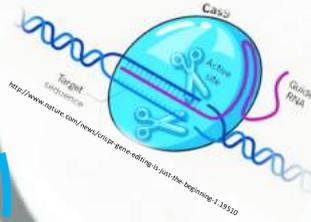


# CRISPR

## DAWN OF A REVOLUTION

**FIND IT. CUT IT.**  
In short, targeted nucleases – that's what CRISPR-associated enzymes are – enable us to modify DNA on unprecedented scale and with mind-blowing accuracy.



**WHAT?**  
The whole scientific world's attention has been recently focused on revelations on the CRISPR system. The new method is currently revolutionizing biological research and by many is announced as the biggest milestone after the introduction of PCR.

**THE HEROES OF CRISPR**  
Apart from the huge scientific impact, there is also an inspiring story behind it – with a message being addressed to microbiologists in particular.

**SO WHAT?**  
The basic microbiological research, persistence of talented scientists and the imponderable serendipity have spurred us to the right track of a new molecular tool of a global application.



### The Heroes of CRISPR

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Three years ago, scientists reported that CRISPR technology can enable precise and efficient genome editing in living eukaryotic cells. Since then, the method has taken the scientific community by storm, with thousands of labs using it for applications from biomedicine to agriculture. Yet, the preceding 20-year journey—the discovery of a strange microbial repeat sequence, its recognition as an adaptive immune system, its biological characterization, and its repurposing for genome engineering—remains little known. This Perspective aims to fill in this backstory—the history of ideas and the stories of pioneers—and draw lessons about the remarkable ecosystem underlying scientific discovery.

**BACTERIA DID IT!**  
I won't take it too far by saying that bacteria have contributed to most of the modern techniques in genetic detection and manipulation. And I am absolutely sure – there is still a lot to be revealed!

### CRISPR-Cas systems for editing, regulating and targeting genomes

Jeffrey D Sander<sup>1,2</sup> & Keith Joung<sup>1,3</sup>

Targeted genome editing using engineered nucleases has rapidly gone from being a niche technology to a mainstream method used by many biological researchers. This widespread adoption has been largely fueled by the emergence of the clustered, regularly interspaced, short palindromic repeat (CRISPR) technology, an inspired new approach for generating RNA-guided nucleases, such as Cas9, with customizable specificities. Genome editing mediated by these nucleases has been used to rapidly and efficiently modify endogenous genes in a wide variety of biologically important cell types and to engineer them conditionally to manipulate genetically. Furthermore, a modified version of the CRISPR-Cas9 system has been developed to control endogenous genes that can regulate endogenous gene expression or target specific genomic loci in living cells. Although the genome-wide specificities of CRISPR-Cas9 systems remain to be fully defined, the power of these systems to achieve targeted, highly efficient alterations of genome sequence and gene expression will undoubtedly transform biological

### Development and Applications of CRISPR-Cas9 for Genome Engineering

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Recent advances in genome engineering technologies based on the CRISPR-associated RNA-guided endonuclease Cas9 are enabling the systematic interrogation of mammalian genome function. Analogous to the search function in modern word processors, Cas9 can be guided to specific locations within complex genomes by a short RNA search string. Using this system, DNA sequences within the endogenous genome and their functional outputs are now easily edited or modulated in virtually any organism of choice. Cas9-mediated genetic perturbation is simple and scalable, empowering researchers to elucidate the functional organization of the genome at the systems level and establish causal linkages between genetic variations and biological phenotypes. In this Review, we describe the development and applications of Cas9 for a variety of research or translational applications while highlighting challenges as well as future directions. Derived from a remarkable microbial defense system, Cas9 is driving innovative applications from basic biology to

nature  
biotechnology

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