

Review of: "Revisiting Immunology Textbooks: Considering Potential Insights Based on the Role of RNA-Guided Antiviral Defense"

Rakesh Pemmada¹

1 University of Alabama at Birmingham

Potential competing interests: No potential competing interests to declare.

- 1. According to the article, RNA interference plays an important role in human antiviral defense, like the CRISPR-Cas systems in prokaryotes. However, it lacks explicit examples of RNA interference mechanisms that actively attack specific viruses in human cells. Can the authors provide data or examples of how RNA interference directly neutralizes viruses in humans?
- 2. The manuscript discusses the CRISPR-Cas system's involvement in prokaryotic adaptive immunity and eukaryotic RNA interference. Can the authors explain how these processes developed from their ancestral objectives to contribute to the complex immune responses observed in humans and other vertebrates?
- 3. The transmission of microRNAs via breast milk is emphasized as an important part of developing infant immunity. Are there any ongoing research or clinical trials to leverage this natural mechanism for medicinal purposes, particularly in disadvantaged populations or those with weakened immune systems?
- 4. Given the complex interaction of multiple immune responses and the possibility for RNA-guided immunity to play a key role, how do the authors recommend incorporating this knowledge into existing immunological models and training materials?
- 5. The study discusses the significance of RNA-guided immunity but lacks quantitative data comparing its antiviral efficacy to that of the adaptive immune system (SIS). Are there studies or models that quantify the role of RNA-guided processes in viral clearance or protection as compared to antibodies and T cells?
- 6. Given the manuscript's emphasis on RNA-guided antiviral defense, there is an opportunity to investigate the interaction of these systems with the human microbiome, namely viral components such as bacteriophages. What impact does RNA-guided immunity have on the microbiome's viral elements, and what are the implications for host health and disease?

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