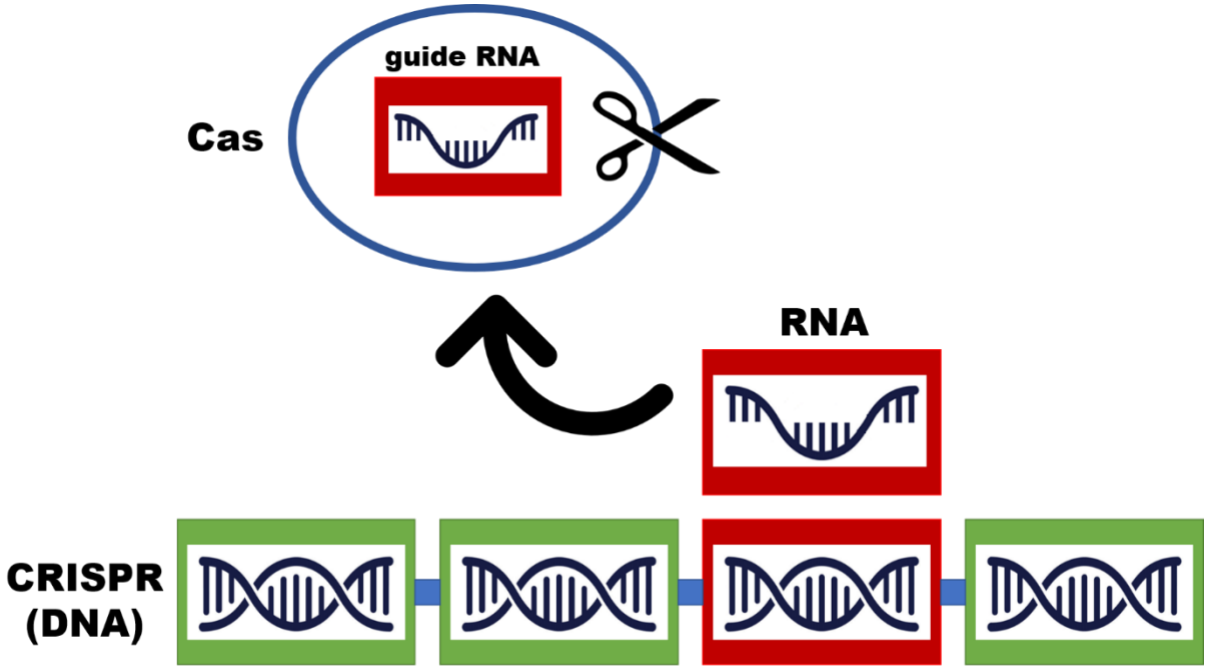
Gene editing with CRISPR/Cas9 molecular scissors

By Krista Thongpanh

What do pesky mosquitos and HIV-1 have in common? Both can potentially be dealt with using CRISPR driven genetic modification. From designer babies to GMOs (genetically modified organisms), CRISPR has gotten a bad reputation in the news lately, but what is it anyway? CRISPR or clustered regularly interspaced short palindromic repeats paired with Cas9 (CRISPR associated protein) is a naturally occurring system in some bacteria. CRISPR/Cas9 is the way that these bacteria fight off harmful viruses, similar to how our immune system helps us fight off the flu. For bacteria, CRISPR is like an old western saloon filled with criminal "Wanted" posters. Cas proteins are like bounty hunters with molecular scissors, ready to cut up anything that matches these criminals' descriptions.

When viruses invade bacteria, Cas9 proteins cut up the viral DNA and then copy it into the CRISPR regions of the bacterial DNA. This integrated viral DNA gets copied into RNA, a different type of genetic language than DNA. The Cas9 protein then binds to the copied RNA and it becomes a guide for the Cas9 protein, helping it search for a match to target and cut up anything matching the guide RNA.



So how does this relate to mosquitos and HIV-1 again? Scientists have found a way to use CRISPR/Cas9 as a gene-editing tool. Remember that guide RNA we talked about, and how Cas9 proteins will readily cut up anything matching the guide RNA? Scientists have discovered how to *make* guide RNA that matches the genes they want to edit and then bind it to Cas9 proteins to do the snipping.

A study performed by Kyrou et al. recently utilized CRISPR/Cas9 gene drives to target a genetic sequence unique to female mosquitoes that carry the deadly human parasite, malaria. The

females that were born with this mutation were unable to further reproduce. Their team studied these mutated mosquitoes in enclosures and found that after 7 to 11 generations, the population of mosquitos was ultimately eradicated. With further research and legislation, this could possibly mean the eventual end of malaria!

In the case of HIV-1, Hartwegar et al. used CRISPR/Cas9 engineered immune cells that can fight against HIV-1. While there are options to treat the symptoms caused by HIV-1, there is currently no treatment to cure it. However, Dr. Hartwegar and his team have found a way to genetically engineer B cells, which are a type of immune cell that secrete antibodies to fight off infections. These CRISPR/Cas9 engineered B cells were genetically modified to secrete bNab, antibodies specific to fighting off HIV strains. In mouse models, the scientists found that these edited B cells were able to neutralize HIV-1 down to a level where the mice were protected against the infection. If this research yields similar results in human clinical trials, these CRISPR/Cas9 engineered B cells could potentially be used to treat HIV-1!

These are just a few examples of the wonderful medical advancements that CRISPR has been able to contribute to. Although the ethics of some CRISPR applications have been legitimately questioned, the beneficial applications of CRISPR for disease treatment and pesky mosquitos is undeniable.

References

Kyrou, Kyros, et al. “A CRISPR–Cas9 Gene Drive Targeting Doublesex Causes Complete Population Suppression in Caged Anopheles Gambiae Mosquitoes.” Nature Biotechnology, vol. 36, no. 11, 2018, pp. 1062–1066., doi:10.1038/nbt.4245.

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