

Stimulation of Inflammation Resolution May Avert Cytokine Storm and Improve Clinical Outcomes Associated with Current Pandemic, Prominent Researchers Proposed

As the current pandemic rages on, several hundred clinical trials are recruiting and ongoing hoping to identify efficacious antiviral and anti-inflammatory strategies. In a new commentary published in the journal *Cancer Metastasis and Reviews* (Springer Nature publishing group),¹ a group of prominent researchers proposed a promising, complementary direction worthy of consideration: targeting inflammation resolution.

Who contributed to this commentary?

The article was led by Dipak Panigrahy, MD, at Beth Israel Deaconess Medical Center of Harvard Medical School, who has had close collaboration with Professor Charles N. Serhan, PhD, DSc, (box) from Brigham and Women's Hospital at Harvard Medical School, Professor Sui Huang, MD, PhD, from Institute of Systems Biology, and Professor Bruce Hammock, PhD, of UCD Comprehensive Cancer Center at University of California, Davis, all of whom contributed to the commentary. Other authors included Molly M. Gilligan and Allison Gartung, PhD, from Beth Israel Deaconess Medical Center; Irene Cortés-Puch, MD, project scientist at Division of Pulmonary at UC Davis Medical Center; Richard P. Phipps, PhD, independent scholar; and Patricia J Sime, MD, Chair of the Department of Internal Medicine at Virginia Commonwealth University.¹

Video: [Charles Serhan, PhD, DSc, describes the role of specialized pro-resolving mediators in adaptive immune response \(length: 1 min 15 sec\)](#)

Video: [Charles Serhan, PhD, DSc, discusses current research for use of specialized pro-resolving mediators \(length: 3 min\)](#)

What did the authors hypothesize?

They hypothesized that controlling excessive pulmonary inflammation via stimulating the resolution of inflammatory responses is as important as antiviral therapies.¹

Serious respiratory viral infection causes massive lung cell destruction and cellular debris that activate inflammasome leading to excessive release of proinflammatory cytokines. Known as cytokine storm, it contributes to severe inflammation and systemic organ failure.²

Specialized pro-resolving mediators are biosynthesized to actively orchestrate key resolution events of acute inflammation. These bioactive compounds, such as resolvins, protectins, and maresins, promote macrophage clearance of cellular debris and counter the release of proinflammatory cytokines, thereby averting cytokine storm and allowing for tissue repair and healing.³

Webinar: [Kara Fitzgerald, ND: inflammasome and inflammation \(free registration\)](#)

Blog: [cytokine storm \(length: 5 min\)](#)

What existing research prompted the authors to propose the use of specialized pro-resolving mediators in the management of the current pandemic?

- In several infectious disease models, specialized pro-resolving mediators enhanced clearance of invading microbes including influenza virus and terminated inflammation.³⁻⁶
- In a mouse model, the specialized pro-resolving mediator 17-hydroxydocosahexaenoic acid (17-HDHA) promoted B lymphocytic activity and increased production of antibodies against influenza virus.⁵
- The specialized pro-resolving mediator resolvin D2 (RvD2) inhibited the activation of NLRP3 inflammasome (the most clinically relevant inflammasome) in macrophages during the resolution process.⁷
- The specialized pro-resolving mediator protectin D1 (PD1) inhibited influenza viral replication in a model of human lung cells, and improved the survival and pathology of severe influenza in mice.⁶
- Thrombosis, a common consequence of infection including the current pandemic, is linked to poor patient outcome.^{8,9} In a mouse model, the specialized pro-resolving mediator resolvin D4 (RvD4) facilitated inflammation resolution, attenuated pathologic thrombosis and promoted clot removal.¹⁰

Video: [Robert Martindale, MD, discusses specialized pro-resolving mediators and patient care \(length: 16 min\)](#)

Blog: [specialized pro-resolving mediators in inflammation and cellular resilience \(length: 15 min\)](#)

How does stimulating inflammation resolution differ from classic anti-inflammation?

Targeting cytokine storm and the hyperinflammatory state as a result of severe viral infection has been challenging. Immunologists have expressed concerns that classic anti-inflammatory medications that aim to target overactive immune response may suppress immunity, delay the elimination of pathogens, and increase susceptibility to secondary infection.¹¹ Also, anti-inflammatory medications targeting individual pro-inflammatory cytokines may not target the right type of cytokines and may not be sufficient in preventing infection progression.¹¹

Authors of the commentary suggested that, by going further upstream to stimulate macrophage-mediated clearance of cellular debris, it may enhance inflammation resolution and may be more effective in countering excessive productions of pro-inflammatory cytokines, thereby averting the potentially fatal cytokine storm. Promoting inflammation resolution therefore may be a novel therapeutic approach to reduce acute respiratory distress syndrome (ARDS) and complications associated with the current pandemic.¹

Video: [Charles Serhan, PhD, DSc, discusses the significance of resolution physiology to human health \(length: 1 min 42 sec\)](#)

Visit [Metagenics Institute](#) for more information on specialized pro-resolving mediators and inflammation resolution

[View the abstract of the commentary](#)

Citations

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