

# Interplay of TLR4 and SARS-CoV-2: Possible Involvement of microRNAs [Response to Letter]

Terence Ndongi Bukong , Clinton Njinju Asaba

Armand-Frappier Sante Biotechnologie Research Center, Institut National de la Recherche Scientifique, Laval, Québec, Canada

Correspondence: Terence Ndongi Bukong, Email [terencendongi.bukong@inrs.ca](mailto:terencendongi.bukong@inrs.ca)

## Dear editor

We have carefully reviewed Gambari and Finotti's letter concerning our recent review, "Interplay of Toll-like Receptor 4 (TLR4) and SARS-CoV-2: Unveiling the Complex Mechanisms of Inflammation and Severity in COVID-19 Infections". Their thoughtful comments provide a valuable perspective that deepens the scientific discourse on therapeutic strategies, particularly by exploring microRNAs (miRNAs) as regulatory agents within the TLR4/MyD88/NF- $\kappa$ B signaling pathway.

Their suggestion to employ specific miRNAs - such as miR-93 and miR-145-5p - as modulators of TLR4 signaling aligns closely with our goal of attenuating the heightened immune response associated with severe COVID-19 cases. As Gambari and Finotti aptly highlight, miRNAs could serve as precise regulators of TLR4-driven cytokine production, thus dampening the intensity of the inflammatory cascade that can lead to adverse clinical outcomes. Specifically, applying miRNA mimics, such as miR-93-5p, which targets pro-inflammatory pathways, offers a promising approach to modulate the TLR4/NF- $\kappa$ B axis, potentially reducing cytokine storm severity.

Their approach to miRNA-based therapeutics introduces a sophisticated therapeutic paradigm. This strategy, which extends beyond the direct inhibition of TLR4, may allow modulation of downstream inflammatory mediators and enable a finely tuned immune response. Such a multi-tiered strategy could address the immune dysregulation observed in severe COVID-19 cases, minimizing hyper-inflammation while preserving essential antiviral functions.

Further, Gambari and Finotti also present evidence indicating that miRNAs can inhibit NF- $\kappa$ B-mediated expression of key pro-inflammatory cytokines, such as IL-8. IL-8 is crucial in recruiting and activating neutrophils, which can amplify inflammation and lead to tissue damage. Elevated IL-8 levels and increased neutrophil counts correlate with severe COVID-19 and poorer clinical outcomes. Targeting this pathway with miRNAs like miR-93 and miR-145-5p may offer a precise approach to modulating inflammation by reducing excessive cytokine production, thus curbing harmful inflammation while preserving essential antiviral responses. This approach suggests that miRNA-targeted therapies could extend beyond TLR4 modulation to affect a wider range of inflammatory pathways. By acting as a secondary regulatory layer, miRNAs could help maintain immune balance, offering a multi-level intervention that enhances therapeutic outcomes. These findings underscore the potential of combining TLR4-targeted treatments with miRNA modulation to manage COVID-19's intricate inflammatory processes effectively.

Taken together, Gambari and Finotti's insights reinforce the significant potential of miRNA-based strategies to precisely regulate the complex inflammatory pathways implicated in COVID-19. Their contributions underscore a promising scientific foundation for leveraging miRNA modulation to achieve targeted immune response control, opening new avenues for robust and effective therapeutic interventions in COVID-19 and beyond.

## Disclosure

The authors have no conflicts of interest regarding this communication.

Dove Medical Press encourages responsible, free and frank academic debate. The content of the Journal of Inflammation Research 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Journal of Inflammation Research editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.

## Journal of Inflammation Research

Dovepress

### Publish your work in this journal

The Journal of Inflammation Research is an international, peer-reviewed open-access journal that welcomes laboratory and clinical findings on the molecular basis, cell biology and pharmacology of inflammation including original research, reviews, symposium reports, hypothesis formation and commentaries on: acute/chronic inflammation; mediators of inflammation; cellular processes; molecular mechanisms; pharmacology and novel anti-inflammatory drugs; clinical conditions involving inflammation. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/journal-of-inflammation-research-journal>

<https://doi.org/10.2147/JIR.S503739>