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When Proteins Write DNA: A Discovery That Redefines Biology

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SUMMARY

The central dogma of molecular biology holds that new DNA is copied from an existing DNA or RNA template, ensuring that genetic information is transmitted with high fidelity across generations. A recently characterized bacterial immune system, Defense-associated Reverse Transcriptase 3 (Drt3), challenges this rule by allowing a protein to dictate the sequence of a newly synthesized DNA strand without reading from any nucleic acid template. This paper reviews how the Drt3 ribonucleoprotein complex detects bacteriophage infection and activates its antiviral response, and how its two catalytic subunits, Drt3a and Drt3b, build a repetitive double-stranded DNA product through different synthesis mechanisms. Drt3a relies on a noncoding RNA template, whereas Drt3b instead uses specific amino acid residues as base mimics to guide accurate synthesis without any template at all. This discovery expands the known pathways of biological information transfer and carries implications for antiviral biology, synthetic biology, and future DNA-writing biotechnology.

INTRODUCTION

A foundational rule of molecular biology is that new DNA is built by copying an existing DNA or RNA template, a process that safeguards the accurate transmission of genetic information from generation to generation. A newly described bacterial defense pathway, Defense-associated Reverse Transcriptase 3 (Drt3), challenges this long-standing assumption by showing that a protein can itself dictate the sequence of a new DNA strand (Deng et al., 2026; Tong, 2026). Bacteria are constantly threatened by bacteriophages, and over evolutionary time they have assembled a diverse toolkit of immune systems capable of recognizing and neutralizing these viral invaders. Drt3 belongs to this toolkit, but it operates through a strategy unlike any previously known antiviral mechanism (Deng et al., 2026).

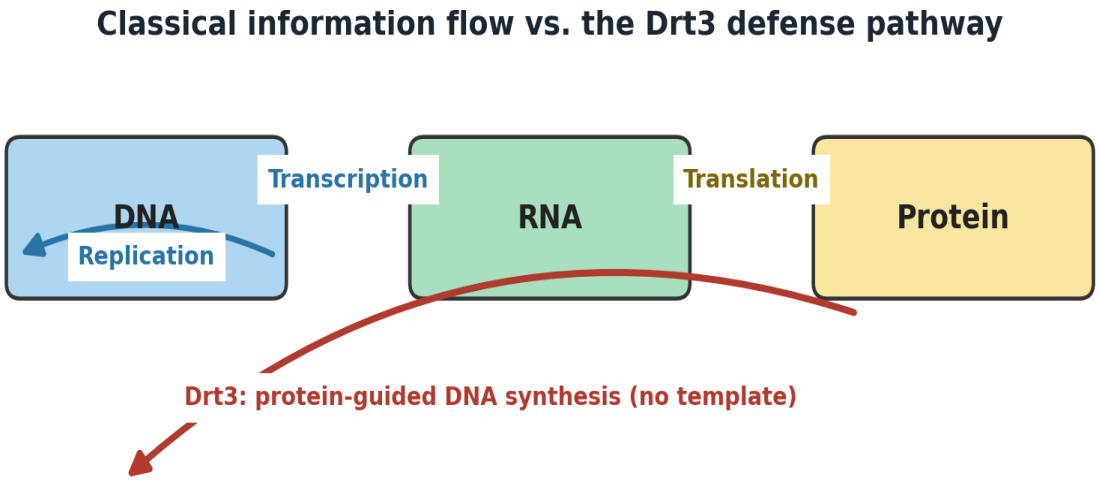

Figure 1. The classical central dogma (DNA ↔ RNA → protein) compared with the Drt3 pathway, in which protein structure guides new DNA synthesis.

Activation and Assembly of the Drt3 Complex

Upon phage infection, Drt3 assembles into a hexameric ribonucleoprotein complex containing six copies each of two reverse transcriptase subunits, Drt3a and Drt3b, together with a noncoding RNA (Deng et al., 2026). This complex remains dormant until it senses a specific phage protein, ST61, at which point it is triggered into an active antiviral state. Once activated, the complex synthesizes a double-stranded DNA product built from repeating poly(GT/AC) sequence blocks (Deng et al., 2026).

