

## IL-6 trans-signaling induces plasminogen activator inhibitor-1 from vascular endothelial cells in cytokine release syndrome

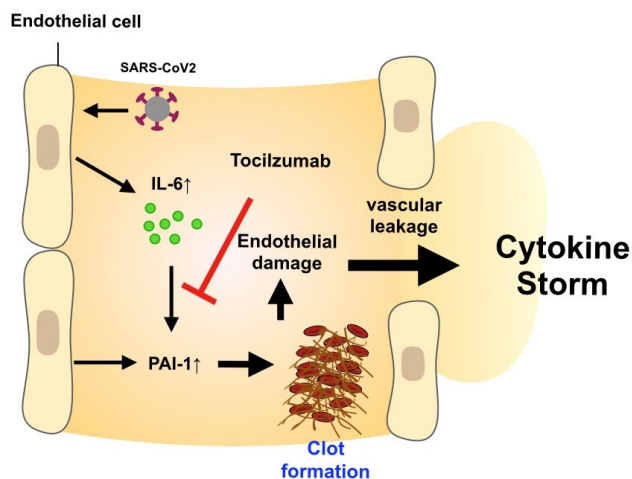
Keywords: IL-6, Tocilizumab, Endothelial cells, CRS, COVID-19

### ❖ Points

- In the early stage of COVID-19, IL-6 increased in blood, and causes the release of PAI-1 from blood vessels.
- PAI-1 causes thrombus in many organs such as lung, and makes pneumonia severe.
- An antibody drug suppressing IL-6 (commercial name: Actemra<sup>®</sup>) is expected to be effective in the early treatment of pneumonia.

### ❖ Abstract

Cytokine release syndrome (CRS) is a life-threatening complication induced by hyperinflammatory responses. However, no specific immunotherapies are available for its treatment. Sujin Kang, Tadamitsu Kishimoto (Immune Regulation, IFReC) and the research group found that interleukin (IL)-6 signaling plays a crucial role in endothelial cell dysfunction during bacterial and viral CRS. Specifically, they identified that the pathogenesis of CRS in patients with sepsis, acute respiratory distress syndrome, and burns involved the IL-6-mediated production of hyperinflammatory cytokines and plasminogen activator inhibitor-1 (PAI-1), which indicates that IL-6 signaling blockade has potential as a therapy for CRS. The group also found that the inhibition of IL-6 signaling by Tocilizumab treatment decreased PAI-1 production and alleviated clinical manifestations in severe COVID-19 patients.



**Figure: How Actemra<sup>®</sup> suppresses inflammation**  
IL-6 in blood promotes thrombus formation via PAI-1. By suppressing IL-6, Actemra prevents severity of the pneumonia due to cytokine storm.

### ❖ Article

**Title:** "IL-6 trans-signaling induces plasminogen activator inhibitor-1 in cytokine release syndrome"

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