# CRISPR-Cas9: an ancient bacterial immune system harnessed into a powerful gene editing technology

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The RNA-programmable CRISPR-Cas9 system has recently emerged as a transforming technology in biological sciences, allowing rapid and efficient targeted genome editing, chromosomal marking and gene regulation. In this system, the endonuclease Cas9 or catalytically inactive Cas9 variants are programmed with single guide RNAs (sgRNAs) to target site-specifically any DNA sequence of interest given the presence of a short sequence (Protospacer Adjacent Motif, PAM) juxtaposed to the complementary region between the sgRNA and target DNA. The system is efficient, versatile and easily programmable.

Originally, CRISPR-Cas is an RNA-mediated adaptive immune system that protects bacteria and archaea from invading mobile genetic elements (phages, plasmids). Short crRNA (CRISPR RNA) molecules containing unique genome-targeting spacers commonly guide Cas protein(s) to the invading cognate nucleic acids to affect their maintenance. CRISPR-Cas has been classified into three main types and further subtypes. CRISPR-Cas9 originates from the type II CRISPR-Cas system that has evolved unique molecular mechanisms for the maturation of crRNAs[a] and the targeting of invading DNA[a,b], which we identified in the human pathogen *Streptococcus pyogenes*. On the basis of the discovery of the DNA targeting mechanism, we proposed that RNA-programmable Cas9 could offer considerable potential for genome editing in cells of the three kingdoms of life for biotechnological, biomedical and gene-therapeutic purposes[b]. As demonstrated by a large number of studies published in the last 18 months, DNA targeting by CRISPR-Cas9 has quickly been adopted by the scientific community to edit and silence genomes in a large variety of cells and organisms including human cells, plants and mice. I will discuss the biological roles of CRISPR-Cas9, the mechanisms involved, the evolution of the type II CRISPR-Cas components tracrRNA, crRNA and Cas9 (formerly named Csn1) in bacterial species and the applications of the system as a novel genome engineering technology.

[a]Deltcheva E et al. 2011. Nature 471(7340):602-607. [b]Jinek M et al. 2012. Science 337(6096):816-821.