Merits of constant expression of CRISPR loci in adaptive immunity of bacteria

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Abstract

Bacteria fend off attack of bacteriophage through a variety of systems such as restriction-modification as well as clustered regularly interspersed short palindromic repeats (CRISPR). CRISPR is an adaptive immune system that provides a molecular memory of past attacks of bacteriophages on the bacterial strain in a vertically inheritable fashion. More importantly, such molecular memory of past phage infection is utilized in guiding a precision attack on the nucleic acids of invading bacteriophages. To do this, snippets of DNA from invading phages that have been neutralized are inserted into CRISPR-loci in the bacterial genome. Transcription of the CRISPR loci provides active RNA variants of the DNA snippets from phages useful for guiding the Cas9 endonuclease to invading phage DNA through complementary base pairing defined by a spacer region. While the system provides real-time surveillance of the bacterial cytoplasm for phage DNA resembling those from past infections, energetic cost of constantly transcribing the CRISPR loci might be high. Specifically, as currently understood, the CRISPR system would express phage DNA snippets catalogued in the CRISPR loci irrespective of environmental and nutritional conditions to help fend off possible infections by the same phages. However, phages responsible for past infections may not be present in the vicinity of the bacterial cell's environment, which meant that expression of the CRISPR loci might be a waste of cellular energy and resources without any gain in fitness advantage to the bacterial cell compared to those from another species in the same environment. Hence, the evolutionary forces that shape the retention of the extant form of CRISPR remains to be understood in the context of how cellular energetics of adaptive immunity connects with bacterial fitness. Theoretically, a better system would involve the selective expression of specific CRISPR loci targeting the DNA or RNA of particular bacteriophage invading the cell. Such a system would incur less energy and resources to maintain, but would require another layer of intracellular surveillance able to identify the type and species of invading bacteriophage. Doing so would return us to the same problem as a molecular surveillance system requires key elements of recognition and actuation where recognition requires a molecular template of sequence information characteristic of particular bacteriophage. Given that DNA is a more stable format for storing sequence information compared to RNA, and that complementary base pairing as recognition mechanism require single stranded nucleic acid, current incarnation of CRISPR loci might be close to optimal in device architecture and functional logic. Hence, could we do better in redesigning bacterial adaptive immune system able to recognize a diversity of phages involved in past infection of a species or strain at reduced energetic and material cost?

Keywords: CRISPR, adaptive immunity, bacteria, bacteriophage, endonuclease, spacer region, complementary base pairing, device architecture, cellular energetics, bacterial fitness,

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