

CRISPR-CAS9

A POWERFUL GENE-EDITING TOOL

There are more bacteriophages in the world than any other organism, including bacteria, combined!



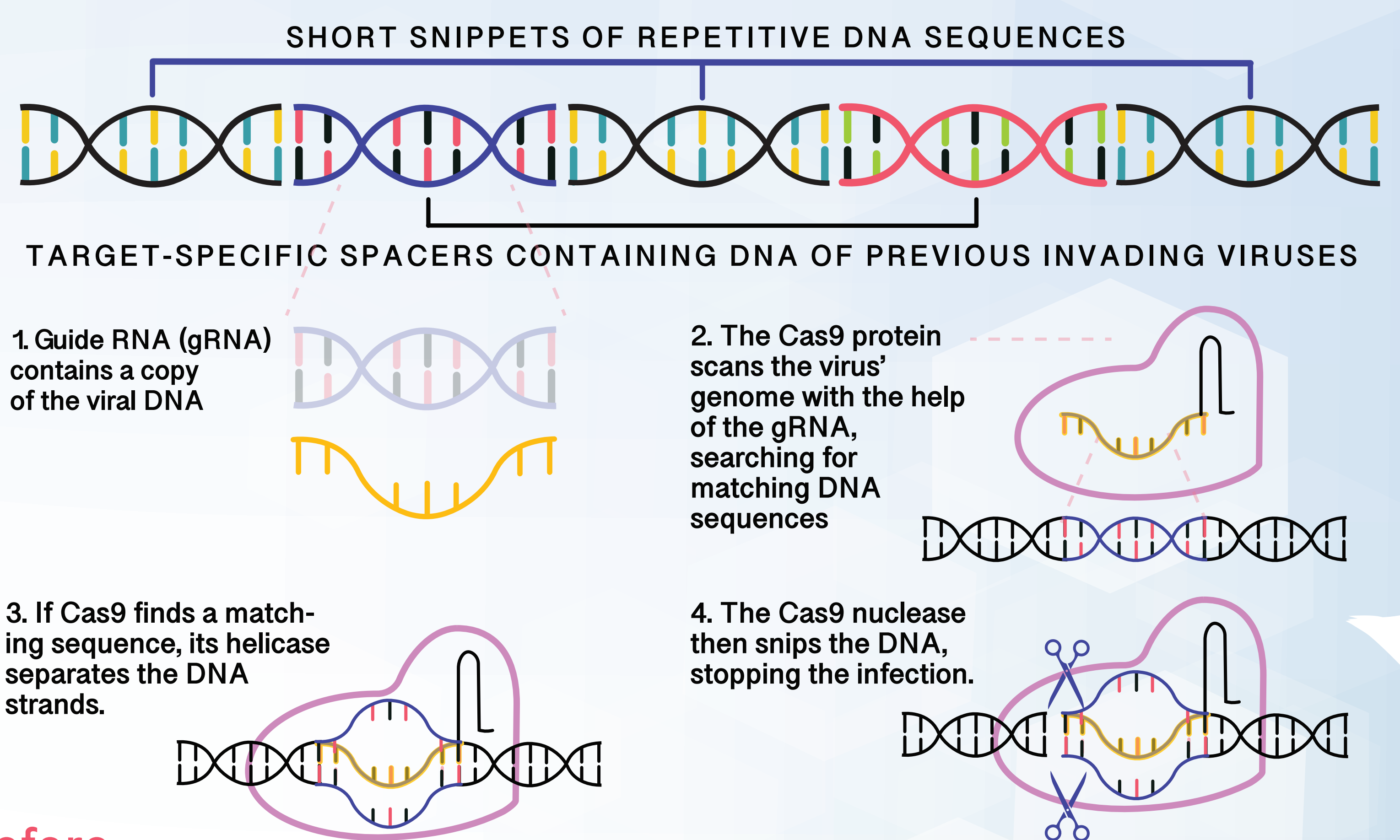
Viruses that attack bacteria are called **bacteriophages** (or phages.) They latch on and insert pieces of their own DNA, where it replicates and takes over the cell. Bacteria have their own **immune defense system** to protect them against these viruses. In the cases where the bacteria survives a phage attack, a copy of the attacker's DNA is stored in its own DNA, allowing it to recognize it if it attacks again **--and slice it up!** This natural process of slicing DNA uses two main components.

The first are short snippets of repetitive DNA sequences called **CRISPR**:

- C**lustered -- means they are found together on the genome.
- R**egularly -- refers to the fact that between these repeats are unique pieces of DNA, called spacers. This is where the viral DNA is stored!
- I**nterspaced --
- S**hort ---- means the sequence is just 20 or 40 base pairs long.
- P**alindromic -- means the sequence can be read the same forward or backward.
- R**epeats -- means this palindromic sequence is repeated over and over.

Scientists discovered they could apply the **find and cut mechanism** of the CRISPR-Cas system to other organisms including **plants, animals, and humans** by adapting different guide RNAs for the use with Cas9. This **guide RNA (gRNA)** helps Cas9 to find the place in the DNA where it is supposed to cut. After it is cut, the DNA then repairs itself. It would then be unreadable. Alternatively, scientists can add a **DNA template** in addition to Cas9 that will then be inserted into the cutting site during the DNA repair process. This allows novel genes to be introduced at a specific site of interest in the genome, therefore enabling researchers to create new features in different organisms. This technique can be used for many purposes in bio-technology and medicine. Of course, ethical concerns need to be taken into consideration.

The second component are Cas proteins, short for **CRISPR-associated proteins**. The Cas genes are located near the CRISPR on the genome. The repeated patterns help the protein to find the invaders' DNA. There are different types of Cas complexes, but **Cas9** was the first adapted for use for human purposes. When a bacterial cell senses bacteriophage invasion, the Cas proteins take a transcript (known as **guide RNA**) of the unique DNA sequences stored in the CRISPR array from previous attacks, and scan the invader's DNA for a matching sequence. If recognized as invading phage, the Cas9 (with the helicase part of the protein) **unwind** and (with the nuclease part of the protein) **chop up** the viral DNA like molecular scissors, destroying it and therefore halting the phage infection.



CURRENT AND FUTURE USES OF CRISPR:

CRISPR is currently used in many aspects of **food production**: from specialized crops to cell-based meat, to modified yoghurt cultures. In **biomedicine**, it has been used to cure sickle-cell disease and beta-thalassemia, and in treating retinal diseases.

Some **current developments** include treating certain genetic diseases, and helping with improved transplant methods and smarter T-cells. It is being developed to engineer crops that can withstand extreme weather conditions and get rid of pests without harmful chemicals, to create enhanced biofuels, aid in environmental conservation, and much more!



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