Two Distinct Synthesis Mechanisms

The two subunits accomplish this synthesis in strikingly different ways. Drt3a follows the conventional reverse-transcriptase logic: it reads the complex's noncoding RNA as a template to assemble a DNA strand of repeating GT bases. Drt3b, in contrast, produces the complementary poly(AC) strand without using any RNA or DNA template at all (Deng et al., 2026). Structural analysis revealed why: in Drt3b, the pocket that would normally accommodate a nucleic acid template is physically occupied by segments of the protein itself, leaving no room for a template strand to bind. Instead, the enzyme relies on its own three-dimensional architecture to select and position each incoming nucleotide. Particular amino acid side chains function as "base mimics," substituting for the missing template bases; for example, Glu26 selectively recognizes incoming adenine nucleotides, while Arg253 helps enforce the correct alternating GT/AC order along the growing chain (Deng et al., 2026; Niazi, 2026). The newly formed DNA also folds into an unusual kinked conformation that stabilizes protein–DNA contacts and preserves the fidelity of the repeating sequence as synthesis proceeds (Deng et al., 2026).

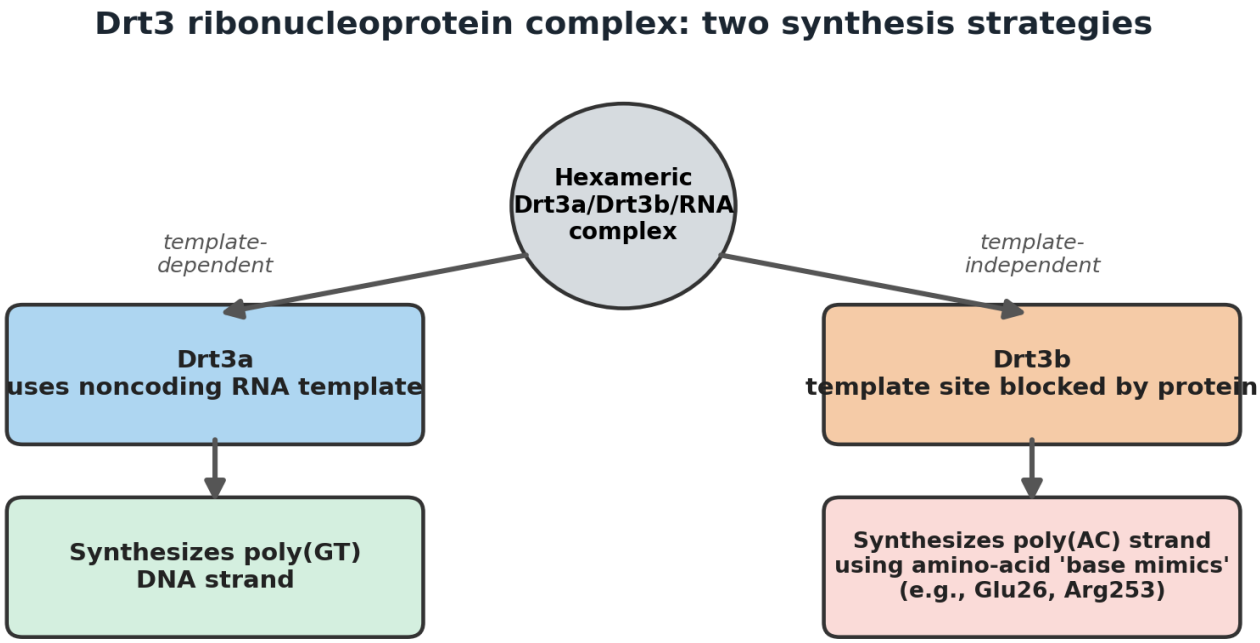

Figure 2. The Drt3a/Drt3b/RNA complex uses two parallel strategies—RNA-templated synthesis by Drt3a and template-independent, protein-guided synthesis by Drt3b—to build the antiviral DNA product.

Broader Significance

The significance of Drt3 extends well beyond a single bacterial defense pathway. Long, sequence-specific DNA synthesis was previously thought to be impossible without a nucleic acid template; Drt3 demonstrates that, under the right conditions, protein structure alone can encode DNA sequence, adding a previously unrecognized route for the flow of biological information (Deng et al., 2026; Niazi, 2026; Tong, 2026). Beyond deepening our understanding of bacterial immunity, this discovery has clear implications for biotechnology and synthetic biology: protein-guided, template-independent DNA synthesis could inform the design of new DNA-writing enzymes, programmable biomolecular tools, and novel therapeutic technologies (Niazi, 2026; Tong, 2026).

CONCLUSION

Drt3 is a reminder that biology continues to reveal exceptions to its own textbook rules. By showing that a protein can independently dictate a DNA sequence without any nucleic acid template, this single antiphage defense system broadens our understanding of how genetic information can be stored, transferred, and protected (Deng et al., 2026; Niazi, 2026; Tong, 2026). Future structural and biochemical studies of Drt3 and related defense-associated reverse transcriptases are likely to refine this model further and may open new avenues for engineering programmable, template-independent DNA-writing tools (Niazi, 2026; Tong, 2026).

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