Bacteria's Defense Against Bacteriophages: CRISPR/Cas-9

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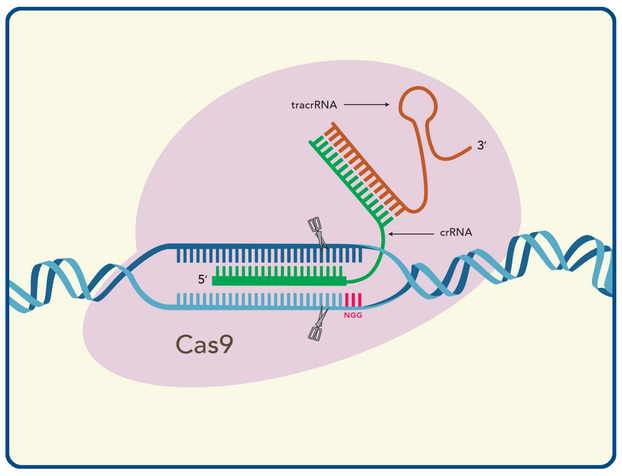
What is CRISPR/Cas-9?

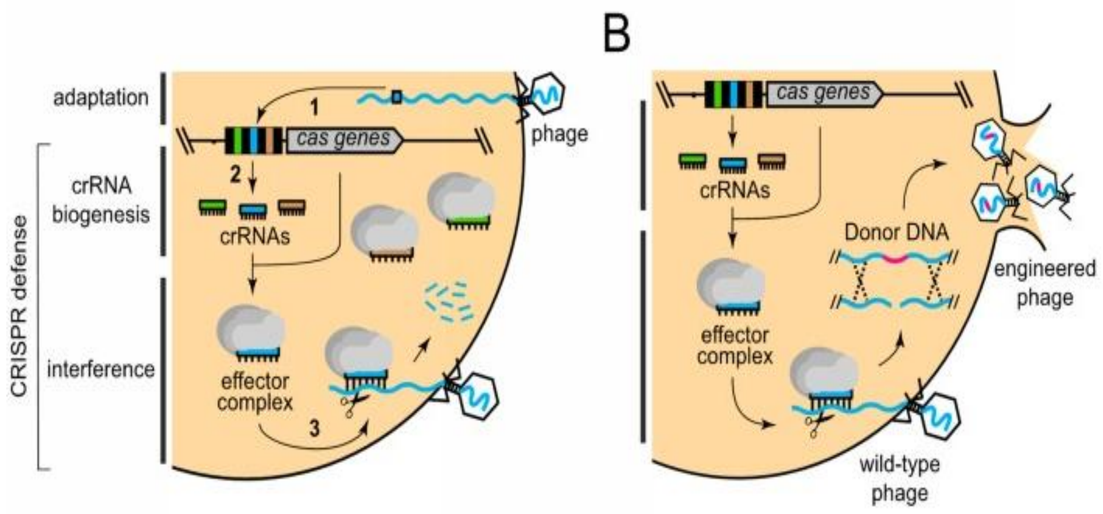
- Clustered Regularly Interspaced Short Palindromic Repeats
  - Gene editing tool – uses enzyme Cas-9 to cut DNA and the CRISPR locus is the memory directing activity against foreign DNA
- Its function is to edit DNA sequences, allowing bacteria to fight against bacteriophages and allowing bacteriophages to target specific bacteria



Source: Integrated DNA Technologies, Inc.

CRISPR & Modification of Phages

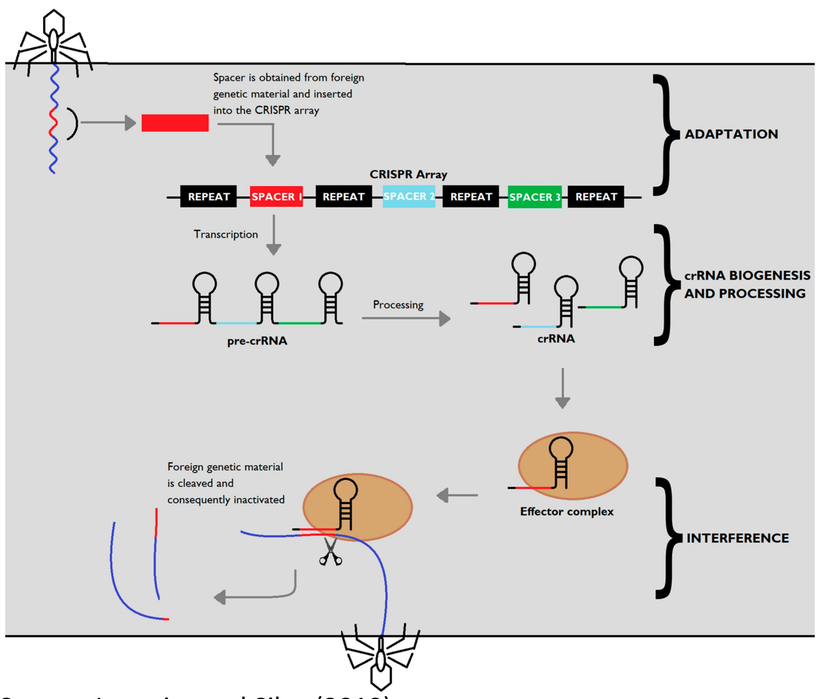
- CRISPR-Cas systems can be utilized to evolve phages in controlled environments to introduce desired mutations
- Health Impacts:
  - Can be used to create gene specific anti-microbial agents
    - Modifications help to control and detect antibiotic resistant bacteria
      - Utilizes homologous recombination
    - Studies have tested modified phages against gram-negative bacteria
      - Example: Engineered phages are used to detect and identify pathogens in food, hospitals, etc.
  - Vehicles for drug delivery and vaccines



Source: Hatoum-Aslan A. Phage Genetic Engineering Using CRISPR¯Cas Systems. *Viruses*. 2018;10(6):335. Published 2018 Jun 19. doi:10.3390/v10060335

CRISPR as a Bacterial Defense Mechanism

- Bacteria are constantly at risk of infection by bacteriophages
- To reduce the effect that phages have on bacterial species, bacteria evolved their own “immune systems"
- This system takes the injected genes from phages that attacked it in the past and “remembers” it
- It uses small sections of this phage DNA of approximately 20 base pairs and attaches it to a Cas-9 protein
- If this section of DNA matches up with another strand of DNA, like another invading phage’s DNA, the Cas-9 protein will cut the DNA, disabling it, and preventing infection



Source: Loureiro and Silva (2019)

Sources:

Loureiro, A.; da Silva, G.J. CRISPR-Cas: Converting A Bacterial Defence Mechanism into A State-of-the-Art Genetic Manipulation Tool. *Antibiotics.* 2019;*8(*1): 1-25.

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