-Cas system can be divided into two main classes, which are further classified into six types and several sub-types. The classification is based on the occurence of effector Cas proteins that convey immunity by cleaving foreign nucleic acids. In class 1 CRISPR-Cas system (types I, III, and IV), the effector module consists of a multi-protein complex whereas class 2 systems (types II, V and VI) use only one effector protein [11–14].

CRISPR-Cas systems caught most attention for their potential in medical applications and numerous other biotechnological applications like crop editing, gene drives and synthetic biology [15]. Challenging issues that remain and

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need to be adressed in the future include off-target cleavage by Cas. These effects are a major concern when precisely remodelling the genomic content of eukaryotic cells. Genetic alterations at off-target sites reveal the need for higher specificity of the technique [16, 17].

Conflicts of interests. Author declares the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

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CRISPR-Cas: короткий огляд

Резюме. CRISPR-Cas — це адаптивний імунітет у прокаріотів проти інфікування вірусами та плазмідами. Масив CRISPR розпізнає сторонні послідовності агентів, а Cas знищує їх. При використанні цієї системи здається можливим знайти небажані послідовності в геномі та знищити або змінити їх за допомогою відповідних інструментів. Ця система здатна не тільки захистити себе від майбутніх інфекцій, а й виправити вроджені патології, що можуть спричинити канцерогенез або деякі вроджені захворювання.

Ключові слова: CRISPR-Cas; адаптивний імунітет; майбутні інфекції; редагування геному; канцерогенез

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Турция

CRISPR-Cas: краткий обзор

Резюме. CRISPR-Cas — это адаптивный иммунитет у прокариот против инфицирования вирусами и плазмидами. Массив CRISPR распознает посторонние последовательности агентов, а Cas уничтожает их. Используя эту систему, представляется возможным найти нежелательные последовательности в геноме и уничтожить или изменить их с помощью соответствующих инструментов. Эта система способна не только защитить себя от будущих инфекций, но и исправить врожденные патологии, которые могут повлечь канцерогенез или некоторые врожденные заболевания.

Ключевые слова: CRISPR-Cas; адаптивный иммунитет; будущие инфекции; изменения генома; канцерогенез